STUDY PROTOCOL

with embedded

STATISTICAL ANALYSIS PLAN

PRIME CARE

Postpartum Remote monitoring and Integration of Mobile health with Engagement from Community heAlth workers for Regulating Elevated blood pressure

A Single-Site, Two-Arm, Parallel-Group, Superiority Randomized Controlled Trial of Telehealth-Enabled Remote Patient Monitoring with Community Health Worker Support vs. Standard of Care for Postpartum Hypertension in Black Women

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1. Protocol Synopsis

Title	PRIME CARE — Postpartum Remote monitoring and Integration of Mobile health with Engagement from Community heAlth workers for Regulating Elevated blood pressure.
Design	Single-site, two-arm, parallel-group, superiority randomized controlled trial with 1:1 individual-level allocation. Open-label with blinded outcome assessors and blinded analysts.
Setting	University of Nebraska Medical Center (UNMC) clinics; ~2,200 deliveries per year, >1,000 with hypertensive disorders annually.
Population	Black women aged 18–50 years with a hypertensive disorder of pregnancy (per 2019 ACOG criteria) currently enrolled in STAMPP-HTN through 6 weeks postpartum.
Intervention	Collaborative Care: telehealth-enabled remote patient monitoring (RPM) with Bluetooth-enabled home BP devices and algorithm-driven community health worker (CHW) support from 6 weeks through 12 months postpartum, layered on guideline-directed antihypertensive therapy.
Comparator	Standard of Care (SOC): AHA/ACOG guideline-directed postpartum hypertension management with standardized automated BP monitors, scheduled clinic visits at 6 weeks, 6 months, and 12 months, and monthly EMR audits of guideline adherence.
Primary objective	Determine whether Collaborative Care improves BP control (<130/80 mmHg) at 12 months postpartum compared with SOC.
Primary outcome	Proportion of participants with BP <130/80 mmHg at 12 months postpartum (dichotomous). Participants who discontinue prior to the 12-month visit are counted as failures in the primary analysis.
Key secondary outcomes	Continuous systolic and diastolic BP at 12 months; patient activation (PAM); trust in healthcare system (Trust in Physician Scale); composite severe maternal morbidity (SMM); time to first SMM event; implementation outcomes per RE-AIM.
Sample size	N = 404 (202 per arm). 82% power for the primary endpoint to detect a 15% absolute reduction in failure (55% SOC → 40% Collaborative Care) at two-sided $\alpha = 0.05$ using a continuity-corrected chi-square test. 80% power for the planned mediation analysis. 93% power for the composite SMM endpoint.
Randomization	1:1, computer-generated via the REDCap randomization module by the study biostatistician; allocation concealed until enrollment confirmation.
Duration	Active recruitment over [TBD] months; 12-month per-participant follow-up; total study duration approximately 4 years.
Safety oversight	Independent five-member Data and Safety Monitoring Board (DSMB) reviews safety annually with weekly intervention-team review of hospitalizations, ED visits, and hypotensive episodes (<90/60 mmHg). Prespecified stopping rule: trial terminated for safety if adverse events in the intervention arm exceed control by >20%.

2. Background and Rationale

2.1 Burden of postpartum hypertensive disease and racial disparities

Hypertensive disorders and other cardiovascular diseases are the leading cause of maternal death in the United States, and more than 90% of these deaths are considered preventable. Black women are three times more likely than White women to die from pregnancy-related complications and six times more likely if they develop hypertensive disorders of pregnancy (HDP). Cardiovascular disease contributes to nearly half of pregnancy-related deaths and has driven a more than 140% rise in pregnancy-related mortality over the past three decades, with two-thirds of deaths occurring postpartum.

Hypertensive disorders of pregnancy — including chronic and gestational hypertension, preeclampsia/eclampsia, and HELLP syndrome — disproportionately affect Black women, who experience earlier onset and greater severity. Black women also face higher rates of progression to stroke, heart failure, and pulmonary edema, with the highest-risk period extending from delivery through six weeks postpartum. CVD-related peripartum mortality for Black women is 8–9 times higher than for White women.

2.2 Evidence supporting RPM and CHW interventions

Remote patient monitoring with telehealth-guided postpartum BP management has demonstrated improvements in short- and long-term cardiovascular outcomes. The POP-HT randomized trial (n = 220) showed that physician-guided antihypertensive titration via RPM reduced 24-hour mean diastolic BP at 9 months (71.2 ± 5.6 vs. 76.6 ± 5.7 mmHg, $p < 0.001$) and reduced BP-related readmissions by 72.5%. The intervention also produced an 8% reduction in left ventricular mass that persisted at 4 years.

Digital health interventions and community health workers (CHWs) have repeatedly improved clinical outcomes in underserved populations. A meta-analysis of 28 studies (N = 8,257) showed that RPM-based digital health interventions yielded superior systolic BP reductions at 6 and 12 months. CHW-led, culturally tailored interventions have improved BP control across multiple trials.

2.3 Investigator preliminary work — STAMPP-HTN

The Systematic Treatment and Management of Postpartum Hypertension (STAMPP-HTN) program, launched at the University of Chicago in January 2019, combines RPM with CHW support, plain-language education, BP-monitor kits, embedded escalation pathways, and CHW services. STAMPP-HTN has enrolled 70–90 patients per month, served more than 6,000 patients, and scaled to 11 health systems in 9 states using the PRISM and RE-AIM frameworks. Key outcomes vs. pre-intervention: visit adherence 83.9% vs. 33.5% ($p < 0.0001$); systolic BP within 24 hours postpartum 136 vs. 149 mmHg ($p < 0.0001$); hypertension (>140/90) reduced from 42.2% at week 1 to 14.3% at week 6 ($p < 0.001$); and near-elimination of racial disparities in visit adherence (Black 81.3% vs. White 88.8%, $p = 0.08$

2.4 Gap addressed by PRIME CARE

A retrospective analysis (n = 1,480, 78% Black, 2018–2020) of women enrolled in STAMPP-HTN revealed care-continuity gaps beyond 6 weeks: 79% had Stage 1 or higher hypertension requiring treatment, yet only 7% had cardiology follow-up and 13% primary care follow-up within one year. Only 10% received guideline-directed therapy and 2% experienced a hypertensive crisis. Notably, patients who did access follow-up achieved 80% BP control (<130/80 mmHg). Recent Medicaid postpartum coverage expansion (48 states) and CHW reimbursement adoption (36 states) create unprecedented scalability potential. PRIME CARE addresses this gap with an RCT extending the STAMPP-HTN framework from 6 weeks to 12 months postpartum, evaluating both effectiveness and mechanisms.

2.5 Risk–benefit assessment

The intervention layers algorithm-driven CHW outreach and RPM onto guideline-directed antihypertensive management. Anticipated risks are minimal and include those inherent to home BP measurement, occasional false-positive alerts triggering provider contact, possible distress from frequent BP monitoring, and standard data-privacy considerations associated with REDCap and EMR-mediated transmission. Anticipated benefits include improved BP control, earlier detection of clinical deterioration, reduced ED visits and readmissions, and increased patient activation and trust. The overall risk–benefit balance is favorable given the population's documented disparities in cardiovascular outcomes.

3. Objectives, Aims, and Hypotheses

3.1 Primary objective and hypothesis

To determine whether Collaborative Care (RPM + algorithm-driven CHW support) improves BP control at 12 months postpartum compared with SOC in Black women with HDP.

Primary hypothesis (H1): The proportion of participants achieving BP <130/80 mmHg at 12 months postpartum will be higher in the Collaborative Care arm than in the SOC arm.

3.2 Secondary objectives and hypotheses

- **Aim 2 —** Identify mechanisms by which Collaborative Care improves BP control, focusing on patient activation (PAM) and trust in the healthcare system (Trust in Physician Scale). H2: Greater activation and increased trust will mediate intervention effects on BP.
- **Aim 3 —** Assess efficacy of Collaborative Care in reducing severe maternal morbidity (SMM). H3: Participants receiving Collaborative Care will experience lower rates of the composite SMM endpoint between randomization and 12 months postpartum.
- **Implementation —** Characterize Reach, Effectiveness, Adoption, Implementation fidelity, and Maintenance using the RE-AIM framework.

3.3 Estimand framework (primary endpoint)

Population	Black women aged 18–50 years with HDP enrolled at 6 weeks postpartum at UNMC who meet all eligibility criteria and are randomized.
Treatment	Assignment to Collaborative Care vs. SOC.
Endpoint	BP <130/80 mmHg at the 12-month postpartum visit window.
Intercurrent events — strategy	Discontinuation of follow-up prior to 12 months: composite (failure) strategy in the primary analysis (treated as not achieving BP control). Treatment switching or non-adherence is handled by treatment-policy strategy (intention-to-treat). Death is treated as failure.
Population-level summary	Risk difference (Collaborative Care minus SOC) in the proportion achieving BP control, with two-sided 95% confidence interval; chi-square test at $\alpha = 0.05$.

4. Study Design

4.1 Overall design

Single-site, two-arm, parallel-group, individually randomized (1:1) superiority RCT comparing Collaborative Care with SOC over 12 months of postpartum follow-up. Open-label design with blinded data collectors and blinded analysts to mitigate ascertainment bias. The trial is preceded by enrollment in STAMPP-HTN, which delivers standard postpartum hypertension care from delivery through 6 weeks postpartum to all eligible patients regardless of subsequent trial participation.

4.2 Schematic of participant flow

Approach → Consent → Eligibility Confirmation (Dr. Rana) → Baseline Assessment (Survey 1) at 6 weeks postpartum → 1:1 Randomization in REDCap → Allocation to Collaborative Care or SOC → Survey 2 (6 months) → Survey 3 + Primary Endpoint Assessment (12 months) → End of Study.

4.3 Schedule of assessments

Procedure / Assessment	Screen	Baseline (6 wks PP)	Month 6	Month 12	Adverse events (ongoing)	Notes
Informed consent	X					Re-consent if protocol amendments materially change risks/benefits
Eligibility confirmation (Dr. Rana)	X	X				HDP diagnosis per 2019 ACOG criteria
Demographics, SDOH, medical/obstetric history		X				From EMR + participant self-report
Randomization (REDCap)		X				1:1 allocation
BP measurement (in-clinic, standardized)	X	X	X	X	X (as indicated)	Primary endpoint at Month 12
Home RPM BP transmissions		X	Continuous	Continuous	Continuous	Intervention arm only

Procedure / Assessment	Screen	Baseline (6 wks PP)	Month 6	Month 12	Adverse events (ongoing)	Notes
Antihypertensive medication review	X	X	X	X	X	Per 4-step algorithm
PAM-13 (Patient Activation)		X	X	X		Mediator
Trust in Physician Scale		X	X	X		Mediator
Lifestyle (smoking, salt, alcohol, exercise, contraception)		X	X	X		Self-report
SMM composite ascertainment		X	X	X	X	EMR + Care Everywhere
CHW interaction log		X	X	X	X	Intervention arm only
Implementation outcomes (RE-AIM)		X	X	X		Patient + staff surveys
AE / SAE assessment		X	X	X	X	DSMB review per safety section

5. Study Population

5.1 Inclusion criteria

1. Self-identified Black race.
2. Age 18–50 years at the time of consent.
3. Diagnosis of a hypertensive disorder of pregnancy in the index pregnancy, per 2019 ACOG criteria, confirmed by the study clinician (Dr. Rana, Co-I).
4. Enrolled in STAMPP-HTN through 6 weeks postpartum at UNMC.
5. Able to provide informed consent in English.
6. Access to a smartphone, tablet, or study-provided SIM-enabled device adequate for RPM data transmission.

5.2 Exclusion criteria

7. Significant kidney disease (eGFR <30 mL/min/1.73 m²) or chronic liver disease that would preclude safe antihypertensive medication titration, per study clinician judgment.
8. Known secondary hypertension requiring specialist care unrelated to HDP, in the judgment of the study team.
9. Current participation in another interventional trial whose intervention overlaps with PRIME CARE.
10. Inability to comply with study procedures or follow-up (e.g., relocation outside of the UNMC catchment area without Care Everywhere connectivity).
11. Any other condition that, in the judgment of the investigator, makes participation unsafe or scientifically inappropriate.

5.3 Recruitment, screening, and consent

Primary enrollment occurs at the 6-week postpartum visit in UNMC clinics. The EMR will be queried daily to flag potentially eligible patients. Trained study staff approach flagged participants in person at clinic visits or by phone/video. Based on existing STAMPP-HTN throughput, approximately 240 eligible Black patients per year (~20 per month) are anticipated, with an expected 70% consent rate.

Consent is obtained using an IRB-approved informed consent form (ICF). The ICF and Health Insurance Portability and Accountability Act (HIPAA) authorization will be reviewed verbally and in writing. Participants are given as much time as needed to consider participation and may withdraw at any time. Documentation of consent will be maintained in REDCap and in source documents.

5.4 Withdrawal, discontinuation, and lost-to-follow-up

Participants may withdraw consent at any time. The study team will distinguish between (a) withdrawal of consent to all study activities (including data use going forward), (b) withdrawal

from the intervention while continuing to permit outcome ascertainment, and (c) loss to follow-up (defined as three documented failed contact attempts across at least two modalities). The reasons for and timing of discontinuation will be captured in REDCap. Analyses will follow the prespecified intercurrent-event strategies in Section 12 of the SAP.

6. Interventions

6.1 Standard of Care arm

All participants in the SOC arm receive AHA/ACOG guideline-based care, including cardiovascular risk counseling, lifestyle modifications, and risk-factor management as determined by their primary care physician. Both arms use the same automated home BP monitor model and complete the same standardized web-based BP-measurement training. BP assessments are performed at 6 weeks, 6 months, and 12 months in conjunction with survey administration. Primary care visits follow standard clinical schedules; medication management is aligned with AHA guidelines. All data are transmitted to a centralized EMR, with monthly EMR audits of guideline adherence and provider feedback as needed.

6.2 Collaborative Care arm

Collaborative Care integrates telehealth-enabled RPM with algorithm-driven CHW support across three layers: automated BP surveillance, risk-stratified clinical responses, and personalized medication optimization. All data are transmitted to the centralized EMR.

6.2.1 RPM BP monitoring protocol

- Baseline (Weeks 1–2 post-randomization): daily BP measurements at consistent times.
- Stabilization (Weeks 3–8): measurement frequency determined by BP stage — Stage 2+ daily, Stage 1 alternate days, normotensive biweekly.
- Maintenance (Weeks 9–52): minimum biweekly measurements; daily during any medication titration.

6.2.2 Automated response algorithm

BP category	Triggered response
Normal (<130/80 mmHg)	Monthly CHW check-ins.
Stage 1 (130–139 / 80–89 mmHg)	Provider review within 1 week; CHW contact within 1 week; lifestyle counseling.
Stage 2 (≥140/90 mmHg)	Provider review within 24 hours; same-day CHW contact; medication adjustment per algorithm.
Severe (≥160/110 mmHg)	Immediate provider alert; CHW within 1 hour; ED referral if symptomatic.

6.2.3 CHW integration and dose

- Weeks 1–2: 3 contacts/week (technology onboarding, medication initiation).
- Weeks 3–8: 2 contacts/week (optimization, adherence barriers).
- Weeks 9–52: 2 contacts/month maintenance plus as-needed escalations triggered by the algorithm.

CHWs verify medication initiation within 48 hours, assess side effects, address access barriers, and coordinate pharmacy services. Dr. Griffith (Co-I), a licensed clinical psychologist, is available for behavioral-health consultation. CHWs document all encounters using a structured REDCap form (Box 1 — [TBD: include in appendix at IRB submission]).

6.2.4 Evidence-based medication algorithm (both arms)

12. Step 1: Monotherapy with lactation-safe agents (labetalol, nifedipine, methyldopa) or ACE-I/ARB for non-breastfeeding women.
13. Step 2: Dual therapy combining different drug classes.
14. Step 3: Triple therapy with referral to a specialist.
15. Step 4: Transition to ACE-I/ARB after weaning for long-term cardiovascular benefit.

6.3 Concomitant medications and prohibited interventions

There are no protocol-prohibited medications. All participants may receive any clinically indicated therapy. Concomitant medications are recorded at each study visit. To avoid contamination, CHW services and the RPM platform are restricted to the Collaborative Care arm; pilot data confirm no cross-arm contamination.

6.4 Adherence and intervention fidelity

Adherence to RPM is monitored via daily transmission counts; missing transmissions for >48 hours trigger CHW outreach. Adherence to CHW dosing is monitored via the structured REDCap encounter log. Intervention fidelity is assessed monthly via random audits of 10% of encounters by the study coordinator, with feedback to CHWs and providers. A fidelity threshold of ≥90% is targeted, consistent with STAMPP-HTN benchmarks.

7. Randomization and Blinding

7.1 Sequence generation

A computer-generated 1:1 randomization sequence will be created a priori by the study biostatistician (Dr. Ying) using a permuted-block design with random block sizes [TBD: 2/4/6 to be finalized in the SAP appendix prior to first randomization]. Stratification factors: HDP subtype (chronic/gestational hypertension vs. preeclampsia spectrum) and antihypertensive use at randomization (yes/no).

7.2 Allocation concealment

The sequence is loaded into REDCap's password-protected randomization module. Allocation is revealed to the study team only after the participant is enrolled and the baseline assessment is complete.

7.3 Implementation

The research coordinator confirms eligibility, obtains consent, completes baseline assessments, and then triggers randomization in REDCap. The participant's arm assignment is communicated to the clinical team and CHW supervisor.

7.4 Blinding

Because the intervention is behavioral and technology-based, participants and treating clinicians cannot be blinded. Bias is minimized by: (1) blinded outcome assessors with no CHW/clinician role; (2) objective primary endpoint (BP at standardized time points) using identical automated devices in both arms; (3) automated capture via RPM and REDCap-administered surveys; and (4) blinded statistical analysis (data files are labeled “Group A” and “Group B” until the final primary-endpoint analysis is locked).

8. Outcomes and Assessments

8.1 Primary outcome

Proportion of participants with BP <130/80 mmHg at the 12-month postpartum study visit. BP is measured using an automated, calibrated home BP monitor of the same model in both arms, following AHA standardized technique (rest 5 min, seated, supported back and arm, two readings 1–2 minutes apart, average recorded). Participants who do not have a 12-month measurement are counted as failures in the primary analysis (see SAP Section 12).

8.2 Secondary outcomes

- Mean systolic and diastolic BP at 12 months (continuous).
- Change from baseline to 6 and 12 months in systolic and diastolic BP (continuous).
- Patient activation — Patient Activation Measure (PAM-13), 0–100, SD ~ 15.
- Trust in healthcare system — Trust in Physician Scale (11 items, range 11–55, α = 0.85–0.90, SD ~ 14).
- Composite severe maternal morbidity (SMM) between randomization and 12 months postpartum: any unplanned ED visit, hospitalization, or qualifying severe morbidity event.
- Time from randomization to first SMM event.
- Individual SMM components (severe hypertension, acute heart failure, pulmonary edema, eclampsia, acute renal failure, shock, sepsis, cardiac arrest, arrhythmias, myocardial infarction, pulmonary embolism, stroke, death).
- BP-related ED visits and readmissions through 12 months.
- Implementation outcomes per RE-AIM: Reach, Effectiveness, Adoption, Implementation fidelity, and Maintenance.

8.3 Other prespecified assessments

Lifestyle covariates collected at each survey: smoking status, dietary salt intake, alcohol consumption, hormonal contraception use, exercise, and physical activity. EMR-derived covariates: age, BMI, hypertensive disorder of pregnancy type, diabetes, insurance status, and gestational age at delivery.

8.4 Definitions of severe morbidity events

9. Safety Monitoring and Adverse Events

9.1 Definitions

- **Adverse event (AE):** Any untoward medical occurrence in a participant, irrespective of relationship to study intervention.
- **Serious adverse event (SAE):** Any AE that is fatal, life-threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability, or is otherwise medically significant.
- **Adverse event of special interest (AESI):** Severe hypertension (≥160/110 mmHg with or without symptoms), symptomatic hypotension (<90/60 mmHg), eclampsia, stroke, acute heart failure, pulmonary edema, acute kidney injury, and any event meeting the SMM composite.

9.2 Ascertainment, recording, and reporting

AEs and SAEs are ascertained at every study contact and via continuous EMR review for the duration of follow-up. SAEs are reported to the IRB and DSMB within [TBD: institution-required interval, typically 24–72 hours]. AEs are recorded in REDCap with onset date, severity (CTCAE v5.0 [TBD: confirm version at IRB submission]), seriousness, relationship to intervention, action taken, and outcome.

9.3 Data and Safety Monitoring Board (DSMB)

An independent five-member DSMB — [TBD: roster names and disciplines, expected to include obstetric medicine, cardiology, biostatistics, ethics/community representation] — meets annually to assess accrual, progress, and safety. The intervention team performs weekly review of hospitalizations, ED visits, and hypotensive episodes (<90/60 mmHg).

9.4 Stopping rule

The trial will terminate if the intervention group has >20% higher adverse event rate than control, as judged by the DSMB at any scheduled or ad-hoc safety review. No formal interim efficacy stopping rules are planned; the DSMB may recommend stopping for futility or safety at its discretion.

9.5 Risk-mitigation strategies

- RPM onboarding support, visual aids, culturally tailored education, and SIM-enabled tablets for participants without smartphone access.
- CHW training in motivational interviewing, trauma-informed care, mental-health first response, and confidentiality.
- Routine algorithm optimization to reduce alert fatigue while preserving clinical safety.
- Established escalation pathways to clinicians for any abnormal BP or concerning symptom report.

10. Data Management

10.1 Data collection and storage

All study data are collected and managed using REDCap hosted at UNMC. Case report forms (CRFs) are designed by the biostatistician with web-based data entry, range checks for continuous variables, consistency checks for dates and key fields, and pull-down menus/radio buttons for categorical variables to minimize errors at entry. Scripts will generate edit queries within and across forms; the research coordinator will reconcile flagged discrepancies.

10.2 Source documents and audit

Source documents include EMR notes, in-clinic BP measurements, signed consent forms, and CHW encounter logs. A data monitor will compare audits of a 20% random sample of REDCap-entered data with source documents every six months. Findings are reviewed with the PI and biostatistician.

10.3 EMR abstraction and Care Everywhere

EMR data are used to capture covariates and outcomes including SMM components. For participants whose follow-up care occurs outside UNMC, Care Everywhere is used to abstract the 12-month BP and SMM endpoints. EMR abstraction is performed by trained staff using structured templates; 10% of abstractions are independently re-abstracted with reconciliation.

10.4 Confidentiality and security

All electronic records are stored on UNMC's secure REDCap and institutional EMR. Access is role-based and audit-logged. A unique study ID links to a separately stored master log accessible only to the PI, coordinator, and biostatistician. The dataset shared for analysis is de-identified except for date variables required for time-to-event analyses, governed by IRB-approved data use procedures.

10.5 Data sharing and code availability

De-identified data and annotated analysis code will be made available consistent with the NIH Data Management and Sharing Policy and the IRB-approved consent. [TBD: confirm repository — e.g., NHLBI BioLINCC, NICHD DASH, or institutional repository — and embargo period at IRB submission.]

11. Ethical and Regulatory Considerations

11.1 IRB and regulatory oversight

The protocol, ICF, and all study materials are reviewed and approved by the UNMC IRB ([TBD: protocol number]) prior to initiation and annually thereafter. Protocol amendments will be submitted to the IRB and, where applicable, to the DSMB and ClinicalTrials.gov. The trial will be registered on ClinicalTrials.gov prior to enrollment ([NCT TBD]).

11.2 Informed consent

Written informed consent and HIPAA authorization are obtained from each participant prior to any study-specific procedure. The consent process includes a verbal review of risks, benefits, study procedures, alternatives, voluntariness, and confidentiality. Re-consent is obtained for material protocol amendments.

11.4 Investigator responsibilities and training

- All study personnel complete CITI Human Subjects Research and Good Clinical Practice training.
- CHWs complete foundational training plus study-developed modules on severe maternal morbidity, hypertension management, RPM, domestic violence screening, mental health, and trauma-informed care.
- Study staff complete implicit-bias training (University of Chicago module) [TBD: confirm UNMC analog if locally required].

11.5 Conflicts of interest

Investigator conflicts of interest are disclosed annually to UNMC and to the funding agency in accordance with NIH financial conflict-of-interest regulations.

11.6 Publication and authorship policy

Results, regardless of direction, will be reported in a peer-reviewed publication consistent with ICMJE authorship criteria and disseminated to community partners and policymakers. The primary outcome analysis is reported within 12 months of database lock. CONSORT 2010 reporting standards will be followed.

12. Statistical Analysis Plan (SAP)

12.1 SAP overview

This SAP is fully prespecified and will be finalized and version-locked prior to first randomization. Any amendments after the start of the trial will be documented with version history, rationale, and approval by the PI, biostatistician, and DSMB (as applicable).

12.2 Analysis populations

Intention-to-treat (ITT) population	All randomized participants analyzed in the arm to which they were assigned, regardless of intervention received. This is the primary analysis population.
Per-protocol (PP) population	Participants who received their assigned intervention without major deviations (definitions of major deviations specified in the SAP appendix prior to first randomization).
Safety population	All randomized participants with any post-randomization safety contact.
Mediation population	ITT participants with non-missing baseline and at least one post-baseline measurement of each mediator (PAM, Trust).

12.3 Sample size and power

Primary endpoint: Using STAMPP-HTN preliminary data (134/394 = 34% Stage 1 hypertensive between 6 and 12 months postpartum) and the POP-HT trial control-arm distribution (DBP mean 76.6, SD 5.7; SBP mean 120.3, SD 9.1) the SOC hypertension rate is estimated at ~35%. Adding 20% dropout (counted as failures) yields a 55% failure rate in SOC. Assuming 25% hypertension and 15% dropout (40% failure rate) in Collaborative Care, a sample of 404 participants (202 per arm) provides 82% power to detect a 15% absolute reduction using a two-sided continuity-corrected chi-square test at $\alpha = 0.05$.

Secondary continuous BP: Based on POP-HT SDs and 20%/15% attrition, the 97.5% CI half-width for diastolic BP difference is ± 1.4 mmHg, and ± 2.3 mmHg for systolic BP (slightly tighter under multiple imputation).

Mediation (Aim 2): Assuming a medium intervention→mediator effect and small mediator→outcome effect, with complete or partial mediation, n = 404 provides 80% power at two-sided $\alpha = 0.05$ using the bias-corrected bootstrap (per Fritz & MacKinnon, 2007).

SMM (Aim 3): Assumed SOC composite SMM rate 36% (severe hypertension 1.5%, ED visits/hospitalizations 34%, stroke/death 0.4%) vs. 20% under Collaborative Care; n = 404 provides 93% power. Under exponential time-to-event distributions, the assumed event rates correspond to HR = 0.5, with 94% power for the log-rank test.

12.4 Primary analysis

Hypothesis: H0: π_CC = π_SOC vs. H1: π_CC ≠ π_SOC, where π is the proportion achieving BP <130/80 mmHg at 12 months postpartum.

The primary analysis is conducted in the ITT population using a two-sided continuity-corrected chi-square test at α = 0.05. Risk difference and risk ratio with 95% confidence intervals are reported alongside the p-value. Participants who discontinue prior to 12 months are counted as failures in both arms (composite intercurrent-event strategy).

12.5 Sensitivity analyses for the primary endpoint

- (S1) Complete-case analysis excluding dropouts.
- (S2) Last-observation-carried-forward of the participant's hypertensive/normotensive status at the time of dropout.
- (S3) Multiple imputation for missing 12-month status using baseline covariates and longitudinal BP measurements (predictors include age, BMI, smoking, HDP subtype, diabetes, insurance, gestational age at delivery, and prior BP readings); 10 imputations; Rubin's rules for inference.
- (S4) Tipping-point analysis varying the assumed control rate among dropouts to identify the threshold at which the primary inference changes.

12.6 Secondary analyses — continuous BP at 12 months

Mean systolic and diastolic BP at 12 months are compared using a two-sample t-test at two-sided α = 0.025 (Bonferroni adjustment for two co-primary BP components). Dropouts and missing values are handled via multiple imputation as described in S3, with baseline covariates and longitudinal BP as predictors; 10 imputations; standard errors via the within/between-imputation variance formula. A rank-based sensitivity analysis is performed in which dropouts receive the worst (highest) BP rank, compared between groups with the Wilcoxon rank-sum test.

12.7 Mediation analysis (Aim 2)

12.7.1 Longitudinal mixed model for binary hypertension

A mixed-effects logistic model is fit using lme4 in R with a random intercept per participant and time dummies for 6 and 12 months (baseline reference). Treatment is included as a main effect and via treatment×time interactions. Patient activation (PAM) and trust are entered as lagged time-varying covariates. The full model (all treatment terms) is compared to a reduced model (treatment terms removed) using likelihood-ratio tests under ML estimation. Effect sizes and 95% CIs are reported for all parameters.

12.7.2 Path analysis via lavaan

Conditional on a detectable intervention effect, separate path models are fit at 6 and 12 months using lavaan, with mediators entered from the prior time point and both mediators included simultaneously. Indirect effects $A_1 \times B_1$ (PAM) and $A_2 \times B_2$ (trust) are reported with bias-corrected

bootstrap 95% CIs (≥5,000 replicates). 95% CIs that exclude zero are considered statistically significant.

12.7.3 Cross-sectional mediation for continuous BP at 1 year

A three-step regression approach is applied to the 12-month continuous BP outcome:

Step 1: $M^{(k)} = \alpha_0^{(k)} + \alpha_1^{(k)} X$ for k = 1, 2.

Step 2: $Y = \beta_0 + \beta_1 X$ (already estimated in Aim 1 secondary analysis).

Step 3: $Y = \gamma_0 + \gamma_1 X + \gamma_2^{(1)} M^{(1)} + \gamma_2^{(2)} M^{(2)}$.

The indirect effect IE = $\hat{\beta}_1 - \hat{\gamma}_1$ is estimated with a bootstrap 95% CI (≥5,000 replicates). Required assumptions: (i) no confounding of X→Y, (ii) no confounding of X→$M^{(k)}$, and (iii) no confounding of $M^{(k)}$→Y. Randomization addresses (i) and (ii); sensitivity analyses per Ding & VanderWeele (2016) and VanderWeele (2016) assess robustness of (iii) by varying two sensitivity parameters governing unmeasured mediator–outcome confounding.

12.8 Aim 3 — severe maternal morbidity

- Primary SMM analysis: the composite SMM proportion between randomization and 12 months is compared between arms using a chi-square test at two-sided α = 0.05.
- Component analyses: each SMM component is compared separately using chi-square or Fisher exact tests as appropriate. No formal multiplicity adjustment is applied to component-level tests; results are interpreted as exploratory.
- Time-to-event: time from randomization to first SMM event is estimated by the Kaplan–Meier method and compared via the log-rank test. Participants without an event are censored at 12 months or last follow-up.
- Adjusted analyses: logistic regression (binary) and Cox proportional hazards regression (time-to-event) including treatment and prespecified prognostic factors (age, BMI, HDP subtype, baseline BP, parity, insurance) identify covariate-adjusted effects.
- Proportional hazards assessment: graphical methods and the Grambsch–Therneau test. If violated, restricted mean survival time (RMST) is compared with 12 months as the restriction time.
- Sensitivity analysis: participants lost to follow-up are treated as having an event at the time of dropout.

12.9 Implementation outcomes (RE-AIM)

- Reach: percentage of eligible participants randomized; consent rate; representativeness vs. UNMC source population, by sociodemographics.
- Effectiveness: described by the Aim 1 and Aim 3 primary analyses.
- Adoption: percentage of approached providers and CHWs who participate; described by provider type.

- Implementation fidelity: percentage of CHW encounters and RPM transmissions meeting protocol thresholds; algorithm-triggered escalation completion rates within target windows.
- Maintenance: described qualitatively by staff end-of-study surveys; sustainability index reported at 12 months and at trial close.

12.10 Missing data

All missingness mechanisms are assessed descriptively (Little's MCAR test for diagnostic purposes only). The primary analysis uses the composite (failure) strategy for missing 12-month status. Sensitivity analyses (S1–S4) span MCAR, MAR (via multiple imputation), and MNAR (via tipping-point) assumptions. Mediator missingness is handled with full-information maximum likelihood (FIML) within lavaan; multiple imputation is used where FIML is infeasible.

12.11 Multiplicity

- Primary endpoint: single test at two-sided $\alpha = 0.05$;
- Continuous BP (secondary):
- Mediation, SMM components, RE-AIM: hierarchical and exploratory; no familywise correction. P-values reported alongside effect sizes and CIs; interpretation emphasizes magnitude and consistency.

12.12 Subgroup analyses (prespecified, exploratory)

- HDP subtype (chronic/gestational hypertension vs. preeclampsia spectrum).
- Baseline BP category at randomization (normotensive on therapy vs. elevated).
- Insurance status (Medicaid vs. commercial vs. other).
- Social determinants of health composite tertile derived from CHW baseline assessment.
- Age (<35 vs. ≥35) and parity (primiparous vs. multiparous).

12.13 Software, reproducibility, and version control

All analyses are performed in R (version locked at SAP finalization; lme4, lavaan, survival, mice, boot). Code is maintained in a private institutional Git repository with versioned releases. Pre- and post-lock code separation is enforced. All analyses are reproducible from the locked database; the final analysis report is generated via R Markdown or Quarto with full session info.

12.14 Reporting

Results are reported per CONSORT 2010 for the main trial, SPIRIT 2013 for the protocol, and StaRI for implementation outcomes. A CONSORT participant-flow diagram is generated at study end.

13. Trial Organization and Roles

Principal Investigator	Sajid Shahul, MD, MPH — scientific oversight, regulatory approvals, publication.
Co-Investigator (clinical)	Dr. Rana — HDP diagnosis confirmation, clinical care oversight, escalation review.
Co-Investigator (biostatistics)	Dr. Ying — randomization sequence, SAP authorship, primary analyses.
Study Coordinator	[TBD] — recruitment, consent, REDCap data management, fidelity audits.
CHW Supervisor	[TBD] — CHW training, supervision, encounter audits.
Data Manager	[TBD] — REDCap configuration, data quality, source-document audits.
DSMB	5 independent members — [TBD: roster, charter to be appended].

14. Risk Management and Contingency Plans

14.1 Low enrollment

Enrollment is monitored monthly. If realized rates fall below 75% of the monthly target for two consecutive months, the team activates surge sites with existing EMR-based daily screening reports are used to ensure no eligible patient is missed.

14.2 Loss to follow-up

Mitigation strategies include diverse communication channels (text, phone, email), travel and assessment stipends, milestone cards for infant birthdays.

14.3 RPM/CHW engagement

Barriers to RPM are addressed via onboarding support, visual aids, culturally tailored education, SIM-enabled tablets for participants without phone access, and user-friendly tools. Barriers to CHW engagement are addressed via motivational interviewing training, culturally concordant CHWs, flexible phone/video options, and clear confidentiality protocols.

14.4 Clinician/CHW workload

The algorithm is iteratively optimized to automate routine tasks, extend timelines for stable participants, and consolidate check-ins, while preserving rapid escalation pathways.

14.5 Protocol deviations and amendments

All deviations are logged in REDCap with date, description, root cause, and corrective action. Material amendments require IRB approval and DSMB notification prior to implementation. The protocol version log is maintained on the first page of the document.

Date: _____