ISRCTN10398081 https://doi.org/10.1186/ISRCTN10398081

Effects of free essential medicines on health outcomes in patients with hypertension or diabetes

Submission date 14/07/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 14/07/2026	**Overall study status** Ongoing	
Last Edited 14/07/2026	**Condition category** Other	

Plain English summary of protocol
Not provided at time of registration

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Study information

Scientific Title
A pragmatic randomized controlled trial evaluating the effect of free essential medicines on survival outcomes among urban and rural residents with hypertension or diabetes

Study objectives
Primary Objectives:
The primary aim of this study is to evaluate the impact of providing national basic antihypertensive and antidiabetic drugs free of charge to patients with hypertension or diabetes on long-term survival outcomes and health equity. The specific objectives include:
Core survival benefit assessment: To evaluate the effect of the free medication intervention on reducing all-cause mortality at the medium-term (5-year) follow-up and to quantify the absolute life expectancy gain over the long-term (10-year) follow-up using Restricted Mean Survival Time (RMST).
Health equity evaluation: To confirm the effectiveness of the free basic medication policy in reducing disparities in long-term survival outcomes between urban and rural residents, thereby providing high-level evidence-based support for the national integrated urban-rural medical security system.

Secondary Objectives:
Secondary clinical endpoint assessment: To evaluate the intervention's effect on cardiovascular and other disease-specific mortality rates, prevention of renal composite endpoints at specific follow-up time points, and to systematically track the long-term dynamic trajectory of all-cause mortality risk over time.
Health economic evaluation: To conduct cost-effectiveness analysis (CEA) and cost-benefit analysis from both societal and healthcare system perspectives, quantifying the long-term economic value of the free provision of basic medications.
Multi-dimensional subgroup analysis: To explore the heterogeneity of treatment effects across populations with different baseline characteristics (such as age groups, sex, and comorbidity profiles) in order to precisely identify the optimal target populations that benefit most from this policy.
Urban-rural interaction and health disparity analysis: To thoroughly assess the differential distribution of intervention effects between urban and rural subgroups and to quantitatively evaluate the specific contribution of the free medication policy to bridging urban-rural health inequalities through rigorous testing of the "urban-rural characteristic × intervention" interaction.
Policy translation staged outputs: To generate a pre-specified "5-Year Interim Information Report." This report will focus on the early results of the 5-year all-cause mortality and urban-rural survival gap, aiming to provide timely real-world evidence for the dynamic optimization of national or local essential medication systems. As an independent policy-oriented deliverable, the release of this interim report will not trigger early termination of the trial and will not involve multiplicity penalties or alpha spending as defined in the statistical analysis plan.

Ethics approval required

Ethics approval required

Ethics approval(s)
Approved 10/03/2020, Medical Ethics Committee of GuCheng County Hospital, Hebei Province (No. 55, Kangning East Road, Gucheng County, Hengshui, 253800, China; +86 (0)186 3285 9887; 1447572629@qq.com), ref: KYSC-2020001

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Health services research, Supportive care

Study type(s)

Health condition(s) or problem(s) studied
Hypertension, diabetes

Interventions
Participants will be randomly assigned to either the intervention group (free medication group) or the control group (routine management group) in a 1:1 ratio. The randomization sequence will be generated by an independent biostatistician using computer software and will employ stratified block randomization by urban/rural area to ensure balance of key baseline characteristics between groups. Allocation concealment will be achieved through a centralized randomization system so that neither study personnel nor participants will know the group assignment before completing the baseline assessment.

Participants in the control group will receive routine chronic disease management. They will purchase or obtain reimbursement for national basic antihypertensive and antidiabetic medications according to the existing social health insurance policy and will continue to receive standardized chronic disease management under the National Basic Public Health Service Program. This includes regular follow-up visits, blood pressure and blood glucose monitoring, health education, and lifestyle guidance. The frequency and content of follow-up assessments will be the same as in the intervention group.

Participants in the intervention group will receive the long-term free basic medication supply policy intervention. Participants will be able to obtain national basic antihypertensive or antidiabetic medications free of charge at designated primary healthcare facilities (village clinics or community health service centers) upon presentation of a doctor’s prescription. The types

and dosages of medications will follow the recommendations in the National Guidelines for Primary Prevention and Management of Hypertension and the National Guidelines for Primary Prevention and Management of Diabetes, with individualized adjustments made by the responsible physician based on the patient's clinical condition.
This study focuses on the core policy intervention of free medication supply. Physicians will primarily provide supervision and prescription management. The free supply mechanism aims to eliminate economic barriers to medication use, thereby improving long-term adherence and survival outcomes.

Intervention Type
Other

Primary outcome(s)
1. All-cause mortality, defined as the time from randomization to death from any cause, measured using multiple complementary sources to ensure high completeness and accuracy, including: active follow-up records from regular visits by village doctors or general practitioners; data linkage with the national or regional Population Death Registry Information System; data linkage with the local medical insurance claims/settlement database. All suspected death events will be reviewed and adjudicated by an independent, blinded Clinical Endpoint Committee (CEC) according to pre-specified standardized criteria. The date of death will be determined based on the date recorded in the official death certificate or the registry system. Measured at continuously from the date of randomization until the end of the 10-year follow-up period. The primary outcome analysis will be performed at the 10-year time point using restricted mean survival time (RMST). A pre-specified interim analysis will be conducted once all participants have completed 5 years of follow-up, reporting 5-year all-cause mortality as an exploratory outcome to support policy decision-making.

Key secondary outcome(s)
1. Cardiovascular, hepatic, renal, and other disease-specific mortality rates, defined as death where the primary cause is attributed to cardiovascular, hepatic, renal, or other specified diseases, measured using linkage with the population death registry system and medical insurance databases, supplemented by active follow-up records. All events will be adjudicated by the independent blinded Clinical Endpoint Committee (CEC) using standardized criteria. Measured at 5 and 10 years after randomization

2. The incidence rate of the renal composite endpoint, defined as the first occurrence of any of the following: progression to end-stage renal disease (ESRD), a sustained decline in estimated glomerular filtration rate (eGFR) of ≥40% or ≥50% from baseline, or death due to renal disease, measured using laboratory measurements (eGFR), active follow-up records, and linkage with medical insurance and death registry databases. All potential events will be adjudicated by the independent blinded Clinical Endpoint Committee (CEC). Measured at 5 and 10 years after randomization

3. The incremental cost-effectiveness ratio: the ratio of the difference in total costs to the difference in effectiveness (measured in quality-adjusted life years, QALYs) between the intervention and control groups. Costs will be assessed from both societal and healthcare system perspectives, including medication costs, outpatient and inpatient care, and other related medical resource utilization. Effectiveness will be measured using quality-adjusted life years (QALYs) derived from utility values collected during follow-up. Measured at 5 and 10 years after randomization

4. Longitudinal medication adherence trajectory: the proportion of participants categorized as highly adherent (proportion of days covered [PDC] >=80%) measured using using Generalized Linear Mixed Models (GLMM) longitudinally at 5 and 10 years after randomization

5. Clinical target achievement rates for blood pressure or glycemic control measured using the proportion of participants achieving protocol-defined clinical targets (blood pressure <140/90 mmHg or HbA1c <7.0%), evaluated longitudinally and adjusted for baseline covariates using Generalized Estimating Equations (GEE) or GLMM, at 5 and 10 years after randomization

6. Differences in 5-year all-cause mortality between urban and rural subgroups measured using Hazard ratio (HR) evaluated via treatment-by-stratum interaction test in a Cox proportional hazards model at 5 years after randomization

7. Variation in 10-year survival benefits between urban and rural subgroups measured using difference in restricted mean survival time (RMST) evaluated via interaction test at 10 years after randomization

8. Treatment effect modification by baseline body mass index (BMI) categories measured using hazard ratio (HR) and restricted mean survival time (RMST) difference evaluated via treatment-by-BMI stratum interaction tests at 5 and 10 years after randomization

9. Heterogeneity of survival benefit stratified by baseline blood pressure and glycemic control measured using interaction tests for treatment effect (5-year HR and 10-year RMST difference) across baseline systolic blood pressure and HbA1c categories/tertiles at 5 and 10 years after randomization

10. Age-related variation in long-term treatment efficacy and survival measured using evaluation of treatment-by-age interaction (<65 vs ≥65 years) using Cox proportional hazards models and RMST difference at 5 and 10 years after randomization

11. Impact of baseline comorbidity burden and polypharmacy on treatment efficacy measured using interaction analysis of treatment effect stratified by baseline Charlson Comorbidity Index (CCI) or number of concurrent medications at 5 and 10 years after randomization

12. Mediating effect of longitudinal medication adherence trajectories on survival outcomes measured using time-dependent Cox regression and landmark analysis evaluating the association between longitudinal adherence rates and mortality risk at 5 and 10 years after randomization

13. Treatment effect modification by baseline kidney function (eGFR and albuminuria) measured using interaction analysis of treatment effect (hazard ratio and RMST difference) stratified by baseline chronic kidney disease stages at 5 and 10 years after randomization

14. Heterogeneity of survival benefit stratified by baseline cardiovascular risk profiles measured using evaluation of treatment-by-risk interaction comparing secondary prevention cohorts (prior CVD events) versus primary prevention cohorts using Cox models at 5 and 10 years after randomization

15. Impact of baseline socioeconomic status and health literacy on treatment efficacy measured using interaction tests assessing the variation in survival benefits (RMST difference) across different tiers of educational attainment or household income at 5 and 10 years after randomization

16. Sex-specific differences in long-term survival and cardiovascular outcomes measured using treatment-by-sex interaction test evaluating the hazard ratio (HR) and RMST differences between male and female subgroups at 5 and 10 years after randomization

17. Treatment efficacy stratified by baseline Frailty Index and multimorbidity burden measured using interaction analysis of survival outcomes across baseline frailty categories (robust, pre-frail, frail) using validated geriatric assessment tools at 5 and 10 years after randomization

Completion date
10/04/2030

Eligibility

Key inclusion criteria
1. Aged 18 years or older
2. Meeting the diagnostic criteria of the National Guidelines for Primary Prevention and Management of Hypertension or the National Guidelines for Primary Prevention and Management of Diabetes, and having established a chronic disease management record at the local village clinic or community health service center
3. At the start of the study, residents with local county household registration or holding a local residence permit and planning to reside in the area long-term (≥5 years), to ensure completion of long-term follow-up
4. No history of significant allergy to the free basic medications, such as anaphylactic shock, urticaria, or severe gastrointestinal intolerance
5. No malignant tumors, and willing to participate and able to provide written informed consent

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
92936

Key exclusion criteria
1. Pregnant or breastfeeding female patients
2. Severe physical illnesses such as cancer
3. Severe cognitive impairment or psychiatric disorders
4. Participation in other clinical trials

Date of first enrolment
10/03/2020

Date of final enrolment
10/05/2020

Locations

Countries of recruitment
China

Sponsor information

Organisation
The People's Government of Gucheng County, Hebei Province

Organisation
Hebei Medical University

ROR
https://ror.org/04eymdx19

Funder(s)

Funder type

Funder Name
The People's Government of Gucheng County, Hebei Province

Results and Publications

Individual participant data (IPD) sharing plan
Upon completion of the study, de-identified individual participant data will be made available to qualified researchers, within reasonable limits and upon reasonable request, in accordance with journal requirements and the International Committee of Medical Journal Editors (ICMJE) data sharing recommendations.

IPD sharing plan summary
Available on request