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Improvement of Care Cascade for Hypertension and Diabetes in Rural China: Protocol for an Implementation Study

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Keywords: care cascade | diabetes | hypertension | implementation study | primary health care

ABSTRACT

The management of hypertension and diabetes poses significant challenges to China's healthcare system, necessitating seamless patient progression through screening, diagnosis, management, and control. Utilizing the care cascade model, this study aims to systematically identify patient drop-offs and devise strategies to address healthcare delivery bottlenecks for hypertension and diabetes in rural China. This study consists of three phases. In Phase 1, qualitative interviews are conducted to explore healthcare experiences and identify determinants across the care cascade. Phase 2 involves systematically assessing barriers identified in Phase 1 and collaborating with local stakeholders using intervention mapping and co-design to generate interventions and implementation strategies. Phase 3 is a cluster randomized controlled trial involving 48 villages, randomly assigned in a 1:1 ratio, to compare changes in hypertension and diabetes care. Intervention villages will implement interventions developed in Phase 2 for 1 year, while control villages will continue with usual care. Primary outcomes include between-group differences in achieving blood pressure and glycemic targets, along with service and implementation outcomes. This study aims to identify the stage with the largest patient retention gap in the care cascade and develop intervention strategies through participatory co-design with practitioners, emphasizing feasible, low-cost approaches. The pragmatic cluster RCT will assess strategy effectiveness, offering valuable insights for practical interventions to enhance hypertension and diabetes care in rural settings, potentially shaping impactful programs and improving healthcare outcomes.

Trial Registration: ClinicalTrials.gov. identifier: NCT06141278

1 | Background

Hypertension and diabetes are two common chronic diseases that present major challenges for health systems [1, 2]. Their effective management is pivotal for mitigating cardiovascular and renal risks, yet rural areas encounter significant hurdles in achieving optimal control [3]. More than 270 million people are living with hypertension in China, and the recorded prevalence of diabetes has risen more than tenfold from less than 1% in 1980 to 12.8% in 2017 [4, 5]. In a national study of 1.7 million participants in 2017, nearly half of the Chinese individuals aged 35–75 years exhibited hypertension [6]. Of the patients with hypertension, a mere third were actively treated, and merely 1 in 12 achieved blood pressure control [6]. A simulation model study predicted that among those 1.7 million participants, gaps in awareness result in an estimated 3,336,000 years of life lost and 3,829,000 quality-adjusted life-years (QALYs) lost; treatment deficits led to 6,318,000 years of life and 7,251,000 QALYs lost; and control shortfalls translated to a staggering toll of 24,914,000 years of life and 28,657,000 QALYs lost [7]. Similarly, a nationally representative survey in 2013, including 170,287 Chinese participants, found that the prevalence of diabetes was 10.9% and only 37% of those with diabetes were aware of their diagnosis, and just 32% received treatment [8]. Effective management of these conditions hinges on seamless progression through screening, diagnosis, management, and control steps—collectively constituting the care cascade.

The care cascade analysis, initially developed for chronic communicable illnesses like HIV and tuberculosis, offers a systematic dissection of disease management into interlinked service steps, addressing patient needs from screening to control [9]. Enhancing linked cascade services relies on robust primary care capacities grounded in evidence-based guidelines to prevent, treat, and manage hypertension and diabetes at the population level. This is challenging for rural areas that encompass limited resources, suboptimal care quality, and inadequately qualified primary care providers [10].

The Healthy China 2030 initiative, aiming to reduce premature deaths from major non-communicable diseases by 30% by 2030, underscores the urgency of developing and evaluating a potent, adaptable, and scalable model for comprehensive hypertension and diabetes care in rural primary settings [11]. Although several population-based surveys illuminate progress along the service continuum in China, scant research delves systematically into inter-stage dynamics and intervenes at each cascade stage.

A recent scoping review of the literature on the care cascade for hypertension and diabetes identified 128 pertinent studies [12]. Despite shared management pathways and the significant opportunity to synergize healthcare systems and implementation strategies for both conditions, a mere 14.1% (18 studies) addressed their joint management. The analysis further revealed a predominance of observational studies, constituting 75.0% (96 studies) of the body of work, with interventional research and implementation studies representing only 18.8% (24 studies) and 6.3% (8 studies), respectively [12]. These findings underscore a critical evidence gap in integrated care strategies for managing hypertension and diabetes. Our implementation study seeks to address this gap by undertaking context-specific implementation research to pinpoint priorities and develop effective strategies, thereby marking a significant advancement in addressing healthcare delivery challenges for these conditions in rural China.

2 | Methods

This study comprises three phases (1) context analysis and need assessment, (2) intervention development, and (3) implementation and evaluation. In the initial phase, qualitative interviews will be conducted with healthcare providers, clinical managers, and hypertensive/diabetic patients to identify facilitators and barriers influencing the continuity of hypertension and diabetes care and inform the development of targeted interventions and implementation strategies. The second phase will involve intervention mapping and engaging in participatory design sessions with experts, local stakeholders, and the implementation team to collaboratively devise implementation strategies. The final phase will include executing a cluster-randomized controlled trial to discern longitudinal changes in hypertension and diabetes care and evaluating the clinical effectiveness of the implemented interventions. A thorough process evaluation will be conducted to analyze alterations in the measures of reach, adoption, implementation, and maintenance, providing insights into the dynamics of intervention implementation. Additionally, an economic evaluation will be undertaken to ascertain the cost-effectiveness of the interventions, ensuring a comprehensive understanding of the economic implications and sustainability of the implemented strategies.

2.1 | Conceptual Framework and Approach

Our theoretical model, depicted in Figure 1, synthesizes elements from the process model, determinant framework, and evaluation framework within the broader context of implementation science (Figure 1). This amalgamation aims to augment traditional trial designs by incorporating measures of implementation fidelity. By embracing diverse implementation theories, models, and frameworks, our approach seeks to unravel the intricacies of implementation processes, generating actionable knowledge essential for scaling up interventions in low- and middle-income settings.

The Consolidated Framework for Implementation Research (CFIR) plays a pivotal role in identifying multilevel factors influencing the implementation of prevailing standards in hypertension and diabetes care. Renowned for its robustness, CFIR operationalizes context-relevant barriers and facilitators across five domains: innovation characteristics, outer setting, inner setting, characteristics of individuals, and the implementation process [13]. This framework serves as a comprehensive lens for dissecting the complex landscape of implementation challenges. We employ intervention mapping to guide the development of interventions [14]. Behavior change theory, specifically the Capability, Opportunity, Motivation, Behavior (COM-B) model, informs our interventions by identifying key behavioral determinants and guiding the selection of appropriate strategies [15, 16]. Implementation

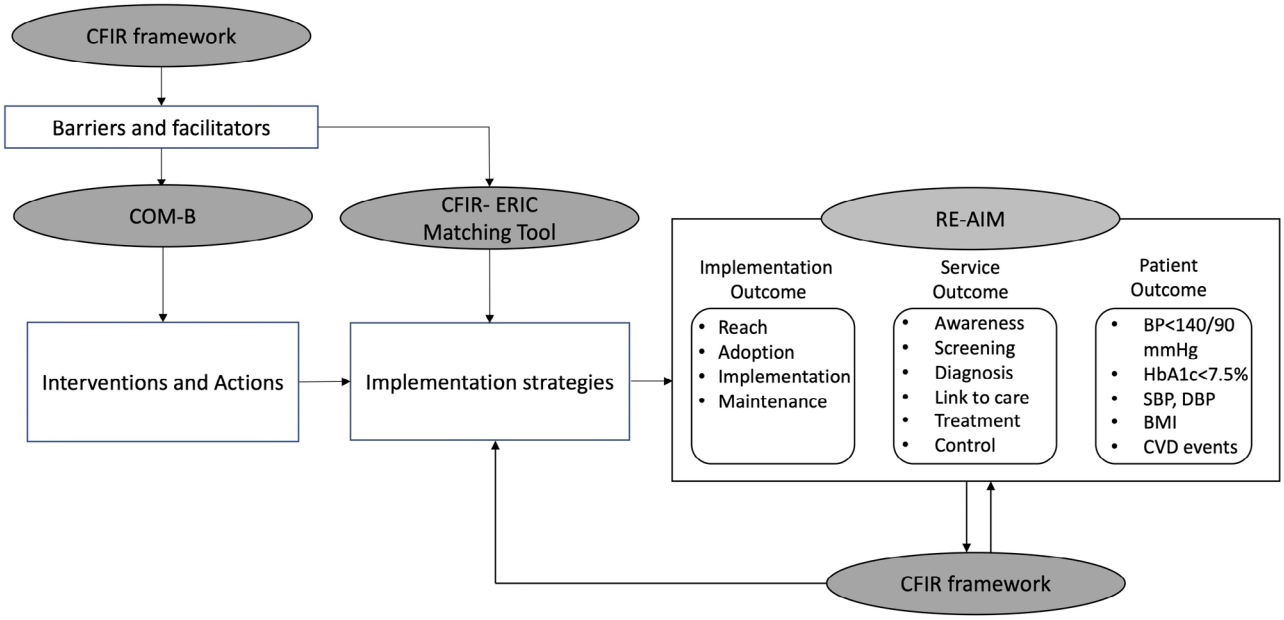

FIGURE 1 | Theoretical model for the study. BMI indicates body mass index; CFIR = consolidated framework for implementation research; COM-B = capability, opportunity, motivation, behavior; CVD=Cardiovascular Disease DBP = diastolic blood pressure; ERIC = Expert Recommendations for Implementation Change; Re-AIM = reach, effectiveness, adoption, implementation, maintenance; SBP = systolic blood pressure.

mapping, combined with the CFIR-ERIC matching tool [17], further refines our approach by systematically assessing barriers and facilitators and prioritizing actions with local stakeholders. The CFIR-ERIC matching tool helps match discrete implementation strategies to specific determinants identified from the CFIR analysis, ensuring that the interventions are contextually relevant and capable of overcoming identified barriers [18]. The RE-AIM (reach, effectiveness, adoption, implementation, maintenance) framework is a practical tool that assesses complex interventions in real-world healthcare system settings, including measures of clinical effectiveness and implementation strategies [19].

2.2 | Setting and Facility Selection

The study will be conducted in Gongyi, Wugang, and Linqu counties of China. Study sites are selected by the study team based on their willingness to participate and their proximity to the research team.

2.3 | Project Activities

2.3.1 | Phase 1: Context Analysis and Need Assessment

2.3.1.1 | Study Participants. We will include key stakeholders in four hierarchical levels (1) policymakers from Provincial, Municipal, and Prefectural Health Commissions and health administrators from Provincial or Municipal Centers for Disease Prevention and Control; (2) administrative or clinical leaders from the county hospitals, including chief physicians, department heads, and senior medical specialists, whose responsibilities included guidance and support to local primary health care facilities; (3) village doctors, who are the sole healthcare providers at village clinics in rural China and perform a range of functions typically covered by doctors, nurses, and pharmacists in other settings; and (4) local residents diagnosed with hypertension and/or diabetes, aged 35–74 years old. For representatives of policymakers and clinical leaders, we will only invite those who have been in the mentioned positions for at least 6 months. For patient representatives, we will ensure that participants represent drop-offs in every stage of cascades. Participants will be excluded if they are unavailable at the time of interviews, unable to communicate with researchers, or unable to provide informed consent. Purposive and snowball sampling methods will be applied to identify interviewees.

2.3.1.2 | Qualitative Data Collection. Individual in-depth interviews will be adopted with semi-structured interview guides. Interview guides will be developed based on the CFIR framework and care cascade model. These guides will be meticulously designed to probe into the nuances of patient engagement with the healthcare continuum, specifically investigating the determinants of patient retention and the reasons behind discontinuation of care. Separate topic guides will be used for different groups of interviewees. Different sets of topic guides will be prepared for distinct groups of interviewees, with a keen focus on understanding patient healthcare-seeking behaviors, reasons for attrition in the care continuum, and factors contributing to successful treatment outcomes. All guides will be pilot-tested and refined before the formal interview. All interviews will be carried out in person by researchers from our project team who possess extensive experience and are well-versed in the cultural and clinical context of rural China. The interviews will take place at the interviewee's office or a private space to allow interviewees to share their views freely and confidentially without being influenced by others. The sample size will be determined by thematic saturation, which occurs when no new theme emerges during the interviews.

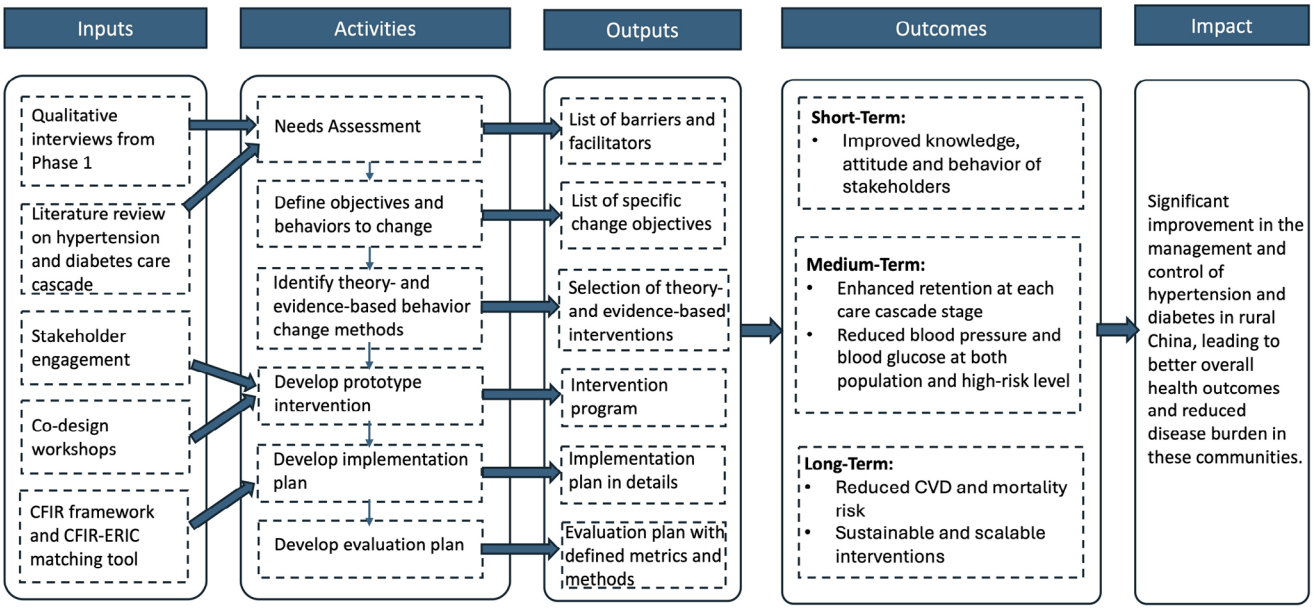

FIGURE 2 | Intervention mapping logical model. CFIR indicates Consolidated Framework for Implementation Research.

2.3.1.3 | Qualitative Data Analysis. All interviews will be audio recorded and transcribed verbatim. Two researchers will independently review the transcripts and inductively generate preliminary codes about influencing factors. Those barriers and facilitators will be summarized under the cascade stages of hypertension and diabetes care, providing a comprehensive overview of the healthcare journey for these conditions. Through this analytical process, summaries of these factors will be developed and further organized into matrices by participant type. This organization will facilitate a detailed mapping of the healthcare pathway, allowing for the identification of critical barriers, facilitators, and actionable recommendations for implementing guideline-based care strategies in rural settings.

2.3.2 | Phase 2: Identify Interventions to Improve Retention in Hypertension and Diabetes Care Cascade

In Phase 2, we employ intervention mapping to systematically develop interventions aimed at improving retention within the hypertension and diabetes care cascade in rural China. Intervention mapping is a structured, iterative process consisting of six consecutive steps, each designed to ensure the development of theory- and evidence-based interventions that integrate the perspectives and needs of target populations [14]. The logic model of intervention development is shown in Figure 2.

2.3.2.1 | Step 1: Needs Assessment. The needs assessment involves a comprehensive evaluation of the target population's requirements, informed by qualitative interviews from Phase 1 and a literature review on hypertension and diabetes care cascades [12]. This assessment aims to establish a detailed understanding of the care cascade, identify the at-risk population, and elucidate the behavioral and environmental causes and determinants of these conditions. The assessment will focus on barriers and facilitators influencing the care cascade stages.

2.3.2.2 | Step 2: Defining the Objectives and Behaviors to Change. In this step, we develop specific change objectives and identify the behaviors that need to change within the target population. Using the findings from the needs assessment, we will identify key behavioral determinants and performance objectives that are necessary to achieve the program goals. The Capability, Opportunity, Motivation, Behavior (COM-B) model will guide this process, focusing on factors crucial for the target population [15]. Performance objectives will specify the actions individuals must take to achieve desired health outcomes.

2.3.2.3 | Step 3: Selection of Theory- and Evidence-Based Behavior Change Methods. This step involves linking behavioral determinants with desired behavioral outcomes and selecting appropriate theory- and evidence-based interventions. By mapping the intervention strategies to these determinants, we aim to identify effective methods for influencing behavior at each care cascade step. This process ensures that the selected interventions are theoretically sound and evidence-based, optimizing the intervention content for maximum impact.

2.3.2.4 | Step 4: Development of a Prototype Intervention. In this step, we integrate the intervention components into a coherent program using delivery channels suited to the local context. The co-design process, involving a series of three workshops with local policymakers, healthcare implementers, selected patient representatives, and village doctors, will ensure that the interventions are feasible, acceptable, and effective for the target population. These workshops will integrate insights from Phase 1 interviews and allow for direct participation by end-users, ensuring that their needs, preferences, and practical considerations are fully represented in the intervention design. Feedback loops and iterative refinement during the workshops will further enhance the alignment of the interventions with real-world conditions (Table 1). Detailed notes and qualitative synthesis

TABLE 1 | Proposed contents of stakeholder workshops.

	Participants	Contents
Workshop 1	Policymakers, local principal investigators, county leadership, clinical managers	Introduce care cascade analysis methods and chronic care models
		Present the main results of Phase 1
		Discuss the strategies developed from the CFIR-ERIC tool
		Develop coordinated care for hypertension and diabetes
		Define the roles and responsibilities of the team members
		Formulate a plan on how to re-design the delivery of hypertension and diabetes care in local practice settings
Workshop 2	Policymakers, local investigators, county leadership, clinical managers	Introduce the evidence-based practice of hypertension and diabetes management in primary care
		Identify potential solutions to improve each stage of hypertension and diabetes care cascade
		Formulate a plan on how to improve the clinical information system in rural area
		Design an audit plan
		Identifying existing resources/data that can be used to improve disease management efficiency
Workshop 3	Local investigators, clinical managers, village doctors, and patient representatives	Discuss the concept and principles of self-management support
		Develop interventions to support participant self-management
		Explore ideas, concerns, and expectations from local implementers
		Design tools to motivate patients to change behavior, including accessing screening, changing lifestyle, getting diagnosis, achieving adherence to therapy, self-monitoring blood pressure, and blood glucose
		Decide on the management tools supporting participants' self-management

of the workshop outcomes will guide the final intervention design.

2.3.2.5 | Step 5: Development of an Implementation Plan. This step involves creating a detailed implementation plan using the implementation mapping [20]. We will systematically assess barriers to care and service delivery bottlenecks, identify priority actions with local service providers, health administrators, and decision-makers, and utilize the ERIC compilation of 73 discrete implementation strategies [18]. The CFIR-ERIC matching tool will help match these strategies to specific determinants identified from the CFIR analysis [17]. The output from this exercise will be discussed with local stakeholders to ensure that implementation strategies are contextually relevant and can overcome identified barriers.

2.3.2.6 | Step 6: Development of an Evaluation Plan. The final step involves creating an evaluation plan to assess the effectiveness and feasibility of the interventions. This plan will include both process and outcome measures, ensuring a comprehensive assessment of the interventions' impact on care retention and overall healthcare outcomes. Metrics will be established to evaluate the interventions' success in achieving blood pressure and glycemic targets, as well as service and implementation outcomes. The evaluation plan will facilitate robust assessment and potential replication of successful interventions.

2.3.3 | Phase 3: A Cluster Randomized Controlled Trial to Implement and Evaluate Interventions for Improving Hypertension and Diabetes Care Cascade

We will conduct a parallel-arm, cluster-randomized trial to evaluate the effectiveness and implementation of an evidence-based intervention for improving the care cascade of hypertension and diabetes (Figure 3).

2.4 | Study Villages

We will purposely select four townships in each county and four villages from each township, giving a total of 48 villages. We will purposefully choose four townships within each county, engaging in informed discussions with local county health authorities to gauge their willingness to participate and the proximity of townships to county centers. The inclusion and exclusion criteria for villages are methodically formulated to uphold homogeneity and practicality within our study framework. Villages with a resident population ranging from 1000 to 2000 individuals are deliberately included, with a focus on two pivotal aspects: convenient transportation and concentrated residency. This deliberate emphasis seeks to streamline logistical considerations and enhance the efficiency of intervention implementation. Furthermore, the demographic composition of each village's residences is meticulously aligned with that of the respective county, thereby mitigating potential confounding

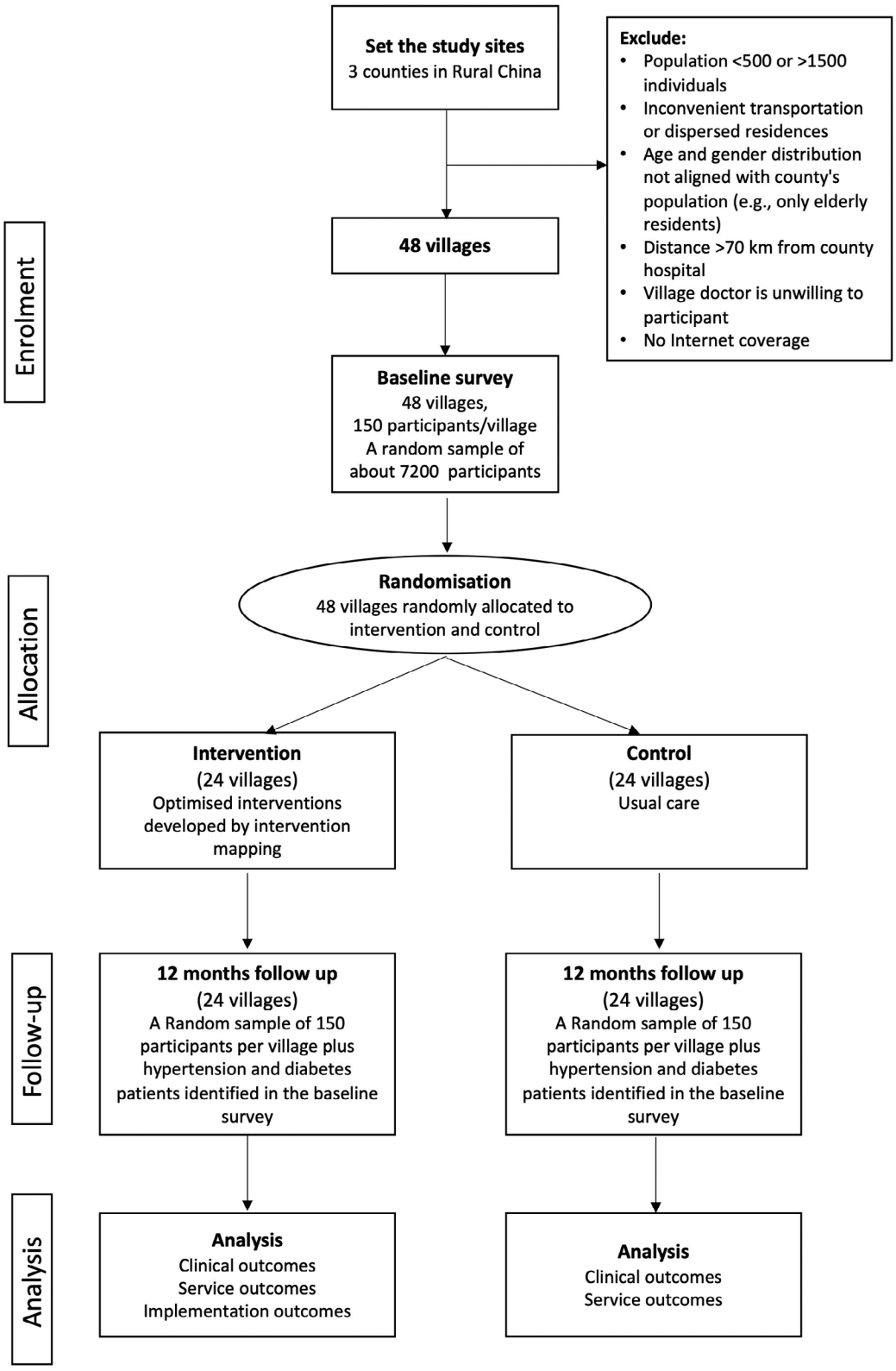

FIGURE 3 | Cluster randomized controlled trial flowchart.

variables and bolstering the internal validity of our study. We will exclude villages primarily inhabited by elderly residents left behind by migrating family members. Such populations typically exhibit an amplified prevalence of chronic diseases, increased healthcare needs, and reduced access to care—factors that can disproportionately influence study outcomes. By excluding these villages, we aim to reduce variability related to healthcare utilization and support mechanisms, thereby ensuring that our findings more accurately reflect the efficacy of the intervention in a typical rural setting. In addition to demographic considerations,

the geographical proximity to the county-level hospital is a critical criterion for inclusion. Villages located within 70 km of the county hospital are strategically chosen to facilitate seamless access for biological sample testing, ensuring the integrity of our data collection process. Moreover, the presence of a village doctor and their demonstrated willingness and capability to implement the prescribed intervention measures are paramount factors influencing village selection. Existing wireless network coverage within the village is a prerequisite for selection, facilitating real-time communication and data transmission vital for the precise monitoring of the intervention and the integrity of data collection processes. It is important to note that the non-random selection of the counties and townships is not a significant issue for a study with this design.

2.5 | Randomization and Blinding

Randomization will be done by computer through the assignment of a random number with stratification by county and a 1:1 allocation of villages to the intervention group or control. Randomization of the village to intervention or control is done only after all participants in the villages have been recruited. As this is a behavioral intervention program, the people delivering the intervention cannot be blinded to the intervention group.

2.6 | Intervention and Control

2.6.1 | Intervention

Villages allocated to the intervention group will implement prioritized hypertension and diabetes management intervention through the strategies developed in Phase 2. The intervention will be applied at the village level. Village doctors from intervention villages will receive the intervention package, which consists of cascade care workshops, intervention equipment, ongoing facilitation, and support.

After randomization, village doctors from the intervention group will receive a 3-day training. This curriculum is designed to underscore the importance of non-communicable disease management, with a focus on diabetes and hypertension. The training will encompass strategies for risk assessment based on dietary habits, physical activity levels, tobacco use, and alcohol consumption; the use of digital sphygmomanometers for blood pressure monitoring; anthropometric measurements; and the protocol for referring patients who present with SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg. Additionally, the program will deliver health education tailored to the principal risk factors for these conditions, underpinned by the Health Belief Model. To ensure the highest quality and relevance, training materials will be crafted in collaboration with domain experts and local stakeholders, followed by a pretesting phase with a select group of township village physicians. The intervention emphasizes the necessity of real-time clinical data for monitoring village doctors' performance in continuous hypertension and diabetes care. Improvement in adherence to the guideline recommendations is facilitated through monthly village doctor performance feedback reports. Village doctors in the intervention group receive monthly supervision visits from district supervisors who are part of the local health authority or designated by the county health department to ensure the fidelity of the intervention's implementation and to provide support where necessary. In terms of resources, village physicians will receive customized support, addressing the specific requirements of their practice settings. This will include the provision of fundamental diagnostic and monitoring equipment, such as validated digital blood pressure monitors, precision scales for weight, stadiometers for height, and blood glucose testing apparatus, necessary for the comprehensive management of patients throughout the 12-month intervention period.

2.6.2 | Control

Villages that have not been enrolled in the intervention will conduct the current standard of care. In China, the Department of Primary Health and National Health Commission has issued standards for the management of hypertension and diabetes in primary care [21–23]. These documents summarize the best evidence available and are periodically updated. The Guidelines incorporate decision-making algorithms, aiming to provide primary healthcare workers with comprehensive recommendations in the field of hypertension and diabetes management.

In our study, the control villages will continue working as normal, and the implementation manager did not visit them or interact with their staff to avoid contamination. However, at the time of the initial data collection, all participants with elevated BP (SBP $\geq$140 mmHg and/or DBP $\geq$ 90 mmHg) or diagnosed with diabetes in both intervention and control villages will be notified of their health status. They will be advised to seek further evaluation from their local health provider. Additionally, these participants will be provided basic health lifestyle advice, including recommendations to (1) limit salt intake to no more than 5 g per day by avoiding foods high in salt and reducing the addition of cooking or table salt to meals; (2) eliminate the use of cooking oils high in saturated fats; (3) consume at least five servings of fruits and vegetables daily to ensure adequate fiber and micronutrient intake; (4) engage in at least 150 min of moderate-intensity aerobic physical activity per week; and (5) abstain from all tobacco products and limit alcohol consumption. Participants who were previously aware of their hypertensive status will be advised to revisit their doctor for a review of their medication and to take their medication as told by their doctor. No further care or advice will be provided during the intervention period. At the end of the intervention period, the participants with hypertension in the control sampling units will be revisited for outcome measures, as outlined below. At the follow-up survey, these participants will receive further advice and recommendations regarding their hypertension status. Furthermore, they will be provided with all the educational material about hypertension and how to manage the disease.

2.7 | Baseline and Post-Intervention Survey

We will independently draw two random samples, before and after randomization, to measure the study outcomes at the population level. Baseline surveys, conducted before randomization, aim to blind study staff from intervention allocation.

The post-intervention survey leverages two distinct components: firstly, a randomly selected survey sample drawn independently, mirroring the pre-intervention approach to assess changes. Secondly, to examine the impact of intervention strategies for the group of individuals with hypertension and diabetes, the post-intervention survey will include follow-up assessments for individuals identified as hypertensive and/or diabetic in the baseline survey. As such, our design provides a nuanced understanding of the interventions' effects for both the general population and the populations of patients with high risk. Both baseline and post-intervention surveys will be conducted in the same season to minimize the variation due to seasonal changes.

2.7.1 | Participants

Inclusion criteria include individuals aged 35–74 who are permanent residents in the selected villages, with a residency duration exceeding 6 months annually. Exclusion criteria encompass individuals with mental disorders or communication barriers, those planning to relocate within the next year, individuals with an expected life span of less than a year, pregnant or lactating women, and those who are absent due to travel, hospitalization, or residing outside the study area during the investigation period. Population censuses (specifically completed for this study or existing polling booth registers) at each selected village will be used to select potential participants randomly. One hundred fifty residents aged 35–74 are selected from each village (for a total of 7200 from 48 villages) to participate in the survey. The total number of individuals will be divided into eight age and sex groups to obtain approximately equal numbers of males and females in the age categories 35–44, 45–54, 55–64, and 65–74 years in each village. Additional sampling will be conducted (10 from each age and sex band) to replace those participants who had migrated, died, or refused to participate. Recruitment for this study will be conducted from December 2023 to May 2024.

In the post-intervention assessment, we will also include high-risk individuals identified in the baseline survey. High-risk individuals encompass those indicating a diagnosis from county hospitals or higher-level healthcare facilities, individuals with an average systolic blood pressure (SBP) of $\geq$ 140 mmHg and/or diastolic blood pressure (DBP) $\geq$ 90 mmHg, and those currently prescribed anti-hypertensive medication(s). Similarly, individuals deemed high-risk for diabetes included those indicating a diagnosis from county hospitals or higher-level facilities, having a fasting plasma glucose of 7.0 mmol/L (126 mg/dL) or higher, a random plasma glucose of 11.1 mmol/L (200 mg/dL) or higher, and an HbA1c measurement of 6.5% or higher. This approach facilitates a nuanced exploration of intervention effects on sustained high-risk profiles for hypertension and diabetes, thereby contributing to a comprehensive understanding of the care cascade dynamics in this critical population subset.

2.7.2 | Data Collection

Our data collection methodology represents a meticulous and scientifically rigorous approach tailored to unveil intricate factors influencing hypertension and diabetes within our study cohort. The structured questionnaire, meticulously devised, spans diverse domains crucial for a comprehensive understanding, encompassing (1) fundamental demographic information, including age, income, gender, marital status, religion, number of children, and occupation; (2) lifestyle-related factors such as physical activity, tobacco use, alcohol consumption, dietary practices, including cooking methods and salt utilization, and aspects of stress and overcrowding; (3) assessment of knowledge pertaining to hypertension, its risk factors, and participants' awareness and reporting of prior blood pressure measurements; (4) an evaluation of medication adherence through a scale assessment [24]; (5) implementation of the Patients Assessment of Chronic Illness Care (PACIC) questionnaire to gauge the alignment of care with the chronic care model [25]; and (6) a specialized questionnaire probing hypertension and diabetes care cascade.

Anthropometric measurements, pivotal for a holistic health assessment, will be conducted using precise instruments. Height and weight, assessed with a portable stadiometer (Seca213, Hamburg, Germany) and weighing scale, will be measured with meticulous precision. Waist and hip circumferences will be measured using non-stretchable tape at defined anatomical points. Blood pressure will be recorded thrice, ensuring reliability and consistency, utilizing a Digital Automatic Blood Pressure Monitor (OMRON HEM-7271) after the participant has rested for at least 15 min.

Spot urine and fasting venous blood samples will be collected from all subjects. Overnight fasting venous blood samples will be collected after non-traumatic venepuncture. Both urine and blood samples will undergo detailed analyses at the county hospital laboratory, employing validated methods to guarantee accuracy and reliability. The urinary profile will include essential indicators such as urinary sodium, urinary potassium, urinary creatinine, and urinary microalbumin. Urinary potassium and urinary sodium levels will be quantified using the ion-selective electrode method, while urinary creatinine was assessed through the enzymatic method. Detection of urinary microalbumin will be conducted utilizing the immunoturbidimetric method. In blood testing, pivotal markers will be assessed to gain comprehensive insights into metabolic and cardiovascular health. These include glycated hemoglobin (HbA1c), blood glucose levels, creatinine, triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). The quantification of these markers will be executed with methodological precision: HbA1c analysis employed the High-Performance Liquid Chromatography (HPLC) method, while total cholesterol (TC), triglycerides (TG), and HDL-C will be analyzed using an enzymatic colorimetric reference method. All blood samples will be processed on an automatic analyzer, ensuring timely assessment of TC, TG, and HDL-C levels within 2 h of collection to maintain sample integrity.

All the data at the patient level will be collected at baseline and follow-up surveys at the end of the trial using the same data collection tools. All investigators and data collectors will be trained regarding the study procedures before the conduct of the study to minimize variability in the method of data collection and ensure standardization. A study-specific training

manual containing step-by-step procedures for all data collection (anthropometric and survey administration) will be provided.

2.8 | Outcome Evaluation

2.8.1 | Patient-Level Clinical Outcomes

The primary study outcomes are the between-group differences in the change in the proportion of patients achieving the BP target of < 140/90 mmHg (from baseline to 1 year) and the change in the proportion of patients achieving the glycemic target of HbA1c < 6.5% among participants with diabetes, respectively. Secondary outcomes encompass between-group differences in the mean change, from baseline to 1 year, in systolic blood pressure (SBP) and diastolic blood pressure (DBP) among hypertensive patients. The changes in the proportions of patients achieving body mass index (BMI) < 23 kg/m^2 will be evaluated. The clinical outcome evaluation will be conducted through direct contact with the trial participant by the outcome assessment team. To mitigate ascertainment bias, the outcome assessment team is completely independent of the village doctors.

2.8.2 | System-level Service Outcomes

Secondary outcomes extend to quantitative measures reflecting successful progression through stages in the hypertension and diabetes care cascade (Table 2). Monthly assessments of process measures will be derived from routinely collected data through the management system over the study period. These service outcomes serve as tangible indicators of the intervention's impact on the broader healthcare system and the seamless progression of patients through crucial care steps.

2.8.3 | Implementation Outcomes

This study aims to yield actionable knowledge on process outcomes and feasibility, delineating core components that are transferrable across contexts while identifying areas necessitating local adaptation for scalable activities. The implementation outcomes thus contribute critical insights into the intervention's real-world applicability and its potential for broader implementation.

2.9 | Sample Size Calculation and Statistical Power

Leveraging prevalence data specific to China, we assume a hypertension prevalence of 35% with a blood pressure control rate of 15% and a diabetes prevalence of 20% with a control rate of 35% [6, 26]. The sample size of 48 clusters (24 intervention and 24 control) and 150 participants in each cluster can provide at least 80% statistical power (with a two-sided alpha = 0.05) to detect an 8% or greater improvement in blood pressure control and a 10% or greater enhancement in blood glucose control in intervention villages compared to control villages. This power estimate is based upon an intra-cluster correlation coefficient (ICC) of 0.02 and a lost follow-up rate of less than 20% [27].

2.10 | Statistical Analysis

For patient-level clinical outcomes, primary analyses will focus on between-group differences in the proportion of patients achieving blood pressure and glycemic targets using a generalized linear mixed-effects model. Mean changes in secondary clinical outcomes will be assessed through linear regression models. To account for clustering within villages, generalized estimating equations (GEE) will be applied, considering the potential correlation among participants within the same cluster. Subgroup analyses will explore variations in intervention effects across prespecified demographic and clinical strata, including age (35-44, 45–54, 55–64, and 65–74 years), gender, baseline health status (e.g., presence of comorbidities), and healthcare utilization patterns. These subgroups have been chosen based on evidence suggesting differential responses to hypertension and diabetes interventions in rural settings. To address potential multiple comparison issues arising from subgroup analyses, adjustments will be made using the Bonferroni correction approach to control for Type I errors. The difference in mean BP changes between the intervention and control groups will be tested using a linear mixed-effects model. In evaluating system-level service, a generalized linear mixed-effects model, while implementation outcomes, will be analyzed descriptively to provide insights into the feasibility and transferability of the intervention. Analyses will be by intention-to-treat.

2.11 | Qualitative Data Collection and Analysis

Qualitative data will be collected through semi-structured interviews with key stakeholders using interview guides developed using the RE-AIM and CFIR framework. Interview guides will contain questions related to feasibility, acceptability, and future adaptations to ensure that important implementation outcomes are represented. Audio recordings will be transcribed and coded using qualitative analytic software. Coding procedures will commence with an initial round using a priori constructs aligned with the study's conceptual model, incorporating relevant implementation outcomes (such as reach, adoption, implementation, and maintenance), and CFIR elements. This coding structure will be documented in a comprehensive codebook, providing explicit definitions and illustrative examples. Thematic analysis will be employed to extract and interpret the perspectives and experiences of stakeholders and patients. To ensure the reliability of the analysis, at least three study investigators will participate in the coding process, establishing inter-rater reliability through a meticulous "check-coding" procedure. The "check-coding" process involves independent coding of the same interview transcripts by all coders, followed by collaborative sessions to compare coding, address any discrepancies, and refine definitions and examples in the codebook. This iterative process continues until coders achieve a shared understanding of domain definitions and coding applications. Subsequently, a new set of interviews will be coded independently, repeating the process to reinforce coder consistency. Upon completion of the coding phase, data will be synthesized using matrix displays. This method facilitates the systematic comparison and contrast of data across diverse sites.

TABLE 2 | Definition of cascade stages of hypertension and diabetes.

Cascade stage	Hypertension	Diabetes
The population in need	Percent of the population with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or previously correctly diagnosed as hypertensive	Percent of the population with DIABETES or previously correctly diagnosed as Diabetes.
Screening	Percent of population with high blood pressure who have had previously had blood pressure measured according to standards	Percent of the population with Diabetes who have ever had a blood glucose test.
Diagnosis	The proportion of people with hypertension in the catchment area of interest who are diagnosed at the facility level, where a diagnosis of hypertension follows at least three measurements of BP on two or more health visits with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg.	The proportion of people with diabetes in the catchment area of interest who have a fasting plasma glucose of 7.0 mmol/L (126 mg/dL) or higher, or have a random plasma glucose of 11.1 mmol/L (200 mg/dL) or higher, or have a HbA1c measurement of 6.5% or higher
Population linked to any care/treatment Initiation	The proportion of people diagnosed with hypertension who initiate any treatment, including lifestyle advice	The proportion of people diagnosed with diabetes who initiate any treatment, including lifestyle advice
Treatment monitoring	The proportion of people who initiate treatment for hypertension, remain in care and are followed up by their service provider. A patient was considered to be monitored by the care provider if there was evidence of BP being measured and recorded every month.	The proportion of people who initiate diabetes treatment, remain in care and are followed up by their service provider. A patient was considered to be monitored by the care provider if there was evidence of blood glucose being measured and recorded every 3 months.
Disease control	The proportion of hypertension patients who have achieved BP control. We defined control as SBP < 140 mmHg and DBP < 90 mmHg in complex cases, such as diabetes comorbidity	The proportion of diabetes patients who have achieved HbA1c < 6.5%

2.12 | Economic Analyses

An economic evaluation is planned using the health services perspective. Detailed information on intervention-related costs will be meticulously gathered from project expense reports. This approach ensures a thorough examination of resource utilization, allowing for a nuanced assessment of the economic implications of the intervention program. Quality of life will be quantified using the EQ-5D instrument, a well-established and validated tool previously employed in rural populations. This instrument offers a standardized and feasible approach to capturing the multifaceted dimensions of participants' quality of life [28]. The study will incorporate health insurance data, specifically from the New Rural Cooperative Medical Scheme, to further enrich the economic analysis. This dataset will provide valuable insights into health services utilization and associated costs, covering various components such as inpatient, outpatient, emergency care, medical tests, and medication use.

The economic evaluation will assess cost-effectiveness per event averted and per life-year saved. Furthermore, the cost per Quality-Adjusted Life Year (QALY) will be computed, offering a comprehensive metric that considers both clinical outcomes and quality of life improvements. These measures will be subjected to modelling techniques, leveraging the data collected during the trial. The models will facilitate the extrapolation of economic outcomes over participants' lifetimes, providing a long-term perspective on the intervention's cost-effectiveness and sustainability.

3 | Discussion

This study is poised to contribute substantially to the advancement of rural healthcare delivery for hypertension and diabetes through a nuanced, multi-phased, and comprehensive implementation approach. By embarking on a qualitative study, the research aims to identify key factors influencing patient retention within the care cascade for these chronic conditions. The intervention strategy, meticulously crafted through participatory co-design with practitioners, emphasizes the importance of adopting acceptable and low-cost strategies to ensure feasibility and sustainability. The pragmatic cluster Randomized Controlled Trial is a robust approach for assessing the effectiveness of these strategies, promising invaluable insights into practical interventions that can significantly enhance healthcare for hypertension and diabetes in rural areas.

Considering the shared risk factors and bidirectional interaction between hypertension and diabetes, the study takes

a holistic approach, recognizing the benefits of simultaneous management. Both conditions follow a similar management pathway, advocating early detection, appropriate treatment, and continuous monitoring. Leveraging the overlap in healthcare systems and implementation strategies for both conditions is deemed efficient and effective, fostering synergistic management. The cascade model's significance is heightened when addressing comorbidities with shared management pathways, facilitating the identification of gaps and bottlenecks in the co-management of multiple conditions. The primary care system plays a pivotal role in enabling holistic and synergistic management, with primary care providers serving as key actors in early diagnosis, timely treatment initiation, and regular follow-up—a proactive approach crucial for mitigating the burden of hypertension and diabetes and their associated complications [29].

This comprehensive implementation study unfolds across multiple phases, with the need assessment in phase one being critical for successful implementation [30]. The implementation cascade analysis in this phase identifies influential factors across the cascade model, surpassing basic descriptions of awareness, prevalence, and control rates. The systematic assessment of barriers and facilitators not only prioritizes improvements but also establishes a robust baseline for tracking project-induced enhancements. The study's scientific rigor and clear methodology promise to enrich the field of implementation science, significantly impacting rural healthcare delivery. One of the key strengths of this study is the use of intervention mapping to develop intervention and implementation strategies in Phase 2. This structured approach allows for a transparent translation of behavioral and environmental determinants into practical and contextually relevant intervention components. It ensures that the interventions are not only scientifically sound but also feasible, acceptable, and sustainable within the rural Chinese healthcare context. Furthermore, the study's innovative co-design methods for strategy development ensure a participatory approach, engaging experts, local stakeholders, and the implementation team. This collaborative design fosters the development of interventions tailored to address challenges identified in the context analysis, ensuring contextually appropriate and locally resonant strategies. Prioritizing actions aligned with local healthcare providers and stakeholders cultivates a sense of ownership and commitment to the interventions [31]. In its final phase, the study executes a cluster-randomized controlled trial, deploying evidence-based guidelines tailored for village doctors. The comprehensive evaluation incorporates stringent quality control measures, including blinded evaluation staff and the separation of intervention and evaluation teams. This approach contributes to resolving debates around high-risk versus population strategies in preventing cardiovascular diseases and other chronic conditions. Additionally, the study employs mixed methods to evaluate implementation outcomes and service outcomes comprehensively. Effectiveness is gauged through service and patient outcomes, while Reach, Adoption, Implementation, and Maintenance are assessed through implementation outcomes. This comprehensive approach ensures a thorough understanding of the impact and sustainability of interventions, contributing to the nuanced field of implementation science. The multidimensional insights derived from both quantitative and qualitative methods promise a nuanced understanding of the implementation process, stakeholders' perspectives, and patient experiences.

Although our study offers valuable insights into the implementation of hypertension and diabetes care interventions in rural China, it is essential to recognize certain limitations that may affect the broader applicability of our findings. One potential limitation lies in the generalizability of results beyond the study context. The study's geographical scope is restricted to three county-level cities in China. However, the intervention design and co-design process are inherently adaptable to other socio-cultural contexts. Using flexible implementation science frameworks, such as the CFIR model, allows for systematic adaptation to different settings. In addition, the participatory co-design approach engages local stakeholders to ensure that the intervention is contextually relevant and scalable. Future research will explore the scalability of the intervention in other rural regions of China, providing further evidence of its generalizability and applicability in diverse settings. In addition, the criteria for village selection, including convenient transportation and proximity to county hospitals, were indeed chosen to optimize the feasibility and integrity of our intervention and data collection processes. The inclusion criteria may introduce a selection bias that may not reflect the broader, more varied rural contexts across China. A potential confounding factor is the ongoing nationwide promotion of community management for hypertension and diabetes in China. China's overarching health policies, articulated in the 5-year development plan and Healthy China 2030, underscore the significance of preventing and managing hypertension. The National Essential Public Health Service Package (NEPHSP) further delineates specific services offered by primary healthcare facilities, encompassing screening, monitoring, routine follow-up, and personalized interventions for hypertension and diabetes [21]. The concurrent implementation of such initiatives may contribute to enhanced routine management practices across both intervention and control groups. This scenario could potentially diminish the distinguishable differences between the two groups, impacting the clarity of observed outcomes. To proactively address the potential impact of concurrent national health initiatives on routine management practices, we have meticulously tailored our intervention strategy within the intervention group. This deliberate differentiation aims to maintain the distinctiveness and integrity of our intervention, ensuring that its effects remain discernible despite external factors. We underscore a strict adherence to the designed intervention components, placing particular emphasis on closely monitoring dosage and fidelity of implementation. Furthermore, the mixed-methods evaluation employed in our study allows for a comprehensive understanding of both the quantitative outcomes and qualitative insights. This dual approach enhances the triangulation of data, providing a more nuanced perspective on the effectiveness and feasibility of our interventions. It also facilitates a deeper exploration of contextual nuances, offering valuable insights into the differential impact of our strategies across diverse settings.

In conclusion, the evidence generated from this study holds significant implications for policy development in China, aligning with the key objective of strengthening primary healthcare in ongoing healthcare reforms. Moreover, the insights gained from this study will have broad applicability to similar,

resource-limited settings in other regions of the world where providing effective care at lower cost remains a universal challenge.

Author Contributions

R.S. and X.Y. conceived of the study. R.S. obtained the study funding. X.Y. drafted the manuscript. Z.W., J.Y., S.H., X.W., J.Z., and N.S. participated in the study design. S.H. designed the statistical analyses. W.F., Q.L., N.L., J.L., J.K., and L.Z. were responsible for data collection, intervention design and implementation in counties. All authors contributed to the editing of the manuscript. All authors read and approved the final manuscript.

Disclosure

The funder played no role in the study design; collection, analysis, and interpretation of the data; the writing of the report; and the decision to submit the article for publication. The authors are solely responsible for the design and conduct of this study, study analyses, and the drafting of this paper.

Ethics Statement

The study protocol received ethics approval from the institutional review boards at the Chinese Academy of Medical Sciences and Peking Union Medical College (CAMS&PUMC-IEC-2023-026). Consent for participation in the project will be sought at the cluster level and the individual level. Cluster-level consent of the community will be obtained through a consultation process involving the government (at a county and township level) and the village leaders. Individual consent will be obtained from all persons selected for participation in the project in the usual way with the provision of a participant information sheet, explanation, and discussion as required, and the collection of written consent from those willing to take part.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data from this study will be available from the corresponding author upon reasonable request.

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