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Brief verbal intervention to address inappropriate prescriptions of chinese patent medicines among western practitioners in primary health care (BRAVERY): a study protocol for an unannounced standardized patient experiment with a factorial design randomized controlled trial in China

Qing Zhao[1,2], Lin Lin[3,4], Ada Kwan[5], Huanyu Hu[1,2], Lei Wu[3,4], Yuanbin Chen[3,4], Zengping Shi[1,2], Bohan Li[2], Jingmin Xiao[3,4], Guangyu Tong[6], Wenjun He[7], Huanyuan Luo[7], Qingqing Li[7], Run Wang[7], Dongmei Zhong[1,2], Siyuan Liu[1,2], Yunyun Xie[1,2], Jiaqi Li[8], Lanping Zhang[9], Zizhen Huang[2], Xiaoqing Zhu[2], Yuting Wan[2], Xiaoshan Chen[2], Wanqing Huang[2], Yaoming Tian[2], Xianwen Li[10], Yuxin Zhou[11], Yiyuan Cai[12] and Dong Roman Xu[1,2,7,13*]

Abstract

Introduction Chinese patent medicines, produced using advanced pharmaceutical techniques and available in various forms, including powders, granules, tablets, pills, and capsules, finds extensive utilization among Western medicine practitioners in primary healthcare (WMP-PHC). However, the inappropriate overprescribing of these medicines has led to significant resource waste and raised considerable concerns. Therefore, we aim to address related knowledge gaps by employing unannounced standardized patients (USPs) as a method, for both measurement and intervention research. Specifically, in this paper, we present a study protocol that aims to develop and evaluate the effectiveness of brief verbal interventions (BVI) delivered by USPs, with the objective of improving the appropriate prescription of Chinese patent medicines. The study aims to equip patients with simple and easily implementable interventions to enhance the appropriate prescription of Chinese patent medicines. Furthermore, The findings from this study will provide valuable insights for policymakers, enabling them to comprehend the current levels of inappropriate Chinese patent medicines prescription and develop targeted policy interventions.

Methods and analysis We will record a total of 576 encounters in primary healthcare (PHC) facilities across two cities in China. The data will be randomized using a 2×2×2×2 factorial design randomized controlled trial (RCT),

*Correspondence:
Dong Roman Xu
romanxu@i.smu.edu.cn; roman.xu@gmail.com

Full list of author information is available at the end of the article

which includes factors such as financial incentives, knowledge and skills, prescribing habits, and patient expectation. USPs will collect data, including retrieving prescriptions and documenting the process of medical encounters. The primary outcome evaluation focuses on the appropriateness of Chinese patent medicines prescriptions. Secondary outcomes include the quality of the consultation process, patient satisfaction, cost information, service time, and appropriateness of antibiotic prescriptions. Descriptive analysis will be performed for the survey results, and the difference in outcomes between interventions and control providers will be compared and statistically tested using generalized linear mixed model (GLMM).

Trial registration number The study has been registered at the China Clinical Trials Registry (ChiCTR2300077913) on 23 November 2023.

Strengths and limitations of this study

•To the best of our knowledge, this study is the first to offer evidence of interventions aimed at addressing inappropriate prescription of Chinese patent medicines in primary healthcare institutions in China.

•Brief verbal intervention as a method of communication-based intervention during medical consultations, focus on prescription adjustments from the patient's perspective, rather than relying on policies that are difficult to change. This approach empowers healthcare consumers in a context of information asymmetry, effectively encouraging doctors to modify their prescribing behaviors. Although this study specifically examines the effect of brief verbal interventions from the patient's perspective on the prescription of Chinese patent medicines by primary care Western physicians, this approach can be expanded. The prescription of Chinese patent medicines serves as a particular context, but the broader concept of brief verbal intervention can be applied to influence Western practitioners' medical decision-making and improve the quality of care they provide.

•The utilization of USPs, which is a method where individuals are trained to depict patients in a standardized manner within medical scenarios, is becoming more prevalent in low-income countries for evaluating the quality of medical care. Research focusing on Chinese patent medicines reveals several advantages to employing this approach. Firstly, USPs can exhibit consistent symptoms, medical history, and emotions, while adhering to predefined standards for consultation, diagnosis, and treatment. This ensures a more objective evaluation of Chinese patent medicines appropriateness. Secondly, USPs are well-suited for introducing BVI, because of the researcher's ability to vary verbal presentation (scripted lines) by the USP, allowing for measuring the effectiveness of the varied intervention while keeping other patient-side confounding factors constant. Lastly, USPs serve as a form of unannounced visits, minimizing the Hawthorne effect and providing researchers with direct and reliable information on appropriate Chinese patent medicines prescriptions.

•The factorial design RCT enables the evaluation of multiple intervention components simultaneously, including the individual effects (main effects) and combined effects (interaction effects) of multiple BVIs. This design ensures robust research evidence and effective control over research costs.

•This study also has limitations. Although we designed different scripted lines for USPs as proxy variables to reflect potential mechanisms such as financial incentives, knowledge and skills, prescribing habits and patient expectation, it should be noted that these scripted lines may not fully capture the mechanisms. Despite our efforts to minimize bias through the inclusion of expert groups and stakeholders in the development of lines, it is important to acknowledge this limitation.

Keywords Chinese patent medicines, Primary health care (PHC), Brief verbal intervention (BVI), Randomized controlled trial (RCT), Unannounced standardized patient (USP), Factorial design

Introduction

In recent years, China has focused on advancing traditional Chinese medicine (TCM), with Chinese patent medicines playing a crucial role. Chinese patent medicines refers to traditional Chinese herbal products manufactured using modern formulation techniques. These formulations come in various forms, including but not limited to powders, granules, tablets, and capsules, distinguishing them from traditional Chinese medicine preparations such as ointments, pills, pellets, and powders, which are typically prepared through methods like decoction or grinding by traditional Chinese medicine practitioners [1, 2]. Under the influence of national policies supporting both TCM and Western medicine, Chinese patent medicines has become widely available in Chinese healthcare system. In the 2023 edition of the National Essential Medicines List, the total number of medications listed in the catalog has reached 3,088, with 1,390 of them being Chinese patent medicines [3]. Chinese patent medicine is also frequently prescribed in clinical practice, constituting approximately 62.13-77.48% of prescriptions in China [4, 5]. The Chinese

patent medicines market has grown significantly, reaching 500 billion RMB in 2023 [6]. As previously mentioned, the inclusion of Chinese patent medicines in the Essential Medicine List, the prescription rates of Chinese patent medicines in clinical practice, and the market value of Chinese patent medicines collectively attest to its widespread utilization in the healthcare sector of China.

The issue of appropriate prescriptions of Chinese patent medicines by WMP-PHC is prominent. According to the World Health Organization's definition, appropriate prescriptions involves patients receiving suitable doses of medications to meet their individual needs, within an appropriate timeframe, and at the lowest cost for their clinical requirements [7]. The issue of appropriate prescriptions of Chinese patent medicines may be observed through under-prescribing, over-prescribing, incorrect prescribing, extravagant prescribing, and multiple prescribing [7, 8]. The unique characteristics of Chinese patent medicines make it easy for WMP-PHC to engage in inappropriate prescriptions. Traditional Chinese medicine emphasizes syndrome differentiation for treatment, where "differentiation" involves analyzing and synthesizing data, symptoms, and signs collected through observation, listening and smelling, questioning, and pulse feeling. This process helps in determining the cause, nature, location, and relationships between pathogenic and healthy factors, leading to the identification of a specific syndrome, which is crucial for treatment [9]. Without systematic training in syndrome differentiation, WMP-PHC may make errors when prescribing Chinese patent medicines. Research indicates that 86.2% of WMP-PHC prescribe Chinese patent medicines without differentiating traditional Chinese medical syndromes, relying solely on Western medical diagnoses [10, 11]. Therefore, there is a significant safety risk associated with WMP-PHC prescribing Chinese patent medicines. The inappropriate prescriptions can compromise patient health, waste healthcare resources, and reduce patient confidence and satisfaction in the healthcare system.

Even though there is ample evidence indicating the low quality of Chinese patent medicines prescriptions issued by WMP-PHC, the existing information lacks comprehensive details concerning content and methods. Firstly, PHC medical records, particularly outpatient records, are often incomplete and may not fully reflect the diagnosis, treatment, and prescription processes. Secondly, medical records can adequately reflect the quality of documentation, but it only serves as a proxy variable for healthcare quality. For instance, if the disease diagnosis is incorrect, prescribing the right medication would still be considered incorrect. However, during prescription review, it may not always be possible to ascertain the accuracy of the disease diagnosis. Thirdly, medical records can partially reflect whether doctors have performed specific diagnostic and treatment procedures but may not accurately reflect their accuracy. For example, while medical records may indicate whether certain examinations have been conducted, they may not reflect whether these examinations were performed in accordance with established standards. To address these limitations, further research is needed to gather data on the inappropriate prescription of Chinese patent medicines by WMP-PHC, using robust measurement tools that capture the nuances of clinical practice in PHC institutions.

Unannounced standardized patients (USPs), which are individuals trained to portray a pre-scripted scenario and later present it to a provider in a typical visit, offer a novel and reliable research method for investigating and assessing interventions [7, 12, 13] to improve the inappropriate prescription of Chinese patent medicines, including: (a) offering an objective and direct evaluation of care during a real visit; (b) being unannounced, thereby eliminating the Hawthorne effect, where individuals alter their behavior in response to awareness of being observed; (c) maintaining standardization in case presentation, providing a natural control for case mix; and (d) ensuring immediate recording of assessment results, minimizing recall bias. Additionally, the use of USPs can allow for identifying the effects of different types of patient presentation through randomly assigning them to sampled providers. The USP method is recognized as a gold standard for evaluating clinical practices due to its objectivity, unannounced nature (eliminating Hawthorne effect), standardized case presentations, and immediate recording of assessment results. Our team has gained extensive experience using USP to assess PHC quality over the past five years through the ACACIA (Primary he**A**lth **C**are qu**A**lity **C**ohort **I**n chin**A**) study: https://www.researchgate.net/project/ACACIA-Study) project [14–16]. We have developed and validated 11 USP cases covering common PHC diseases. ACACIA collaborates with the National Health Commission Statistical Information Center to ensure provider representativeness and conducting 2,200 USP-clinician encounters nationwide in China. In this research, our evaluation focuses on Chinese patent medicines prescription appropriateness, considering diagnosis, symptoms, medical history, and treatment goals, guided by TCM principles and evidence-based medicine. We have been developing evaluation indicators and methods, combining the principles of TCM with evidence-based medicine, for assessing the appropriate prescription of CPM, and we have just completed *the clinical guidelines on treating influenza in adult patients with Chinese patent medicines* [17]. In this study, we will also refer to it as USP cases. Currently, while the USP method has primarily been used to study antibiotic prescriptions [18], it can be expanded to include the research field of Chinese patent medicines. By leveraging the strengths of

the USP method, we can gather valuable insights into the inappropriate prescription of Chinese patent medicines and develop effective interventions to improve more appropriate use. In short, we could use USPs to create experimental conditions while keeping other USP factors constant, enabling us to conduct multi-group randomized controlled trials. This comprehensive approach aims to shed light on Chinese patent medicines inappropriate prescription and develop effective strategies to address it. In addition, we will collect data on the appropriateness of antibiotic prescriptions. This will allow us to contrast the appropriateness prescriptions for Chinese patent medicines with those for antibiotics, providing insights into prescription practices for both types of medication in China.

In the challenging context of healthcare system transformation, it is valuable to investigate how patients themselves contribute to shaping healthcare quality within the dynamics of doctor-patient interactions. Brief verbal intervention (BVI) is a commonly used, simple, and effective method in PHC institutions, such as smoking cessation interventions and reducing alcohol intake [19]. It refers to an approach where patients offer concise suggestions or consultations to doctors. In this study, we will use the USP approach to test BVIs in improving inappropriate prescriptions of Chinese patent medicines. The design of the BVI is primarily tailored to address the issue of over-prescribing. Firstly, we will conduct training for USP to ensure their accurate communication of BVI. Secondly, we can modify specific components (e.g., different scripted lines presented by USPs corresponding to BVI interventions) across healthcare providers while maintaining consistency in other USP case presentation. Consequently, any variations in intervention measures can be entirely attributed to this specific component. Therefore, any changes in the intervention can be attributed solely to that specific component. The choice of a factorial design randomized controlled trial (RCT), primarily considers its efficiency, allowing multiple interventions to be tested with a smaller sample size and the ability to examine interactions between interventions [20]. This design is suitable for detecting the effects of multiple interventions on various mechanisms in our study. Specifically, negative BVIs in the factorial design RCT will be addressed as cross-sectional survey results.

The key aims of this study are as follows: 1.To conduct an in-depth analysis of the factors influencing the appropriate prescription of Chinese patent medicines. 2. To depict the types, quantities, and costs of Chinese patent medicines prescription. 3. To evaluate the effectiveness of BVI in improving the quality of Chinese patent medicines prescriptions.

Trial design and methods

Development of USP cases

We plan to develop 2 USP cases, and in the elaboration of this protocol, we will use influenza cases as examples to illustrate the methodological details in each section. The case development team and case review expert team, comprising an evidence-based researcher, clinical specialists, PHC practitioners, and a coordinator, will collaborate in the development of USP cases. Their focus will be on reviewing the case prototypes, clinical scenarios, disguise plan, USP-clinician encounter, and quality checklist sheets. The details of our checklist development protocol were described in another paper [14]. These aspects will be based on clinical evidence-based guidelines [17], including history, physical examinations, laboratory and imaging studies, diagnosis, and management plans. Differential diagnosis and treatment in Chinese patent medicines prescriptions, as seen in traditional Chinese medicine internal medicine, will also be considered. For example, influenza can be categorized as wind-colds, wind-heats, colds with a deficiency in *qi*, colds with a deficiency in *yin*, summer-heat colds, and damp colds (Table 1 serves as an illustrative example to demonstrate the difference between wind-colds and wind-heats [17, 21]).

Table 1 Wind-heat and wind-cold syndrome of influenza

	Wind-heat syndrome (mild)	Wind-cold syndrome (mild)
Main symptoms	Excessive body heat, slight aversion to wind, lack of sweating, dry or sore red swollen throat, nasal congestion, yellow and cloudy nasal discharge, and a floating pulse are characteristic symptoms of a wind-heat syndrome in traditional Chinese medicine. These symptoms indicate an imbalance of the body's energy, with heat and wind playing a prominent role.	Severe aversion to cold, mild fever, lack of sweating, headache, sore limbs, heavy nasal congestion, occasional runny nasal discharge, and a floating or tight pulse are characteristic symptoms of a wind-cold syndrome in traditional Chinese medicine. These symptoms indicate an imbalance of the body's energy, with cold and wind playing a prominent role.
Secondary symptoms	Headache and pain, cough, sticky or yellow phlegm, thirst, and desire to drink, along with a thin white and yellowish tongue coating and a red tip of the tongue, are indicative of a wind-heat in traditional Chinese medicine.	Itchy throat, cough, thin and white phlegm, not feeling thirsty or desiring hot drinks, along with a thin white and moist tongue coating, are characteristic symptoms of a wind-cold type of influenza in traditional Chinese medicine. These symptoms indicate an invasion of cold energy into the body.
Treatment	Disperse heat; resolving exterior with pungent and cool natured drugs	Disperse cold; relieving exterior syndrome with pungent and warm natured drugs

Brief verbal interventions

In September 2022, our research team conducted an independent study using a multi-stage stratified sampling method with 214 doctors from primary healthcare institutions in Gansu Province as research subjects. Through a questionnaire survey and employing the mixed logit model in a discrete choice experiment, the results revealed that economic incentives, patient willingness, disease severity, drug effectiveness, and drug adverse reactions all significantly influence the prescription behavior of WMP-PHC [5]. Based on these five intervention strategies and project resources, we have determined that the final intervention strategies for this proposed study are to include financial incentives, knowledge and skills, prescribing habits and patient expectation.

The design of the BVI is primarily tailored to address the issue of over-prescribing. We will develop BVIs using an expert panel approach. The focus group will include 1 WMP-PHC, 1 expert in anthropology and sociology, 1 USP with ACACIA experience, and 2 actual patients with demographics and economic profiles similar to our USP cases. Attendees will discuss and revise the BVIs based on scripted lines design requirements, which include: (1) the ability to curtail or enhance the appropriate prescriptions of Chinese patent medicines, (2) brevity for easy memorization and execution by USP, (3) clear and explicit meaning, and (4) a tone and content consistent with the identity of USP in the case design. For the purpose outlined in this protocol, we have initially crafted BVIs for influenza cases for USPs, as indicated in Fig. 1, drawing from our current experience.

BVIs are brief interventions that will be started and concluded with a single USP visit, so we expect few or no cases of discontinuing an allocated intervention. In the case a provider refuses to provide health service, the USP will record the reason and visit a replacement provider with similar characteristics.

Study design and setting

The study is designed as a prospective, single-blinded, multi-center factorial trial with 4 factors. This protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist [22], and the study flowchart is presented in Fig. 2. The study will be

1. **Financial incentives** - Saying before prescribing, '*I don't want to buy drugs here because I don't have local health insurance, I have to go back to my hometown for more reimbursement*' (Doctors prescribing medication is often linked to their own economic interests. To address this, we remove financial incentives between PHC practitioners and Chinese patent medicines as well as antibiotics by refraining from purchasing these medications);

2. **Knowledge and skills** - After receiving a diagnosis from the doctor but before a prescription is issued, inquiring about the prescribed medication. If the doctor intends to prescribe Chinese patent medicines: '*Doctor, I see you prescribe Chinese patent medicines. My father is a Chinese medicine practitioner, and he often says that wind-cold and wind-heat require different Chinese patent medicines'* (PHC practitioner is inspired to differentiate the syndromes through this reminder);

3. **Prescribing habits** - Saying before prescribing: '*I came across an article online today suggesting that some doctors may frequently prescribe Chinese patent medicines or antibiotics out of routine rather than a genuine medical necessity.*' (USP remind PHC practitioner to prescribe based on the medical need, not just habit).

4. **Patient expectation** - Saying before prescribing: '*Doctor, it's okay if you don't prescribe medication.*' (This statement aims to alleviate the PHC practitioner's concerns that the patient may expect or request Chinese patent medicines or antibiotics).

Fig. 1 Example of BVIs in influenza case for USP. Note: The specific interventions will be refined during the project implementation. The provided examples serve as illustrations only

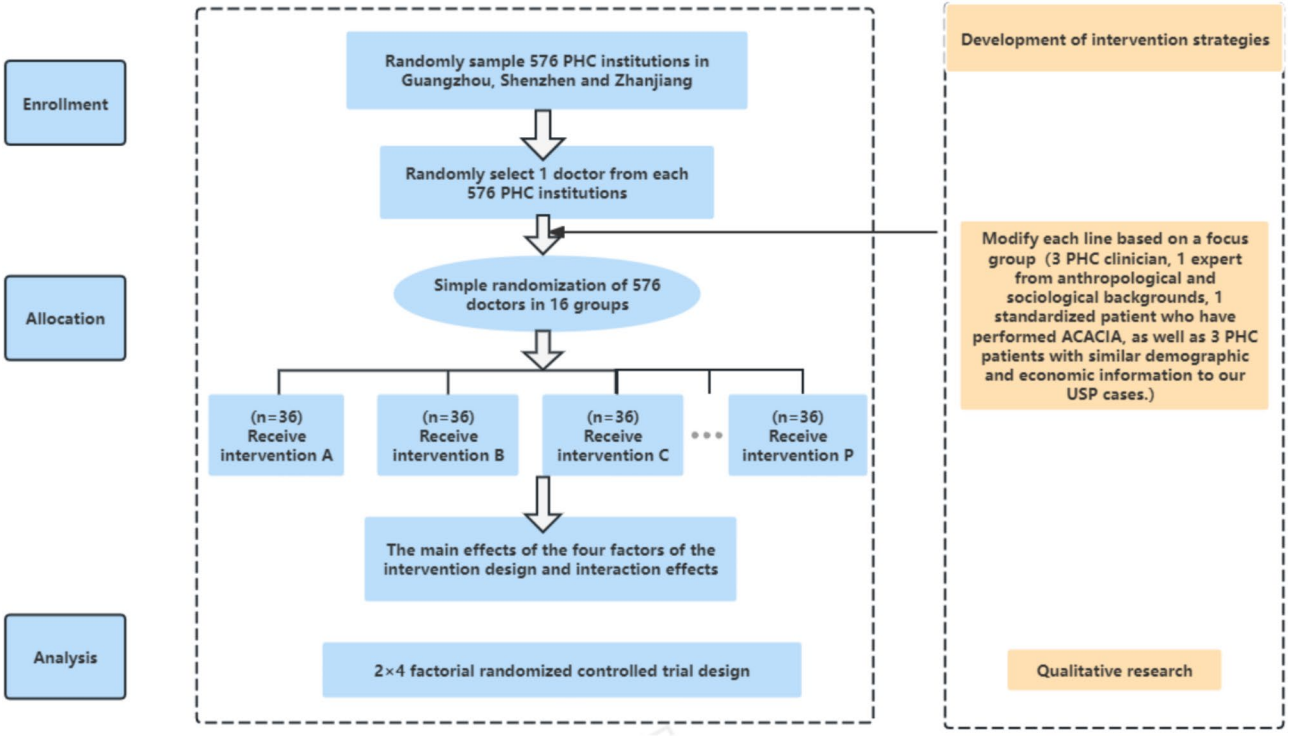

Fig. 2 The study flow chart

conducted in primary healthcare institutions in Guangzhou, Shenzhan and Zhanjiang. Guangzhou is renowned for its traditional Chinese medicine and advanced economy. Shenzhen, a city with a large immigrant population, has experienced rapid economic development, attracting people from various regions across the country. In contrast, Zhanjiang has a relatively modest economic development, with a population primarily consisting of indigenous residents. These three cities collectively provide a diverse representation of the research settings.

Factorial design RCT is an efficient choice for identifying what component to include in a multicomponent intervention [23]. By combining data across multiple factors, factorial design RCT increases statistical power to test the marginal treatment effects compared to separate trials on individual components [24]. The joint modeling of multiple main effects and interactions also enhances the partition of variance and further increases estimation efficiency and statistical power [25]. Notably, factorial design RCT allows for the examination of interaction effects among different interventions. When 4 BVIs are tested, the saturated analytical model can include 6 two-way interactions, 4 three-way interactions, and 1 four-way interactions (Fig. 3). It should be noted that among the 16 combinations of intervention components in the factorial design RCT, the focus of the test is the 4 marginal effects of BVIs. Multiple testing adjustments are debatable (e.g., Freidlin, B., & Korn, E. L. (2017). Two-by-two factorial cancer treatment trials: is sufficient attention being paid to possible interactions?. *JNCI: Journal of the National Cancer Institute*, *109*(9), djx146.) and not considered in this studied.

Participants and recruitment

For the purpose of this study, we will adopt the following inclusion and exclusion of PHC institutions and practitioners:

- (1). PHC institutions: this includes outpatient services provided by the internal medicine departments at secondary PHC institutions, primary PHC institutions, and institutions of undefined level. Institutions with unstable operations, as well as specialty care hospitals and clinics, will be excluded from the study.
- (2). WMP-PHC: WMP-PHC can be classified into three main types: licensed physicians, licensed assistant physicians, and certified village doctors. Their scope of practice is confined to general medicine, internal medicine, obstetrics, and pediatrics.

Sampling frame, sampling and sample size

We will develop the sampling frame of all PHC institutions in Guangzhou, Shenzhen and Zhanjiang that meet our inclusion and exclusion criteria by collaborating with

	Financial Incentives	**Knowledge and skills**	**Prescribing Habits**	**Patient expectations**
Experimental Conditions (EC)	*I don't want to buy drugs here because I don't have local health insurance, I have to go back to my hometown for more reimbursement*	*Doctor, I see you prescribe Chinese patent medicines. My father is a Chinese medicine practitioner, and he often says that wind-cold and wind-heat require different Chinese patent medicines*	*I came across an article online today suggesting that some doctors may frequently prescribe Chinese patent medicines or antibiotics out of routine rather than a genuine medical necessity*	*Doctor, it's okay if you don't prescribe medication*
EC 1	-[1]	-	-	-
EC 2	-	-	+	-
EC 3	-	+	-	-
EC 4	-	+	+	-
EC 5	+	-	-	-
EC 6	+	-	+	-
EC 7	+	+	-	-
EC 8	+	+	+	-
EC 9	-	-	-	+
EC 10	-	-	+	+
EC 11	-	+	-	+
EC 12	-	+	+	+
EC 13	+	-	-	+
EC 14	+	-	+	+
EC 15	+	+	-	+
EC 16	+	+	+	+

Fig. 3 Combination of intervention in factorial design RCT. Note: the symbol '-' represents 'no' or absence of an intervention mechanism, while the symbol '+' represents 'yes' or presence of an intervention mechanism

local health authorities. We will employ a random digit table method to sample institutions, ensuring an unbiased and representative sample for the study. Each PHC institution will be visited once by USPs.

For the factorial design RCT, based on the current ACACIA project, the expected appropriate prescription rate of Chinese patent medicines is 50% in the control [26]. A 25% decrease can be considered clinically significant based on discussions with health economists, implementation science experts, and clinical physicians at the early stages of this project. In a two-proportion test for factorial design RCT on the main effect of each component, a sample size across all 16 combinational conditions of 384 (24 physicians each) can attain 80% power with a two-sided type- I error rate of 0.05. This study conducted a randomized controlled trial in three cities, taking into account the relatively consistent healthcare quality across provinces and regions, with an ICC set at 0.001. As a result, the calculated design effect (Deff) is 1.127, leading to a required sample size of 433. Additionally, considering the three cities (Guangzhou, Shenzhen, and Zhanjiang), PHC institutions Level (three levels of PHC institutions-secondary PHC institutions, primary PHC institutions, and undefined-level PHC institutions), profit model (two types of hospital profit models-public and private) as well as 2 case types and 16 interventions, a total of 576 visits (18*2*16 = 576) is needed. Therefore, the final sample size is determined to be 576 visits, with 36 visits per intervention group.

Randomization and group allocation

First, within the overall sampling frame of the cities of Guangzhou, Shenzhen, and Zhanjiang, the random seed was set using R software. Stratification was performed based on three hospital levels, two profit models, and two case types. Second, within each stratum, random numbers were generated using Excel to assign hospitals to one of the 16 experimental conditions of the factorial trial through complete random assignment. Subsequently, these clinics will be allocated to different experimental conditions according to the order of the assigned random numbers. Each serial number will be assigned one USP visit. This entire process will be carried out by a statistician unaffiliated with the project, using R software. The goal is to address sample imbalance and enhance the comparability of samples across different intervention groups.

Blinding

In this study, the WMP-PHC will not be informed about the visits by USPs, ensuring a single-blind design. However, USPs will be aware of the intervention and data collection procedures, so the study cannot be fully double-blinded. Nevertheless, data analysts will be blinded to reduce subjective analysis. Data will be de-identified, and the BVI grouping information will be concealed during analysis to maintain anonymity.

Since informed consent will not be obtained, the likelihood of unblinding occurring at the level of PHC institutions is minimal, if not impossible. However, in the event that unblinding does occur, a replacement provider with similar characteristics will be identified to conduct the visit.

Data collection

USP disguise plan

USPs will mention having had a fever the previous day and taking antipyretics. Symptoms like a yellow nose and sore throat will further enhance the portrayal of wind-heat syndrome. The effectiveness of this disguise plan has been tested in the ACACIA project with a 0% detection rate. All USPs will undergo intensive training to present a letter containing their university's contact information, explaining their role in the research. This is to address any potential confrontations and to ensure they avoid any potentially harmful examinations.

USP validation

This study will employ Delphi expert method to validate the USP measurement, following the COSMIN theoretical framework [27]. The validation methods are described in detail in our ACACIA research protocol [14] and Supplement Table 1.

USP recruitment

We will mobilize the universities involved in the ACACIA project research network to recruit local survey participants through social media, offline posters, and promotion by researchers. We will recruit and train USPs to implement interventions in different groups. All USPs must meet the following criteria to be eligible for the study: (1) people with a suitable age and physique to portray the case; (2) fluent native speakers of the local language in the area; and (3) having a good memory.

Patient and public involvement

When developing USP cases and designing BVI scripts, we will invite patients with a history of the relevant disease to participate in the development process. However, when conducting formal USP visits, patients will not be involved.

Outcomes

The primary outcome of this study will be the appropriateness of Chinese patent medicines prescription, a dichotomous variable. This outcome will be evaluated by a team of traditional Chinese medicine experts, who will assess the appropriateness of Chinese patent medicines

Table 2 Variables and their definitions

Variables		Definition	Data source	Data collection
Primary outcome	The appropriateness of Chinese patent medicines prescription	Appropriateness	Quality checklist, data collection form	USP, TCM panel
Secondary outcome	Effectiveness and safety ***(based on IOM framework)***	The percentage of recommended procedures performed	Quality checklist	USP
	Patient-centeredness ***(based on IOM framework)***	Whether it is patient-centered	Patient Perspective Patient-Centeredness Rating Scale	USP
	Efficiency ***(based on IOM framework)***	Expenditure of treatment	Data collection form	USP
	The appropriateness of antibiotic prescription	Appropriateness	Quality checklist, data collection form	USP
Variables of interest (baseline data)	Socio-demographic characteristics of the doctors	Gender, age, ethnicity, education level, TCM training	Doctor Information Collection Form	Routine reporting, USP
	Basic information about the institution	Name, location, level and grade, medical equipment, environment, department setting, etc.	PHC institution annual report	Routine reporting, USP

prescriptions for the selected cases based on the principles of traditional Chinese medicine and evidence from evidence-based medicine, and we have just completed the clinical guidelines on treating influenza in adult patients with Chinese patent medicines [17].

Specifically, the appropriateness of Chinese patent medicines prescriptions will be assessed based on two dimensions: indication and dosage.

- For dimension 1 (indication), the traditional Chinese medicine experts will classify each prescribed medication according to guidelines as either "recommended prescription," "completely useless but harmless treatment," or "harmful prescription." The prescription will be considered appropriate if it meets the following criteria:

D1 (appropriate prescription) = (#1 AND #2 AND #3) OR #4.

1. It includes the indication "recommended prescription".

2. It does not include the indication "completely useless but harmless prescription".

3. It does not include the indication "harmful prescription".

4. no traditional Chinese medicine is prescribed under this dimension.

Prescriptions that do not meet these criteria will be classified as not meeting the indication (1-D1).

- For dimension 2 (dosage), the dosage will be considered appropriate (D2) if it complies with the instructions provided in the medication's package insert. Prescriptions that do not meet this criterion will be classified as inappropriate (1-D2).

Chinese patent medicines prescriptions will be considered appropriate only if it meets both criteria: it meets the indication and the dosage is appropriate (D1∩D2).

Antibiotics prescribed for viral respiratory tract infections will be considered inappropriate. Therefore, if no antibiotic prescription is provided, it is considered appropriate, while any other situation is deemed inappropriate.

We will collect a variety of quality information and other related explanatory variables. In this study, we adopted Institute of Medicine (IOM) framework [28, 29], which defines six dimensions of healthcare quality: effectiveness (avoiding underuse and misuse), safety (avoiding harm), patient-centeredness (respecting and responding to individual preferences), timeliness, efficiency (avoiding waste), and equity (ensuring healthcare quality does not vary based on individual characteristics). In this intervention study, considering the content of BVI, we posit that improvements cannot be made in the dimensions of timeliness and equity.

Effectiveness (avoiding underuse and misuse) and safety (avoiding harm), traditional technical goals of quality of care, will be evaluated through the quality checklist sheets discussed above. In short, we will also evaluate WMP-PHC adherence to best practices as the secondary outcome, such as the percentage of adherence to guideline-recommended procedures performed. The patient experience will be assessed with patient-centeredness (PPPC-R) rating scale by USPs [30, 31]. Employing a 4-point Likert scale, the PPPC Rating Scale appraises patient-centeredness across three dimensions: exploration of disease and illness experiences, understanding the whole person, and establishing common ground. A detailed outcome evaluation will include the appropriateness of Chinese patent medicines prescription, quality of consultation process, patient satisfaction, cost information and service time. Table 2 summarizes all outcomes to be collected.

Almost all data will be collected through visits conducted by USPs. USPs will visit accompanied by a peer as a 'friend'. When a USP is being examined by a WMP-PHC, the companion will observe the facility environment and treatment procedures. At the end of each encounter, the USPs will request treatment prescriptions. Each USP and the companion will jointly complete quality checklists and other data forms on a smartphone within 15 min after leaving the sampled PHC institution.

Data analysis

The data will be analyzed based on the intention-to-treat (ITT) principle to compare the primary and secondary outcomes of the initially assigned groups. For continuous variables (based on the distribution), the baseline characteristics of each group will be described using the mean (standard deviation, SD) or median (interquartile range, IQR). For categorical variables, the frequencies (percentages) will be used to describe them. The analysis will involve the use of a logistic regression model for factorial design RCT. Continuous outcomes will be analyzed using generalized linear mixed model (GLMM). Additionally, we will employ logistic regression to investigate the factors associated with appropriate prescriptions in Chinese patent medicines, including categories, quantities, costs, and appropriateness. Subgroup analyses will be performed, focusing on factors limited to type of disease, geographic region, type of healthcare institution, and type of physician. The comparison of the appropriateness of antibiotic prescriptions and Chinese patent medicines prescriptions will be conducted using the chi-square test. Missing data will be imputed using multiple imputation in the GLMM.

We anticipate a low dropout rate as the intervention is provided by USPs, and WMP-PHC will passively receive the intervention. Additionally, the intervention will take place within a short timeframe of a single encounter, hence there will be no follow-up encounters. After the encounter is concluded, all data will be immediately entered into the REDCap. REDCap incorporates bank-level security features, granting access to the data exclusively to the investigators involved in this study. All study forms, including signed consent forms, will be securely and conveniently stored within the REDCap system. All data analyses will be performed with R version 4.3.0 and two-sided P value < 0.05 will be deemed significant.

Trial organization and monitoring

USPs will be assigned specific roles and must accurately portray them, maintain fidelity, and complete the reporting forms competently. A project manager will monitor all sites and hold weekly conferences to address performance issues. Field information will be collected using REDCap app on mobile phones, which ensures data security and de-identifies facility and physician identifiers during analysis [32].

Discussion

This factorial randomized controlled trial aims to investigate the impact of BVIs delivered by USPs on reducing the inappropriate prescription of Chinese patent medicines in PHC institutions in China. The design of the BVI is primarily tailored to address the issue of overprescribing [7]. To the best of our knowledge, this study represents the first attempt to explore the intervention strategies and mechanisms for addressing this issue. The results of this study will not only provide essential empirical evidence for policymakers, healthcare providers, and patients to ensure the provision of high-quality Chinese patent medicines prescriptions, as BVIs can be self-implemented by patients. Additionally, the study holds significance in identifying the most effective intervention and potentially uncovering robust underlying mechanisms contributing to its efficacy. The utilization of USPs in this study provides a reliable approach for measuring and intervening the quality of services.

This study has several strengths. Firstly, it adopts a progressive approach, examining the current situation of inappropriate prescription of Chinese patent medicines, understanding the underlying mechanisms, and implementing BVIs to improve appropriate prescription. This comprehensive approach will provide valuable evidence and information for the prescription of Chinese patent medicines in PHC institutions. Secondly, BVI can offer a practical and feasible solution to improve the appropriate prescription of Chinese patent medicines, and its effectiveness can shed light on the underlying mechanisms. It also empowers patients to advocate for their health rights. Additionally, the study utilizes the USP approach, which is a valuable tool for prescription evaluation and intervention. USPs provide consistent symptoms and standardized consultation, diagnosis, and treatment, enabling objective evaluation of Chinese patent medicines appropriateness. The unannounced visit nature of USPs reduces Hawthorne effect and enhances the reliability of data. The factorial design RCT employed in this study allows for the examination of multiple interventions and their interaction effects, optimizing research evidence while controlling costs.

However, there are some limitations to the USP methodology. Firstly, the limited number of USP cases may restrict the range of prescriptions providers can make, potentially affecting prescription volume and expenditure. Secondly, although we designed different lines scripted for USPs to present as proxy variables to reflect potential mechanisms, it should be noted that these lines may not fully capture the mechanisms. Despite our efforts to minimize bias through the inclusion of expert

groups and stakeholders in the development of line, it is important to acknowledge this limitation.

Through the use of the USP method, this study aims to shed light on the underlying factors that lead to the inappropriate prescription of Chinese patent medicines. By collecting and analyzing actual clinical interactions, the findings will contribute to our understanding of effective strategies for promoting appropriate Chinese patent medicines prescription in PHC institutions. By assessing the impact of this intervention on WMP-PHC prescription practices, the study aims to determine whether patient-focused interventions can play a role in improving the appropriate prescription of Zhongchengyao. We can provide consumers with clear instructions to safeguard their interests and promote healthcare value. Furthermore, the study seeks to identify and validate potential mechanisms, such as financial incentives, prescribing habits, knowledge and skills, and patient expectations, that may influence the inappropriate prescription of Chinese patent medicines. This empirical validation will provide valuable insights into the reasons behind such inappropriate practices.

Ethical considerations and dissemination

This study has received ethical approval from the Institutional Review Board (IRB) of Southern Medical University, China, with a waiver of informed consent from participating general practitioners (Approval #Southern Medical Audit (2023) No. 060). The protocol includes comprehensive descriptions of ethical considerations such as confidentiality, informed consent materials, as well as data management, access, and security protocols. Furthermore, the study has been registered at the China Clinical Trials Registry (ChiCTR2300077913).

Upon completion of the study, the findings will be disseminated to National Health Commission of the People's Republic of China. The results will also be presented at national and international conferences and published in international peer-reviewed journals. This widespread dissemination of the study's outcomes will contribute to knowledge sharing and facilitate informed decision-making in healthcare practice.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12906-025-04870-6.

Supplementary Material 1

Author contributions

DX conceived the project concept. QZ and Ada. K developed the first protocol draft. DX and QZ developed the sampling design. QZ, LL, HH, LW, YC, and JX developed case scripts. GT, WH, HL, QL, RW, DZ, SL, and YX provided original data from the previous studies for the sample size estimation and calculated some summary statistics. QZ, ZS, BL, and HH worked on the SP field execution. JL, LZ, ZH, XZ, YW, XC, WH, YT, XL, YZ, YC reviewed the content and edited the manuscript and GC reviewed the statistical plan. All coauthors participated in the revision and approved this manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

This study has received trial registration before patient recruitment and the approval from the Institutional Review Board of Southern Medical University with a waiver of informed consent from each participating western practitioners.

Patient consent for publication

Not required.

Protocol amendments

Any protocol modifications will be communicated to the relevant parties through an amendment. If the amendments impact USP participants in any way, they will be notified of the changes. If necessary, additional consent will be obtained and recorded. Additionally, online trial registries will be updated accordingly.

Provenance and peer review

Not commissioned; externally peer reviewed.

Ethics and dissemination

This protocol has obtained ethical approval from the Institutional Review Board (IRB) of Southern Medical University (#Southern Medical Audit (2023) No. 060). The authors plan to publish the findings in a peer-reviewed publication.

Author details

[1]Acacia Lab for Implementation Science, School of Public Health, Southern Medical University, Guangzhou, China
[2]Acacia Lab for Implementation Science, School of Health Management, Southern Medical University, Guangzhou, China
[3]The Second Clinical College of Guangzhou, University of Chinese Medicine, Guangzhou, China
[4]Guangdong Provincial Hospital of Chinese Medicine, Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, China
[5]Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, USA
[6]Department of Internal Medicine, Yale School of Medicine, New Haven, USA
[7]Southern Medical University Institute for Global Health (SIGHT), Dermatology Hospital of Southern Medical University (SMU), Guangzhou, China
[8]Guangdong Provincial Center for Disease Prevention and Control (GDCDC), Guangzhou, China
[9]The Third Department of Pulmonary Disease, Shenzhen Third People's Hospital, Shenzhen, China
[10]School of Nursing, Nanjing Medical University, Nanjing, China
[11]Cicely Saunders Institute of Palliative Care, Policy and Rehabilitation, Florence Nightingale Faculty of Nursing Midwifery & Palliative Care, King's College London, London, UK

[12]Department of Epidemiology and Health Statistics, School of Public Health, Guizhou Medical University, Guizhou, China
[13]Center for World Health Organization Studies, Department of Health Management, School of Health Management of Southern Medical University, Guangzhou, China

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References

1. Wu J, Ma B. Formulas and Chinese patent medicines. People's Medical Publishing House; 2013.
2. Jin R, Zhao K, Guo G, et al. Expert consensus on prescription comment of Chinese traditional patent medicine for promoting the rational use of drugs in Beijing. China J Chin Materia Med. 2018;43(5):1049–53. https://doi.org/10.19540/j.cnki.cjcmm.2018.0036.
3. 2023 National Medical Insurance Drug List. Baidu Encyclopedia. Accessed February 29. 2024. https://baike.baidu.hk/item/2023%E5%B9%B4%E5%9B%BD%E5%AE%B6%E5%8C%BB%E4%BF%9D%E8%8D%AF%E5%93%81%E7%9B%AE%E5%BD%95/63154710
4. Liu X, Wen Y, Wang Y, Feng J. Investigation and analysis of the clinical use of Chinese patent medicines in a community hospital. Guangzhou Med J. 2014;45(6):3. https://doi.org/10.3969/j.issn.1000-8535.2014.06.028.
5. Hu W. A study on current situation of proprietary Chinese medicine use and physicians' prescription preference in primary health care institutions in China. Lanzhou university; 2023.
6. Analysis of the Current Market Demand for the Chinese Medicine Industry in 2023. Accessed February 25. 2024. https://m.baidu.com/bh/m/detail/ar_8991588556023752079
7. Ofori-Asenso R, Agyeman A. Irrational use of Medicines-A summary of key concepts. Pharmacy. 2016;4(4):35. https://doi.org/10.3390/pharmacy4040035.
8. Dutta DS. Rational Use Of Medicines: A Review.:5.
9. Jiang M, Lu C, Zhang C, et al. Syndrome differentiation in modern research of traditional Chinese medicine. J Ethnopharmacol. 2012;140(3):634–42. https://doi.org/10.1016/j.jep.2012.01.033.
10. Zhang J, Sun T. Analysis of irrational use of Chinese medicine in community healthcare center. Journal of Pharmaceutical Research. 2021;(09 vo 40):624–627. https://doi.org/10.13506/j.cnki.jpr.2021.09.014
11. Zhu H, Jin Z. Evaluation and analysis of combined prescriptions of Chinese patent medicines at a community health service center. Chin J Clin Ration Drug Use. Published online 2016. https://doi.org/10.15887/j.cnki.13-1389/r.2016.04.054
12. He B, Cao X. Survey and analysis of Western physicians' use of Chinese patent medicines. Chin J Gen Practitioners. 2012;11(4):1. https://doi.org/10.3760/cma.j.issn.1671-7368.2012.04.034.
13. Hu J, Zhang J, Zhao W, Zhang Y, Zhang L, Shang H. Cochrane Systematic Reviews of Chinese Herbal Medicines: An Overview. Verbeek JH, ed. PLoS ONE. 2011;6(12):e28696. https://doi.org/10.1371/journal.pone.0028696
14. Xu DR, Hu M, He W, et al. Assessing the quality of primary healthcare in seven Chinese provinces with unannounced standardised patients: protocol of a cross-sectional survey. BMJ Open. 2019;9(2):e023997. https://doi.org/10.1136/bmjopen-2018-023997.
15. Xu D, Pan J, Dai X, et al. Comparing quality of primary healthcare between public and private providers in China: study protocol of a cross-sectional study using unannounced standardised patients in seven provinces of China. BMJ Open. 2021;11(1):e040792. https://doi.org/10.1136/bmjopen-2020-040792.
16. Xu D (Roman), Cai Y, Wang X Improving Data Surveillance Resilience Beyond COVID-19, et al. editors. Experiences of Primary heAlth Care quAlity Cohort In ChinA (ACACIA) Using Unannounced Standardized Patients. Am J Public Health. 2022;112(6):913–922. https://doi.org/10.2105/AJPH.2022.306779
17. Wu L, Chen Y, Ma Y, et al. Clinical practice guideline on treating influenza in adult patients with Chinese patent medicines. Pharmacol Res. 2020;160:105101. https://doi.org/10.1016/j.phrs.2020.105101.
18. Currie J, Lin W, Meng J. Addressing antibiotic abuse in China: an experimental audit study. J Dev Econ. 2014;110:39–51. 10/gfppmg.
19. Xue W. Clinical guidelines for the proper use of Chinese patent medicines. Gansu Med J. 2010;29(3):5. https://doi.org/10.3969/j.issn.1004-2725.2010.03.014.
20. Collins LM. Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST). Springer International Publishing; 2018. Accessed October 7, 2023. http://link.springer.com/https://doi.org/10.1007/978-3-319-72206-1
21. Fang B, Cui Y, Li Z, et al. Expert consensus on application of Chinese patent medicine for acute upper respiratory tract infection. Chin J Integr Traditional Western Med Intensive Crit Care. 2019;2129–38. https://doi.org/10.3969/j.issn.1008-9691.2019.02.001.
22. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200. https://doi.org/10.7326/0003-4819-158-3-201302050-00583.
23. Collins LM, Dziak JJ, Kugler KC, Trail JB. Factorial experiments: efficient tools for evaluation of intervention components. Am J Prev Med. 2014;47(4):498–504. https://doi.org/10.1016/j.amepre.2014.06.021.
24. Tian Z, Esserman D, Tong G, et al. Sample size calculation in hierarchical 2×2 factorial trials with unequal cluster sizes. Stat Med. 2022;41(4):645–64. https://doi.org/10.1002/sim.9284.
25. Tong G, Esserman D, Li F. Accounting for unequal cluster sizes in designing cluster randomized trials to detect treatment effect heterogeneity. Stat Med. 2022;41(8):1376–96. https://doi.org/10.1002/sim.9283.
26. Lin M, Wu Q. Survey and analysis of 1,034 outpatient prescriptions of Chinese patent medicines. J Clin Ration Drug Use. 2012;5(23):149–50. https://doi.org/10.15887/j.cnki.13-1389/r.2012.23.028.
27. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. J Clin Epidemiol. 2010;63(7):737–45. https://doi.org/10.1016/j.jclinepi.2010.02.006.
28. Baker A, Book. Crossing the quality chasm: A new health system for the 21st century. BMJ. 2001;323(7322):1192–1192. https://doi.org/10.1136/bmj.323.7322.1192.
29. Shojania KG, Grimshaw JM. Evidence-Based quality improvement: the state of the science. Health Aff. 2005;24(1):138–50. https://doi.org/10.1377/hlthaff.24.1.138.
30. Zill JM, Scholl I, Härter M, Dirmaier J. Which dimensions of Patient-Centeredness Matter? - Results of a Web-Based expert Delphi survey. PLoS ONE. 2015;10(11):e0141978. https://doi.org/10.1371/journal.pone.0141978.
31. NHS Patient Experience Framework. GOV.UK. Accessed July 13. 2023. https://www.gov.uk/government/publications/nhs-patient-experience-framework
32. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377–81. https://doi.org/10.1016/j.jbi.2008.08.010.

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