STATISTICAL DESIGN AND POWER

The statistical design of the study intervention includes evaluation of effectiveness and implementation outcomes. For effectiveness outcomes, we will use an interrupted time series design with analysis plans and power calculations outlined below, which use conservative baseline treatment rates, effect sizes, and temporal trend rates to minimize the risk of being underpowered to detect a difference while operating within a feasible project size, timeline, and budget. For implementation outcomes, we will use mixed methods analysis using the RE-AIM framework to triangulate both routinely collected quantitative data and qualitative data to evaluate the reach, adoption, implementation, and maintenance, acceptability, and cost of the interventions.

Analysis plan for Aims 1 and 2.1. We will evaluate change in temporal trends for primary and secondary outcomes through segmented linear regression, aggregating data across primary health care centers by month (centered to time=0 when intervention is implemented) and allowing for autocorrelated errors. To evaluate the individual effects of KPNC components and time variance in implementation on our primary outcomes, we will use patient-level mixed effects models including random effects to account for clustering at the clinic level. We will perform sensitivity analyses by both excluding and restricting repeated measures of the same patients over the study period. Because we know of no concurrent, community-based representative studies that will evaluate hypertension treatment and control rates in Nigeria over the funding period, we will use historical controls and any intercurrent reports (e.g. Global Burden of Disease) for triangulation of our results.

Power for Aims 1 and 2.1. Using a conservatively high baseline hypertension treatment rate of 20% based on previous estimates in Nigeria (to ensure that we are not underpowered),[41] recruiting 1,200 participants per month across 50 sites over 9 months of baseline and 39 months of intervention provides over 80% power to detect a difference in slope of 0.57% per month compared to underlying trend of 0.10% per month, resulting in hypertension treatment rate of 42.5% at the end of 48 months. Similarly, using a conservative baseline hypertension control rate of 10%, we will have over 80% power to detect a difference in slope of 0.44% per month compared to underlying trend of 0.05% per month, resulting in hypertension control rate of 27.0% at the end of 48 months. These effect sizes are conservative based on the KPNC experience to account for differences in the study populations, baseline treatment and control rates, and sites. These baseline trends are also conservatively high so that we are not underpowered if the background hypertension control rates improve during the study period. We will have more power for larger effects as well as secondary/exploratory outcomes.

Analysis plan for Aim 2.2. We will use analysis of covariance (ANCOVA), controlling for baseline clinic-measured SBP and medication (including treatment with fixed-dose combination) to estimate the effect of health coaching including home blood pressure monitoring on 12-month change in SBP compared with propensity matched individuals in sites that did not participate in Aim 2.2 as controls. Secondary analysis will use data from all time points in generalized linear mixed models (identify, logit or log-link for continuous, binary or count outcomes, respectively) adjusting for baseline covariates and including a random participant effect.

Power for Aims 2.2. Health coaching lowers SBP by −3.9 mmHg (95% CI: −5.4, −2.3; 38 trials) and of home blood pressure monitoring lowers SBP by −2.7 mmHg (−3.6 to −1.7; 26 trials). Individual participant data meta-analyses estimate the effect of home blood pressure monitoring plus health worker support to be -6.1 mmHg (95% CI: −9.0, −3.2) lower SBP (5 trials). Assuming a two-sided alpha=0.05, we will have 80% power to detect a 6 mmHg clinic SBP difference (pre-intervention clinic SBP=160 mmHg compared with post-intervention clinic SBP=154 mmHg [group standard deviation =15]) between and after participants receive health coaching and home blood pressure monitoring with **120 participants** (random, age- and sex-stratified sample; 50% women) from 10 primary health centers, assuming a conservative intraclass correlation coefficient (ICC)=0.1 (which compares favorably with a previous ICC=0.06 from a cluster randomized trial of hypertension control in Nigeria). Because home blood pressure monitoring has a lower variance than clinic blood pressure (12 mmHg versus 15 mmHg), we will have 92% power to detect the same difference using home blood pressure data (separate standard deviations).