Community health worker–led hypertension management with independent prescribing in rural Lesotho: a cluster-randomised non-inferiority trial

Felix Gerber PhD[1,2,3]*, Giuliana Sanchez-Samaniego PhD[1,2], Ravi Gupta MD[4], Thabo Ishmael Lejone MSc[1,2], Thesar Tahirsylaj BSc[1,2], Fabian Raeber MSc[1,2], Iliana Esquivel-Valdés MSc[1,2], Elis Belen Saavedra MSc[1,2], Malebona Mathulise[4], Thuso Kabi[4], Mosoetsi Mokaeane[4], Malehloa Maphenchane[4], Manthabiseng Molulela[4], Makhebe Khomolishoele[4], Mota Mota[4], Manthati Mofokeng[4], Mamoronts'ane Pauline Sematle[4], Lebohang Sao MD[5], Mosa Tlahali MD[5], Malitaba Litaba MD[5], Dave Brian Basler MSc[1], Kevin Kindler MSc[1], Irene Ayakaka MD[4], Pauline Grimm PhD[6], Thilo Burkard Prof[7,8], Frédérique Chammartin PD[1,2], Alain Amstutz PhD[1,2,9,10¶], Niklaus Daniel Labhardt Prof[1,2¶*]

[1]Division of Clinical Epidemiology, Department of Clinical Research, University Hospital Basel, Basel, Switzerland
[2] University of Basel, Basel, Switzerland
[3] University Department of Medicine, Division of General Internal and Emergency Medicine, Kantonsspital Aarau, Aarau, Switzerland
[4] SolidarMed Lesotho, Maseru, Lesotho
[5] Ministry of Health Lesotho, Maseru, Lesotho
[6] SolidarMed Switzerland, Lucerne, Switzerland
[7] Medical Outpatient Department and Hypertension Centre, ESH Hypertension Centre of Excellence, University Hospital Basel, Basel, Switzerland
[8] Department of Cardiology, University Hospital Basel, Basel, Switzerland
[9] Oslo Center for Biostatistics and Epidemiology, Oslo University Hospital, University of Oslo, Oslo, Norway
[10] Electronic Health Records Group, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom

* Corresponding authors:

Felix Gerber, Division of Clinical Epidemiology, University Hospital Basel, Totengässlein 3, 4051 Basel, Switzerland; +41767208249; felix.gerber@usb.ch

Niklaus D. Labhardt, Division of Clinical Epidemiology, University Hospital Basel, Totengässlein 3, 4051 Basel, Switzerland; +41612653821; niklaus.labhardt@usb.ch

¶ These authors contributed equally to this work and share last-authorship

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Summary

Background

Hypertension is the leading global cause of premature mortality, yet treatment coverage and control remain poor. Whether community health workers (CHWs) can safely manage hypertension, including independent prescribing and titrating of antihypertensive therapy, remains unknown.

Methods

We conducted a pragmatic, cluster-randomised, open-label, non-inferiority trial in 103 villages in rural Lesotho. Adults with treated, controlled hypertension (<140/90 mmHg) were eligible. Villages were randomised 1:1 to CHW-led hypertension care, including independent prescribing and titrating of antihypertensive therapy (amlodipine-hydrochlorothiazide combination pill at 5/12·5mg or 10/25mg) with clinical decision support, or to usual nurse-led, facility-based care. The primary endpoint was blood pressure control at 12 months among all randomised participants except those who became pregnant during follow-up, with a non-inferiority margin of –10% absolute risk difference. The study is completed and registered with ClinicalTrials.gov (NCT05684055).

Findings

Between September 08, 2023, and January 31, 2024, we enrolled 807 participants (417 in 51 control villages, 390 in 50 intervention villages; 2 empty clusters; mean age 64.4 years; 82·3% women). At 12 months, blood pressure was controlled in 300 of 386 (77·7%) participants in the intervention group and 303 of 412 (73·5%) participants in the control group; 9 participants were excluded due to pregnancy. The absolute risk difference was 5·1% (95% CI, –0·9 to 11·2), meeting the criterion for non-inferiority. Mean 12-month systolic and diastolic blood pressures were 122·5 and 78·7 mmHg in the intervention group and 123·6 and 79·4 mmHg in the control group. Serious adverse events were similar in the two groups, with no excess events attributed to the intervention.

Interpretation

These findings support decentralised, community-based hypertension care with task-sharing to trained CHWs as a scalable strategy to expand access to long-term chronic disease management in resource-limited settings.

Funding

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Research in Context

Evidence before this study

We searched PubMed from database inception to April 13, 2026, without language restrictions, using terms related to hypertension, community-based care, community health workers (CHWs), task-sharing, and randomised trials, and screened reference lists of relevant articles.

Previous randomised trials in low- and middle-income countries have shown that community-based and CHW-supported interventions can improve blood pressure control, particularly among individuals with uncontrolled hypertension. In most approaches, CHWs functioned as an adjunct to existing services, with prescribing authority retained by healthcare professionals.

Evidence on independent antihypertensive prescribing by community-based non-physician providers is limited and largely restricted to rural China, where providers have substantially more formal training than lay CHWs in other settings.

Recent evidence from sub-Saharan Africa suggests that community-based care can improve or maintain blood pressure control, including among clinically stable patients with chronic conditions compared to

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facility-based care. However, these approaches did not evaluate independent prescribing, titration, or de-escalation of antihypertensive therapy by lay CHWs.

We found no randomised trials assessing whether independent CHW-led prescribing, titration, and de-escalation within community-based care can safely maintain blood pressure control among individuals already receiving antihypertensive therapy. A parallel trial in the same setting showed improved blood pressure control among individuals with uncontrolled hypertension.

Added value of this study

This pragmatic, cluster-randomised, non-inferiority trial shows that lay CHWs, supported by a mobile clinical decision support application, can independently prescribe, titrate, and de-escalate antihypertensive therapy among adults with treated, controlled hypertension. CHW-led care was non-inferior to nurse-led, facility-based care in maintaining blood pressure control at 12 months, with no meaningful between-group differences in blood pressure levels and no excess in serious adverse events attributable to the intervention. This study extends previous evidence by focusing on maintenance of control rather than initiation or intensification of therapy and by evaluating independent antihypertensive management by lay CHWs embedded within a routine government programme in a rural low-income setting.

Implications of all the available evidence

Taken together, the available evidence supports community-based, CHW-supported hypertension care as part of long-term chronic disease management in resource-limited settings. Our trial adds that, with standardised treatment algorithms and digital clinical decision support, lay CHWs can independently prescribe, titrate, and de-escalate first-line antihypertensive therapy while maintaining blood pressure control among individuals already receiving treatment. This expanded role could improve access to care, reduce reliance on facility-based services, and support more equitable chronic disease management. Further research should evaluate long-term outcomes, integration with care for other chronic conditions, and cost-effectiveness to inform scale-up.

Introduction

Hypertension is the leading global cause of premature death, contributing to over 10 million deaths each year.[1] Ensuring equitable access to hypertension care is a major global health priority.[2] Despite the availability of effective, low-cost medications, treatment coverage and blood pressure control remain poor in low- and middle-income countries.[3] A major barrier is the limited number of physicians and nurses to diagnose hypertension and provide sustained treatment follow-up.[4]

Task-sharing with community health workers (CHWs) has contributed substantially to the scale-up of HIV and tuberculosis care and has improved access, adherence, and retention in chronic care programmes.[5] In trials conducted across low- and middle-income countries, CHW-led interventions have improved blood pressure control through home-based screening, monitoring, adherence support, medication delivery, or linkage to facility care.[6,7] However, in most of these models, CHWs function as an adjunct to existing services, with prescribing authority retained by nurses or physicians.[8] Although such models may improve health outcomes, they do not reduce reliance on professional health workers. A review of community-based hypertension programmes in sub-Saharan Africa did not identify interventions granting prescribing authority to CHWs.[9] Evidence for independent prescribing by community-based providers is otherwise limited to China, where the CHW-equivalent cadre receives several years of formal training,[10] in contrast to most low- and middle-income countries, where CHWs are lay workers with only brief training.

Standardised treatment protocols improve blood pressure control compared with usual care and a recent meta-analysis reported that interventions led by non-physicians, including CHWs, result in higher blood pressure reductions than those delivered by nurses or physicians alone.[8,11] Mobile clinical decision support applications that provide algorithmic guidance for diagnosis and treatment may enable CHWs to deliver

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standardised hypertension care while reducing the workload of professional health workers. However, evidence from randomised trials on the safety and effectiveness of independent CHW-led hypertension care with digital clinical decision support is lacking.

Previous trials have focused predominantly on adults with uncontrolled blood pressure and evaluated strategies for treatment initiation or intensification, leaving limited evidence on whether community-based models can safely maintain blood pressure control among individuals already receiving treatment.[6,7,12] As treatment coverage expands, health systems must sustain care for growing numbers of individuals with controlled hypertension, placing additional demands on already constrained primary care services.[4] Although recent evidence from sub-Saharan Africa shows that community-based delivery of chronic care can achieve outcomes comparable to facility-based care among clinically stable patients with hypertension and other chronic conditions, this approach did not include independent prescribing or titration of antihypertensive therapy by lay CHWs.[13]

To address this gap, we conducted a pragmatic, cluster-randomised, non-inferiority trial within the Community-Based chronic Care Lesotho (ComBaCaL) cohort to evaluate CHW-led hypertension care with independent prescribing supported by a mobile clinical decision support application. Among adults with treated hypertension and controlled blood pressure at baseline, we assessed whether this model could maintain blood pressure control comparable to that achieved with usual nurse-led, facility-based care.

Methods

Study design

We conducted a pragmatic, cluster-randomised, open-label, non-inferiority trial nested within the ComBaCaL cohort study following the Trials within Cohorts (TwiCs) design.[14] The ComBaCaL cohort study includes all consenting residents of 103 randomly selected villages in the rural districts of Butha-Buthe and Mokhotlong, in Lesotho.[15] In each village, a CHW was elected by the community according to the national policies. CHWs play an important role in the Lesotho healthcare system providing health promotion services and linking the community to facility-based care. The trial was designed and implemented in partnership with the Lesotho Ministry of Health and community representatives. A pilot study conducted in the same setting informed the final design of the intervention.[16,17] The trial was approved by the National Health Research and Ethics Committee of Lesotho (ID: ID 102-2022 Nested) and by the Ethikkomission Nordwest- und Zentralschweiz (ID AO_2022_00074). The study protocol has been previously published.[18] The trial was registered with ClinicalTrials.gov (NCT05684055, registration date January 04, 2023), where a full protocol and statistical analysis plan are available.

Participants

Participants were recruited from the ComBaCaL cohort. Cohort participants aged 18 years or older were screened for hypertension by their CHW during home visits according to the diagnostic algorithm of the Lesotho Standard Treatment Guidelines. Nonpregnant adults who reported current use of antihypertensive medication and had controlled blood pressure (<140/90 mmHg) were eligible. Cohort participants with uncontrolled blood pressure (≥140/90 mmHg) were enrolled in a concurrent, separate superiority trial evaluating the same intervention.[12] Following the TwiCs design, written informed consent for participation in the ComBaCaL cohort included consent for randomisation into future nested trials that evaluate low-risk interventions.[19] Thus, eligible cohort participants were automatically enrolled in the trial after screening. Participants in intervention villages were offered the intervention by their CHW and could accept or decline any of the offered services (oral intervention consent). Consent procedures accommodated participants with limited literacy, and consent could be withdrawn at any time. Details on the design and consent procedures of the ComBaCaL cohort and nested trials have been published previously.[15,18,19]

At enrolment, CHWs collected sociodemographic and clinical information and measured blood pressure using automated devices (Omron M3 Comfort [HEM7131-E]).[20] Measurements were taken after selecting

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the appropriate cuff size, with participants seated after at least five minutes of rest. At the initial visit, blood pressure was measured in both arms with subsequent measurements taken from the arm with the higher systolic pressure. The blood pressure value was calculated as the mean of the last two out of three consecutive measurements obtained at one-minute intervals.

Randomisation and masking

Villages were randomly assigned in a 1:1 ratio to the intervention or control group by an independent statistician before initiation of hypertension screening. Randomisation was stratified by district (Butha-Buthe versus Mokhotlong) and access to health facilities (easy versus difficult access, defined as needing to cross a mountain or river or travel >10 km to the nearest health facility). Because of the cluster-randomised, open-label design, CHWs were aware of group assignment. Participants in control villages were not informed that the intervention was being implemented in other villages.

Procedures

Each village had one CHW equipped with a password-protected tablet containing a tailored clinical decision support application that provided algorithmic guidance for study procedures and served as data collection tool. The application was configured using the open-source Community Health Toolkit Core Framework (versions 3·12, 3·14, 4·6 and 4·13)[21] and provided automated task scheduling and structured questionnaires with decision logic based on individual participant characteristics. Data were synchronized to a secure server and monitored locally and centrally.

All CHWs received a one-week training in data collection and hypertension screening and diagnosis. CHWs in intervention villages received an additional two days of training on the intervention services. In both control and intervention villages, CHWs received the regular government stipend of ZAR 800 (circa USD 40) per month and an additional ZAR 400 (circa USD 20) per month to compensate for study-related work. In control villages, CHWs provided lifestyle counselling and referred participants to the closest health facility for continuation of nurse-led hypertension care, with a check-up and repeated referral at 6 months. In intervention villages, CHWs provided community-based hypertension care, including lifestyle counseling and independent prescription and titration of a fixed-dose combination of amlodipine–hydrochlorothiazide (5 mg/12·5 mg or 10 mg/25 mg), guided by a prespecified treatment algorithm embedded in the clinical decision support application. Treatment was intensified from low to high dose when systolic blood pressure was ≥140 mmHg or diastolic blood pressure ≥90 mmHg and de-escalated (dose reduction or discontinuation at low dose) when systolic blood pressure was <120 mmHg and diastolic blood pressure <90 mmHg. Participants with inadequate blood pressure control despite high-dose therapy, contraindications or intolerance to amlodipine or hydrochlorothiazide, clinical alarm signs or symptoms, or those declining CHW-led care were referred to a health facility, with continued bi-monthly follow-up by the CHW. Visit intervals were one month after dose adjustment and two months when treatment was unchanged. Lipid-lowering therapy (atorvastatin, 10mg) and antiplatelet therapy (acetylsalicylic acid, 100mg) were provided to eligible participants at elevated cardiovascular risk. All care was aligned with the Lesotho Standard Treatment Guidelines.[22] The detailed treatment algorithm is provided in the Supplementary Appendix (Figure S1). CHWs were supervised through both trial-specific and routine health-system mechanisms. Study nurses supervised CHWs at a ratio of approximately 1:25. Information uploaded from the clinical decision support application was reviewed centrally every week, and nurses followed up with CHWs when inconsistencies, clinical concerns, or possible treatment-related problems were identified. CHWs could also contact their supervising study nurse by telephone. In parallel, CHWs remained integrated in the national supervision system and attended routine monthly meetings at their referral health facility, where they could discuss problems, review possible referrals, and obtain medication refills for participants receiving community-based care.

All data were collected by CHWs during home visits. During follow-up visits, CHWs inquired about the occurrence of possible adverse events. In addition, CHWs solicited adverse events through reporting by

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participants, friends or relatives, screening of participants' personal health booklet, and reporting by routine health facility staff any time during the follow-up period.
Adverse events reported by the CHWs were followed up by supervising study nurses to collect further clinical information. The pseudonymized reports were submitted to the study physician for final classification.

Outcomes

The primary outcome was blood pressure control (<140/90 mmHg) at 12 months. Secondary outcomes were blood pressure control at 6 months, mean systolic and diastolic blood pressure, engagement in care (reporting current use of antihypertensive medication or reaching treatment targets without medication), self-reported adherence to antihypertensive therapy, 10-year cardiovascular risk using the WHO cardiovascular disease risk prediction tool,[23] Body-mass index, abdominal circumference, blood lipid status, physical activity using the International Physical Activity Questionnaire Short Form (IPAQ-SF),[24] alcohol consumption, tobacco use, and dietary habits using a short food frequency questionnaire adapted from an assessment tool for obesity used in South Africa,[25] fruit, vegetable and salt consumption using the WHO STEPS instrument[26] assessed at 6 and 12 months. Adherence was defined as no missed doses of antihypertensive medication during the previous four days. Exploratory outcomes included the use of statins among people with elevated cardiovascular risk, blood pressure control without medication use, and eligibility for and acceptance of CHW-led care in intervention villages.
For 6-month endpoints a window of 150 to 240 days, and for 12 months' endpoints, a window of 300 to 420 days after enrolment applied.
Safety outcomes were the occurrence of serious adverse events and adverse events of special interest within 6 and 12 months after enrolment. Adverse events of special interest included hypertension-related complications (myocardial infarction, stroke, heart failure or chronic kidney disease) and antihypertensive medication-related adverse events leading to treatment discontinuation.

Statistical analysis

Assuming a mean cluster size of 10 participants, a blood pressure control rate of 80% in the control group, an intra-cluster correlation coefficient of 0·015,[27] a one-sided type I error rate of 0·025, and 80% power, a total sample size of 780 participants (390 per group, 39 clusters per study group) was required to demonstrate non-inferiority using a prespecified margin of -10 percentage points for the absolute risk difference in blood pressure control. For operational reasons all 103 ComBaCaL cohort villages were included, resulting in an anticipated sample size exceeding the minimum requirement.
Analyses followed standard methods for cluster-randomised trials.[28] The primary analysis followed a modified intention-to-treat (mITT) principle and excluded participants who became pregnant during follow-up. Participants without a follow-up blood pressure measurement (e.g., owing to loss to follow-up or missed visits) were classified as having uncontrolled blood pressure. The prespecified primary analysis used a mixed-effects logistic regression model with adjustment for stratification factors (district and access to a health facility), age, and sex. Because the variance component of the cluster random effect was negligible and resulted in singular model fits, the final model was estimated without the random intercept for cluster. Absolute risk differences and 95% confidence intervals were derived from marginal predicted probabilities using bootstrap resampling. Non-inferiority was declared if the lower bound of the two-sided 95% confidence interval exceeded −10 percentage points. Missing primary outcomes were classified as uncontrolled blood pressure.
A prespecified complete-case sensitivity analysis included only participants with available endpoint measurements. A strict per-protocol analysis was not performed. However, a prespecified restricted-population analysis approximating a per-protocol population included participants with at least one hypertension care visit with a CHW in intervention clusters and at least one hypertension care visit at a health facility in control clusters. Two additional prespecified exploratory restricted-population analyses were conducted: one excluding participants who were not eligible for pharmacological treatment by CHWs

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at baseline (those requiring three or more antihypertensive drugs, presenting with hypertensive emergency or alarm symptoms, or with contraindications or intolerance to amlodipine or hydrochlorothiazide), and one excluding participants with low baseline BP (SBP <120 mmHg and DBP <70 mmHg) suggestive of possible overtreatment or misdiagnosis.

Effect modification of the intervention on the primary endpoint was assessed for the prespecified variables age, sex, engagement in antihypertensive care at baseline, engagement in HIV care at baseline, and access to a health facility, by including interaction terms in the primary analysis model. Subgroup-specific estimates and subgroup credibility assessments were examined only when the interaction p value was less than 0·10. All subgroup and population-restricted analyses were considered exploratory.

Secondary outcomes were analysed using mixed-effects logistic or linear regression models adjusted for baseline outcomes in addition to stratification factors, without formal testing. Confidence intervals were not adjusted for multiplicity. When a variance component of the mixed effects was estimated as negligible and led to singularity diagnostics, the corresponding random effect was omitted.

Serious adverse events and adverse events of special interest were summarised descriptively.

Data management was performed using R version 4·3·3 and data analysis using Stata IC version 16·0. This study was conducted and reported according to the Consolidated Standards of Reporting Trials (CONSORT) extension for cluster-randomised trials.[29] The checklist is available in the Supplementary Appendix (Table S6).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between September 08, 2023, and January 31, 2024, lay CHWs screened 8,034 out of 9,052 eligible adult cohort participants during home visits across 103 villages. Of 1,490 participants with hypertension, 807 (417 control, 390 intervention) from 101 villages (50 intervention, 51 control) had controlled blood pressure levels (<140/90 mmHg), were not pregnant and enrolled in the trial; two randomised clusters contained no eligible participants and therefore contributed no participants to the analysis (Fig. 1).

Figure 1 Participant flow chart. BP: blood pressure; mITT: modified intention-to-treat

Trial participants had a mean age of 64·4 years and a mean blood pressure of 116·4 mmHg (standard deviation [SD] 11·7) over 76·2 mmHg (SD 7·7); 82·3% were female; all reported use of antihypertensive medication at enrolment; 24·4% were smokers, 15·2% had diabetes; 15·1% reported living with HIV; 1·4% had heart failure and 6·3% had a history of stroke or myocardial infarction. No substantial imbalance across the groups was observed (Table 1 and Supplementary Appendix Table S1).

Table 1 Baseline characteristics of participants by study group.

For the primary outcome of blood pressure control (<140/90 mmHg) at 12 months, the modified intention-to-treat analysis included 798 participants (nine exclusions due to pregnancy during follow-up). Blood pressure control was achieved in 300 of 386 participants (77·7%) in the intervention group and 303 of 412 participants (73·5%) in the control group (adjusted odds ratio [aOR], 1·29; 95% confidence interval [CI], 0·93 to 1·80). The absolute difference in blood pressure control was 5·1 percentage points (95% CI, −0·9 to 11·2). Because the lower boundary of the 95% confidence interval exceeded the prespecified non-inferiority margin of −10 percentage points, the criterion for non-inferiority was met.

In the predefined complete-case sensitivity analysis, blood pressure control rates were higher in the intervention group (aOR, 2·19; 95% CI, 1·31 to 3·65). In the prespecified restricted-population analysis approximating a per-protocol population, blood pressure control rates at 12 months were 299 of 368

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(81·3%) in the intervention group and 300 of 376 (79·8%) in the control group (aOR, 0·92; 95% CI, 0·62 to 1·36). Results of the prespecified restricted-population analysis were consistent with those of the primary analysis (Table 2).

Table 2 Intervention effects on primary and selected secondary and prespecified exploratory endpoints. Effects on all other secondary endpoints are available in the Supplementary Appendix Table S2.

Interaction p-values for the prespecified potential effect modifiers were all greater than 0·1, indicating no evidence of effect modification (Supplementary Appendix, Table S5 and Figure S2).

At 6 months, blood pressure control in the modified intention-to-treat analysis was observed in 281 of 387 (72·6%) in the intervention group and 315 of 413 (76·3%) in the control group (aOR, 0·87; 95% CI, 0·59 to 1·29). At 12 months, mean systolic blood pressure was 122·5 mm Hg (SD, 12·6) in the intervention group and 123·6 mm Hg (SD, 15·0) in the control group, and mean diastolic blood pressure was 78·7 mm Hg (SD, 8·2) and 79·4 mm Hg (SD, 9·6), respectively; the adjusted mean differences were −0·6 mm Hg (95% CI, −2·8 to 1·6) for systolic pressure and −0·7 mm Hg (95% CI, −2·3 to 0·9) for diastolic pressure.

At 6 months, 328 of 387 (84·8%) participants in the intervention group and 378 of 413 (91·5%) in the control group were engaged in care (aOR, 0·56; 95% CI, 0·31 to 1·00) (Table 2). At 12 months, engagement in care was reported for 328 of 386 participants (85·0%) in the intervention group and for 367 of 412 participants (89·1%) in the control group (aOR, 0·72; 95% CI, 0·47 to 1·09).

Among participants eligible for statin therapy, statin use at 12 months was higher in the intervention group than in the control group (aOR, 3·26; 95% CI, 2·19 to 4·85). At 12 months, blood pressure control without antihypertensive medication was achieved in 68 of 386 participants (17·6%) in the intervention group and in 5 of 412 participants (1·2%) in the control group. There were no meaningful between-group differences in behavioural risk factors, including physical activity, smoking, alcohol use, or dietary measures (Table 2 and Supplementary Appendix, Table S2). Additional outcome data at 6 and 12 months are provided in the Supplementary Appendix (Tables S3 and S4).

Among participants engaged in care in the intervention group, 208 of 328 (63·4%) were managed by their CHW at 6 months and 213 of 328 (64·9%) at 12 months, with the remainder receiving facility-based care.

By 12 months, 8 participants in the control group and 9 in the intervention group had died; 6 participants in the control group and 7 participants in the intervention group were hospitalized; one participant in the intervention group experienced a life-threatening event during the hospitalization. None of the events were considered to be related to the intervention. No adverse events of special interest were reported in the control group. In the intervention group, 15 participants experienced adverse events associated with antihypertensive medication use, most commonly ankle swelling (12 participants) and dizziness (3 participants), all of which resolved after modification of therapy.

Table 3 Safety endpoints by study group

Discussion

In this cluster-randomised non-inferiority trial in rural Lesotho, CHW-led hypertension care supported by a digital clinical decision support application was non-inferior to nurse-led, facility-based care in maintaining blood pressure control at 12 months among participants with treated, controlled hypertension at baseline. The intervention was delivered within the routine government CHW system and was not associated with safety concerns. These findings indicate that lay CHWs, when supported by standardised algorithms and digital decision support, can safely deliver and adjust ongoing hypertension management for individuals with stable disease.

These findings complement those of a parallel cluster-randomised trial conducted in the same setting, in which the same CHWs used an identical clinical decision support–guided approach to manage adults with uncontrolled hypertension at baseline. In that trial, participants in intervention villages were significantly

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more likely to achieve blood pressure control than those receiving usual facility-based care.[12] Taken together, the two trials suggest that CHW-led care with algorithm-guided prescribing can support both the achievement of blood pressure control among individuals with uncontrolled hypertension and the maintenance of control among those already receiving treatment.

Large-scale trials have shown that community-based hypertension interventions combining CHW-led screening, counselling, monitoring and medication delivery with physician or nurse prescribing can improve blood pressure control and be cost-effective among people with uncontrolled hypertension.[6] A recent randomised trial in rural South Africa demonstrated that a home-based hypertension care model involving CHWs, supported by digital decision support and remote nurse-led prescribing, led to significant reductions in systolic blood pressure compared with standard clinic-based care.[7] However, because prescribing authority remained with physicians or nurses, such models may have limited impact on reducing professional workload, limit scalability, and constrain timely treatment initiation and adjustment in rural settings.

To our knowledge, only one previous randomised trial has evaluated a model that included independent antihypertensive prescribing and titration by community-based nonphysician providers. This trial, conducted in rural China, demonstrated significant reductions in blood pressure and mortality among participants with uncontrolled hypertension.[10] However, the generalizability of those findings to other low- and middle-income countries may be limited by the substantially higher level of training of the involved providers ("village doctors"), the provision of blood pressure monitors to participants, and reliance on health system incentives and medication subsidies that may be difficult to implement and sustain elsewhere.

Our trial evaluated a pragmatic model in which lay CHWs after brief training independently initiated, titrated, and discontinued antihypertensive therapy using a standardised, guideline-based algorithm embedded in a mobile clinical decision support application. The trial addresses several of the top research priorities for improving hypertension care identified by the World Health Organization and responds to calls for contextualised clinical and health system hypertension research in Africa.[2] The intervention was co-developed with the Lesotho Ministry of Health and community leaders and was integrated into routine supervision and medication supply systems. The clinical decision support application was based on an open-source, offline-first, interoperable software platform widely used in low- and middle-income countries.[21] Because screening, diagnosis and treatment algorithms followed national guidelines with no formal facility-level intervention, the model may be readily adoptable and scalable in settings with established CHW programmes. At 12 months, CHWs in the intervention group independently managed nearly two-thirds of participants engaged in care, indicating a substantial reduction in reliance on facility-based services.

A distinguishing feature of this trial is its focus on the maintenance of blood pressure control among individuals already receiving antihypertensive therapy at baseline. Most community-based hypertension trials have enrolled participants with uncontrolled blood pressure and evaluated strategies for treatment initiation or intensification. In routine care, however, hypertension programmes must also provide ongoing care for large numbers of individuals with controlled blood pressure. Maintaining control over time requires regular monitoring, appropriate dose adjustment, and timely de-escalation of therapy.

Recent evidence from sub-Saharan Africa shows that community-based care for clinically stable patients with controlled hypertension can achieve outcomes comparable to facility-based care.[13] However, the approach assessed in this trial did not include independent prescribing, titration, or de-escalation of antihypertensive therapy by CHWs.

In our trial, these treatment-management functions were delivered through a standardised, algorithm-based approach that explicitly guided intensification and de-escalation of antihypertensive therapy by CHWs operating independently. Notably, 17% of participants in the intervention group achieved blood pressure control without antihypertensive medication at 12 months. This finding suggests that some individuals may have been overtreated at baseline, either because of misdiagnosis or excessive treatment

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among those correctly diagnosed, and highlights the potential of algorithm-guided care to improve not only access to treatment but also the appropriateness of hypertension management.[30] In many hypertension programmes, treatment algorithms emphasise escalation but provide limited guidance on dose reduction or withdrawal; our results suggest that structured deprescribing may be an important component of long-term hypertension care.

The intervention also incorporated a cardiovascular risk assessment and CHW-led statin prescription, resulting in higher statin use among eligible participants, thereby demonstrating the feasibility of algorithm-guided cardiovascular risk management at the community level. As in previous studies, we did not observe relevant effects on behavioural cardiovascular risk factors and associated outcomes highlighting the need for improved strategies to enhance the effectiveness of lifestyle counselling within community-based hypertension programmes.

This study has several limitations. First, it focused on participants with treated and controlled hypertension at baseline and, therefore, addresses the maintenance of blood pressure control rather than treatment initiation or intensification; these complementary questions were examined in a parallel trial conducted in the same setting among participants with uncontrolled hypertension.[12] Second, blood pressure and other outcomes were assessed by the same CHWs who delivered the intervention, which may have introduced measurement or reporting bias; however, standardised measurement protocols and automated averaging of repeated readings were used, limiting the potential impact on the primary outcome. Third, the pragmatic treatment algorithm was limited to a fixed-dose combination of amlodipine and hydrochlorothiazide and a uniform treatment target, which may have resulted in suboptimal management for some participants with comorbidities. Future work may explore whether more complex algorithms can be safely implemented by lay CHWs with digital support. Finally, although the intervention was embedded within the government CHW system, scale-up will require careful consideration of workload, supervision, and sustainable compensation, supported by formal cost-effectiveness evaluations.

In conclusion, this cluster-randomised non-inferiority trial shows that lay CHWs supported by a mobile clinical decision support application can independently manage uncomplicated hypertension while maintaining blood pressure control comparable to nurse-led facility-based care. These findings, considered alongside related evidence from the same setting among adults with uncontrolled hypertension, suggest that algorithm-guided task-shifting to CHWs may represent a scalable strategy to expand access to high-quality, long-term hypertension care.

Contributions

AA and NDL were the principal investigators, they acquired the funding, led the project, and conceptualized the study together with FG. FG drafted the study protocol and the final manuscript, led the clinical development of the CDSS application together with TT and FR, and the local implementation together with RG, IA, and PG. TIL, TK, MalebM, MalehM, MosM, MotM, ManMof, ManMol, MK, and MPS were responsible for the local implementation through training and supervision of CHWs and local data monitoring. GSS was responsible for central data management, supported by EBS and IE. LS, MT and ML were involved in the conceptualization of the study and ensured alignment with local guidelines and practices. DB and KK led the technical development of the CDSS application. TB reviewed and approved the clinical algorithms. FC wrote the statistical analysis plan, conducted sample size calculations and all analyses. FC, GSS, IE, and FG accessed and verified the underlying data. All authors had full access to the data, read and approved the final manuscript, and accept responsibility for the decision to submit for publication.

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Declarations of interests

NDL reports having received additional research grants outside the scope of this work by the Swiss National Science Foundation as well as support to attend two conferences by Gilead Sciences. TB reports having received research grants outside the scope of this work by the Swiss National Science Foundation, the Cardiovascular Research Foundation, and through research contracts with Astra Zeneca, Daiichi Sankyo, Novartis, Menarini, Sanofi, Novo Nordisk and Collabree AG. TB has further received consulting fees from Astra Zeneca for his role in an advisory board and payment or honoraria for lectures, presentations or educational events by Servier, Medtronic, Novartis, Novo Nordisk, Sanofi, Daiichi Sankyo and Astra Zeneca (all outside submitted work and paid to institution). TB has further received support for attending meetings by Servier and Novo Nordisk (outside submitted work and paid to institution). TB serves as member of the executive board of the Swiss Society of Hypertension.

Data sharing

Deidentified individual participant data that underlie the results reported in this article and the statistical analysis code, will be made publicly available at the time of publication and remain available for at least 25 years at Zenodo (DOI: 10.5281/zenodo.19350982). The trial was registered at ClinicalTrials.gov (NCT05684055), where the full study protocol and statistical analysis plan are available; a detailed protocol manuscript has also been published previously.

Code Availability Statement

The source code for the clinical decision support system used by CHWs for data collection and service delivery is publicly available at https://github.com/clinepi-usb/cht-combacal. Access to a test environment of the clinical decision support application may be requested from the corresponding author; requests will be evaluated on the basis of feasibility and relevance, and access credentials will be provided upon approval.

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work FG used ChatGPT to assist with language editing and refinement of wording. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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9052 screening-eligible adult ComBaCaL cohort participants in 103 villages

Cluster-randomization stratified by district and access to health facility

51 villages assigned to control with 4601 screening-eligible adults

15 refused screening
404 screening pending or incomplete

59 refused screening
540 screening pending or incomplete

52 villages assigned to intervention with 4451 screening-eligible adults

4182 adults screened in 51 control villages

3436 no hypertension
323 hypertension with uncontrolled BP
6 hypertension and pregnant

3108 no hypertension
352 hypertension with uncontrolled BP
2 hypertension and pregnant

3852 adults screened in 52 intervention villages

417 with hypertension and controlled BP enrolled in 51 control villages

4 pregnant

3 pregnant

390 with hypertension and controlled BP enrolled in 50 intervention villages

413 in 51 control villages included in six months mITT analysis
- 379 with BP measurement
- 18 moved away
- 2 died
- 10 missing
- 4 withdrew consent

1 pregnant

1 pregnant

387 in 50 intervention villages included in six months mITT analysis
- 345 with BP measurement
- 19 moved away
- 8 died
- 8 withdrew consent
- 7 missing

412 in 51 control villages included in twelve months mITT analysis
- 370 with BP measurement
- 27 moved away
- 8 died
- 7 withdrew consent

386 in 50 intervention villages included in twelve months mITT analysis
- 332 with BP measurement
- 32 moved away
- 9 died
- 13 withdrew consent

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Tables

Table 1 Baseline characteristics of participants by study group.

Cluster-level characteristics	Control	Intervention	Total
Villages — no.	51	50	101
Adult cohort participants eligible for screening per village — median (IQR)	85.0 (67.8, 101.3)	78.0 (67.5, 99.0)	81.0 (67.5, 101.0)
Trial participants per village — n, median (IQR)	8.0 (4.0, 10.5)	7.5 (4.0, 10.75)	8.0 (4.0, 11.0)
Range — n	1-22	1-23	1-23
Village with hard access to health facility[1] — no. (%)	26 (51.0)	26 (52.0)	52 (51.5)
District Butha Buthe (versus Mokhotlong) — no. (%)	27 (52.9)	24 (48.0)	51 (50.5)
Individual-level characteristics			
Participants — n	417	390	807
Demographics and anthropometrics			
Female — no. (%)	341 (81.8)	323 (82.8)	664 (82.3)
Age — years, mean (SD)	64.8 (14.1)	64.0 (14.5)	64.4 (14.3)
Body mass index — kg/m^2, mean (SD)	27.6 (6.2)	27.9 (6.3)	27.7 (6.3)
Abdominal circumference — cm, mean (SD)	92.0 (13.2)	91.8 (13.8)	91.9 (13.5)
Education at secondary school or higher — no. (%)	88 (21.2)	86 (22.1)	174 (21.6)
Working for pay or self-employed — no. (%)	168 (40.4)	152 (39.0)	320 (39.7)
Married or in a stable relationship — no. (%)	205 (49.3)	208 (53.3)	413 (51.2)
Blood pressure			
Systolic blood pressure — mmHg, mean (SD)	117.4 (11.6)	115.4 (11.7)	116.4 (11.7)
Diastolic blood pressure — mmHg, mean (SD)	76.6 (7.5)	75.7 (7.9)	76.2 (7.7)
Engaged in hypertension care[2] — no. (%)	417 (100)	390 (100)	807 (100)
CVD risk, lifestyle and comorbidities			
Cardiovascular disease risk ≥10%[3] — no. (%)	165 (41.4)	152 (42.6)	317 (41.9)
Current smoking — no. (%)	101 (24.2)	96 (24.6)	197 (24.4)
Alcohol consumption ≥1 day/week — no. (%)	49 (11.8)	42 (10.8)	91 (11.3)
Moderate or high physical activity[4] — no. (%)	328 (79.2)	325 (84.0)	653 (81.5)
In facility care for another chronic condition[5] — no. (%)	101 (26.4)	115 (29.5)	225 (27.9)
Heart failure — no. (%)	7 (1.7)	4 (1.0)	11 (1.4)
History of stroke or myocardial infarction — no. (%)	25 (6.0)	26 (6.7)	51 (6.3)
Diabetes — no. (%)	57 (13.7)	66 (16.9)	123 (15.2)
HIV — no. (%)	67 (16.1)	55 (14.1)	122 (15.1)
Statin use among eligible participants[6] — no. (%)	8 (3.5)	22 (9.9)	30 (6.7)
Total cholesterol — mg/dl, mean (SD)	154.0 (39.8)	154.9 (45.0)	154.4 (42.3)
Always or often adding salt to food while eating[7] — no. (%)	41 (9.8)	62 (15.9)	103 (12.8)

Table 1 legend

1: Needing to cross a mountain or river or travel >10 km to the nearest health facility

2: Reporting current use of antihypertensive medication

3: 10-year risk for a cardiovascular event, using the WHO laboratory-based cardiovascular risk calculator[23]

4: Self-reported physical activity using the International Physical Activity Questionnaire Short Form (IPAQ-S)[24]

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5: HIV and/or diabetes
6: Participants with history of stroke, myocardial infarction, diabetes, or chronic kidney disease or aged ≥50 years and having a BMI of ≥30kg/m^2 or aged ≥50 years and currently smoking were eligible for statin. Number of participants eligible is 451 (229 in control and 222 in intervention)
7: Assessed using the WHO STEPS instrument[26]
Abbreviations: SD: standard deviation; CVD: cardiovascular disease

Missing data: BMI: 0 control, 8 intervention; abdominal circumference: 4, 20; education: 2, 0; employment status: 1, 0; WHO cardiovascular risk: 18, 33; alcohol consumption: 1, 2; physical activity: 3, 3; total cholesterol: 18, 33.

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Table 2 Intervention effects on primary and selected secondary and prespecified exploratory endpoints. Effects on all other secondary endpoints are available in the Supplementary Appendix Table S2.

	Control	Intervention	aOR or adjusted mean difference (95% CIs)[1]
Primary endpoint analysis[2]	N=412	N=386	
BP <140/90 mmHg at 12 months, mITT[3, §] — no. (%)	303 (73.5)	300 (77.7)	1.29 (0.93; 1.80)
Sensitivity analysis at 12 months[2]	N= 370	N=332	
BP <140/90 mmHg, complete case[4, #] — no. (%)	303 (81.9)	300 (90.4)	2.19 (1.31; 3.65)
Restricted-population analyses at 12 months[2]			
BP <140/90 mmHg, approximating PP analysis[5] — no. (%)	300 (79.8)	299 (81.3)	0.92 (0.62; 1.36)
BP <140/90 mmHg, baseline eligible for CHW care[6] — no. (%)	268 (73.8)	254 (78.4)	1.17 (0.83; 1.66)
BP <140/90 mmHg, baseline BP ≥120/70 mmHg[7] — no. (%)	251 (72.3)	240 (77.2)	1.32 (0.93; 1.89)
Secondary endpoints at 12 months[2]	N=412	N=386	
SBP — mmHg, mean (SD)[†]	123.6 (15.0)	122.5 (12.7)	-0.6 (-2.8; 1.6)
DBP — mmHg, mean (SD)[†]	79.4 (9.6)	78.7 (8.2)	-0.7 (-2.3; 0.9)
Engagement in care[8], ITT[9] — no. (%)	367 (89.1)	328 (85.0)	0.72 (0.47; 1.09)
Engagement in care[8], complete case[10] — no. (%)	367 (99.2)	328 (98.8)	0.86 (0.18; 4.01)
Adherence to antihypertensive medication[11] — no. (%)	332 (92.0)	219 (84.5)	0.51 (0.23; 1.17)
Not using antihypertensive medication — n	50	126	
Cardiovascular disease risk ≥10%[12] — no. (%)	184 (49.9)	165 (50.0)	1.08 (0.58; 2.00)
Total cholesterol — mg/dl, mean (SD)	162.5 (42.8)	158.1 (47.5)	-4.2 (-13.4; 5.0)
Current smoking — no. (%)	111 (30.0)	102 (30.7)	1.19 (0.45; 3.15)
Exploratory endpoints at 12 months[2]	N=412	N=386	
BP <140/90 mmHg without medication — no. (%)	5 (1.2)	68 (17.6)	24.0 (7.2; 79.9)
Statin use among eligible participants[13] — no. (%)	11 (5.0)	53 (29.3)	3.26 (2.19; 4.85)
Not eligible for statin use — n	149	151	
Managed by CHW — no. (%)	0 (0)	213 (64.9)	
Not engaged in care — n	45	58	
Secondary endpoints at 6 months[14]	N=413	N=387	
BP <140/90 mmHg, ITT[3, *] — no. (%)	315 (76.3)	281 (72.6)	0.87 (0.59; 1.29)
BP <140/90 mmHg, complete case[15, *] — no. (%)	315 (83.1)	281 (81.9)	0.93 (0.58; 1.48)
SBP — mmHg, mean (SD) [¶]	122.8 (15.1)	123.6 (14.3)	1.4 (-1.1; 4.0)
DBP — mmHg, mean (SD) [¶]	79.2 (9.3)	79.5 (9.1)	0.3 (-1.2; 1.8)
Engagement in care[8], ITT[9] — no. (%)	378 (91.5)	328 (84.8)	0.56 (0.31; 1.0)
Engagement in care[8], complete case[16] — no. (%)	378 (99.7)	328 (95.1)	0.05 (0.01; 0.38)
Adherence to antihypertensive medication[11] — no. (%)	348 (93.0)	236 (88.7)	0.68 (0.22; 2.17)
Not using antihypertensive medication — n	39	121	
Cardiovascular risk ≥10%[12] — no. (%)	179 (48.0)	159 (49.1)	1.10 (0.62; 1.97)
Total cholesterol — mg/dl, mean (SD)	158.3 (38.7)	159.3 (45.6)	1.1 (-6.3; 8.5)
Current smoking — no. (%)	102 (26.9)	94 (27.2)	0.86 (0.39; 1.91)
Exploratory endpoints at 6 months[2]	N=413	N=387	
BP <140/90 mmHg without medication— no. (%)	4 (1.0)	63 (16.3)	30.1 (7.8; 116.6)
Statin use among eligible participants[13] — no. (%)	10 (4.6)	70 (38.0)	4.94 (2.84; 8.61)
Not eligible for statin use — n	161	162	
Managed by CHW — no. (%)	0 (0)	208 (63.4)	

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	Control	Intervention	aOR or adjusted mean difference (95% CIs)[1]
Not engaged in care — n	35	59	

Table 2 legend

1: Effects are derived from regression models adjusted for sex, age, district, facility access, and baseline values when appropriate. Because the variance of the cluster random effect was negligible and resulted in singular fits, the cluster random effect was omitted from the final models.
2: Nine participants excluded due to pregnancy between enrolment and 12 months
3: Participants with missing BP measurement were considered as having a BP ≥140/90 mmHg
4: Only including participants with available BP measurement at 12 months: 370 control, 332 intervention
5: Only including participants with at least one hypertension care visit with a CHW in intervention clusters and at least one hypertension care visit at a health facility in control clusters: 376 control, 368 intervention.
6: Only including participants who were eligible for pharmacological treatment by CHWs at baseline (requiring less than three antihypertensive drugs, not presenting with hypertensive emergency or alarm symptoms, no contraindications or intolerance to amlodipine or hydrochlorothiazide: 363 control, 324 intervention.
7: Only including participants with baseline BP not suggestive of possible overtreatment or misdiagnosis (SBP ≥120 mmHg or DBP ≥70 mmHg): 347 control, 311 intervention.
8: Reporting current use of antihypertensive medication or reaching treatment target without medication
9: Participants with missing measurement were considered as not being engaged in care
10: Only including participants with available endpoint data at 12 months: 370 control, 332 intervention
11: Reporting no dose of antihypertensive medication missed over the last four days
12: 10-year risk for a cardiovascular event, using the WHO laboratory-based cardiovascular risk calculator[23]
13: Prespecified exploratory endpoint. Statin eligible: participants with history of stroke, myocardial infarction, diabetes, or chronic kidney disease or aged ≥50 years and having a BMI of ≥30kg/m^2 or aged ≥50 years and currently smoking
14: Seven participants excluded due to pregnancy between enrolment and 6 months
15: Only including participants with available BP measurement at 6 months: 379 control, 343 intervention
16: Only including participants with available endpoint data at 6 months: 379 control, 346 intervention

Abbreviations: BP: blood pressure; SD: standard deviation; SBP: systolic blood pressure; DBP: diastolic blood pressure; ITT: intention-to-treat

§ intra-cluster correlation coefficient (ICC) not estimable
# ICC 0.06
† ICC SBP 0.03; ICC DBP 0.08
* ICC 0.06
‡ ICC 0.08
¶ ICC SBP 0.07; ICC DBP 0.07

Missing data at 12 months: SBP and DBP: 42 control, 54 intervention; self-reported adherence: 1, 1; smoking: 42, 54; cardiovascular risk: 43, 56; total cholesterol: 43, 56.

Missing data at 6 months. SBP and DBP: 34 control, 42 intervention. smoking: 34, 41; cardiovascular risk: 40, 63; total cholesterol: 40, 63.

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Table 3 Safety endpoints by study group

	Control	Intervention
Safety endpoints at 12 months	N=417	N=390
Deaths — no. (%)	8 (1.9)	9 (2.3)
Non-fatal serious adverse event[1] — no. (%)	6 (1.4)	8 (2.1)
Hospitalization — no. (%)	6 (1.4)	7 (1.8)
Hospitalization with life-threatening event — no. (%)	0 (0.0)	1 (0.3)
Adverse events of special interest[2] — no. (%)	0 (0.0)	15 (3.8)
Side effects of antihypertensive medication — no. (%)	0 (0.0)	15 (3.8)

Table 3 legend

1: Serious adverse events defined as death, hospitalization, life-threatening event, event leading to persistent disability
2: Adverse events of special interest defined as adverse events consistent with hypertension complications, such as myocardial infarction, stroke, heart failure or chronic kidney disease as well as adverse events related to the intake of antihypertensive medication leading to the discontinuation of the medication concerned.

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