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Randomized Trial of an Intervention to Improve Blood Pressure Control in Stroke Survivors

See Editorial by Burke and Nallamothu

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BACKGROUND: We conducted the first-of-its kind randomized stroke trial in Africa to test whether a THRIVES (Tailored Hospital-based Risk reduction to Impede Vascular Events after Stroke) intervention improved blood pressure (BP) control among patients with stroke.

METHODS AND RESULTS: Intervention comprised a patient global risk factor control report card, personalized phone text-messaging, and educational video. Four hundred patients recruited from 4 distinct medical facilities in Nigeria, aged ≥18 years with stroke-onset within one-year, were randomized to THRIVES intervention and control group. The control group also received text messages, and both groups received modest financial incentives. The primary outcome was mean change in systolic BP (SBP) at 12 months. There were 36.5% females, 72.3% with ischemic stroke; mean age was 57.2±11.7 years; 93.5% had hypertension and mean SBP was 138.33 (23.64) mm Hg. At 12 months, there was no significant difference in SBP reduction from baseline in the THRIVES versus control group (2.32 versus 2.01 mm Hg, *P*=0.82). In an exploratory analysis of subjects with baseline BP >140/90 mm Hg (n=168), THRIVES showed a significant mean SBP (diastolic BP) decrease of 11.7 (7.0) mm Hg while control group showed a significant mean SBP (diastolic BP) decrease of 11.2 (7.9) mm Hg at 12 months.

CONCLUSIONS: THRIVES intervention did not significantly reduce SBP compared with controls. However, there was similar significant decrease in mean BP in both treatment arms in the subgroup with baseline hypertension. As text-messaging and a modest financial incentive were the common elements between both treatment arms, further research is required to establish whether these measures alone can improve BP control among stroke survivors.

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Key Words: blood pressure ■ hypertension ■ risk factor ■ secondary prevention ■ stroke

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WHAT IS KNOWN

- Use of evidence-based therapies for stroke prevention in sub-Saharan Africa is extremely poor and few if any stroke prevention trials have been conducted in the region.
- Elevated blood pressure (BP) is the premier modifiable risk factor for stroke, and recurrent stroke risk is minimized with a systolic BP optimized between 120 and 140 mm Hg in stroke survivors.

WHAT THIS STUDY ADDS

- We designed a culturally appropriate, contextually relevant multipronged intervention using elements of the Chronic Care Model with involvement of all key stakeholders. In a randomized controlled trial, we tested the intervention which comprised a patient global risk factor control report card, educational video, and motivational text messages.
- At 12 months, the change in mean systolic BP among those randomized to the intervention was not better than the controls. In a subset analysis of subjects with baseline BP >140/90 mm Hg (n=168), THRIVES (Tailored Hospital-based Risk reduction to Impede Vascular Events after Stroke) showed a significant mean systolic BP (diastolic BP) decrease of 11.7 (7.0) mm Hg and control group showed a significant mean systolic BP (diastolic BP) decrease of 11.2 (7.9) mm Hg at 12 months.
- As text-messaging and modest financial incentive were the common elements between both treatment arms, further research is required to establish whether these measures alone can improve BP control among stroke survivors.

Rates of stroke occurrence in low-and middle-income countries have approximately doubled over the past 4 decades in contrast to high-income countries where the burden has decreased.[1,2] In particular, sub-Saharan Africa has the highest prevalence, incidence and 3-year fatality for stroke, and the burden continues to increase due to ongoing epidemiological transition.[3–5]

The stroke quadrangle (surveillance, prevention, acute care, rehabilitation), of which prevention is a key component, has been proposed to combat this escalating burden.[6] Longitudinal studies, including Stroke Investigative Research and Educational Network, have identified a number of modifiable risk factors, which if properly modified could substantially lessen the burden of stroke.[7] In Africa, hypertension is the leading risk factor.[7] Therefore, optimal blood pressure (BP) control needs to be at the center of any serious effort to lessen the burden of stroke in Africa. Indeed a 10 mm Hg reduction in systolic BP (SBP) reduces the risk of stroke by 60%.[8,9] However, there have been few, if any, dedicated clinical trials of stroke in sub-Saharan Africa, to seek to optimize BP control within the setting of limited resources.

In this first-of-its-kind implementation science trial of BP control in stroke survivors in Africa, we developed, and tested, in a blinded randomized controlled trial, whether a multipronged tailored THRIVES (Tailored Hospital-based Risk reduction to Impede Vascular Events after Stroke) intervention improves SBP control among a cohort of 400 patients with a recent stroke discharged from 4 diverse medical facilities settings in Nigeria.

METHODS

Details of the study protocol are published elsewhere.[10] However, all essential aspects are highlighted below. Our analysis follows the Consolidated Standards of Reporting Trials (CONSORT) 2010 recommendations for analysis of randomized controlled trial data. The data that support the findings of this study are available from the corresponding author on reasonable request.

Setting and Sites

Nigeria, the most populous African country, provides an ideal setting for this initiative to develop and test the efficacy of a tool to control BP levels among stroke survivors in low-and middle-income countries. Over 90% of the population had access to mobile phones.[11] The study was conducted at 4 sites in Nigeria. These 4 facilities were chosen to capture key aspects of the diverse South-western Nigeria population as well as hospital types: the University College Hospital Ibadan, the first teaching hospital in Nigeria, which receives referral from all over Nigeria and Africa; Blossom Center for Neuro-Rehabilitation, Ibadan, a rehabilitation referral center which accommodates and provides physical therapy, occupational therapy, and speech/cognitive therapy facilities for neurologically impaired patients; Federal Medical Center, Abeokuta, a 250–bed regional tertiary center which receives patients from neighboring counties and states; and Sacred Heart Hospital, Abeokuta, a Catholic missionary hospital, which provides secondary medical care to a low-income community in South West Nigeria.

Eligibility Criteria

Patients aged ≥18 years, with stroke-onset within one-year, and access to mobile phone were included. Hypertension was not an inclusion criterion. We excluded those with severe aphasia or difficulty with communication, any medical condition that would limit participation in follow-up assessments such as severe cognitive impairment/dementia (modified Community Screening Instrument for Dementia- score ≤20), or severe global disability (modified Rankin Score ≥3). CONSORT diagram is presented in Figure 1.

Baseline Assessment

Baseline socio-demographic and clinical data were obtained from all patients using a standardized questionnaire. This included the patient's demographic status, vascular risk data, stroke type and severity, anthropometric measurements and BP.

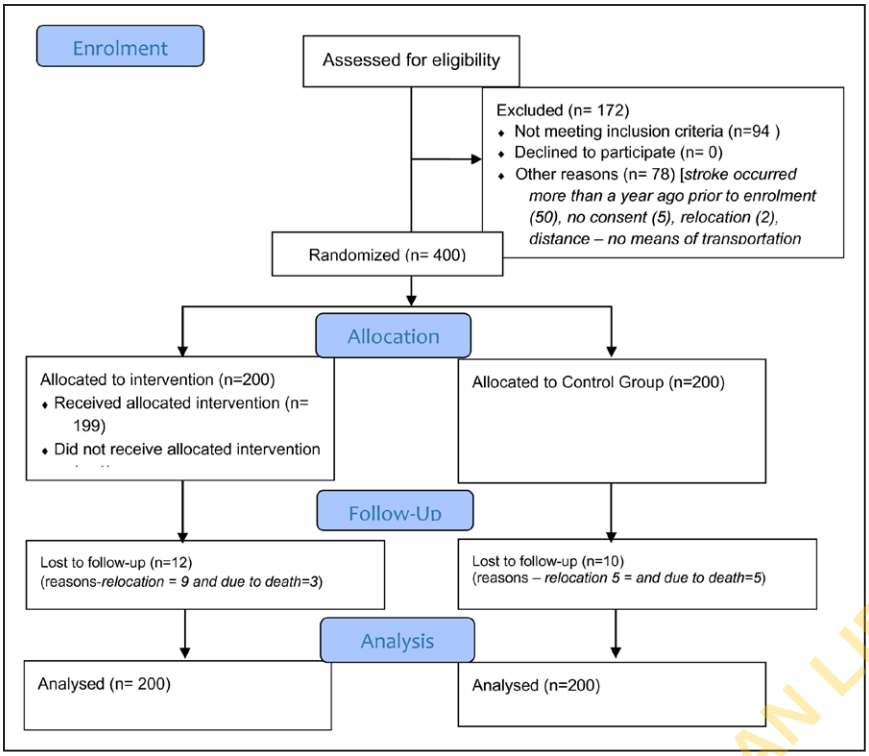

Figure 1. CONSORT flow diagram.

Randomization

Once eligibility and consent were confirmed, participants were randomly assigned to THRIVES intervention versus standard post-discharge management in a 1:1 allocation ratio, stratified by study site, stroke type, and by time from qualifying stroke occurrence (<2 weeks versus >2 weeks). The randomization scheme was developed and maintained by the study biostatistician. We randomized patients instead of clusters, because it is the most statistically efficient method for demonstrating efficacy, and thus would require the smallest sample size.

Experimental Group (THRIVES Intervention)

The intervention comprised the chronic care model components of delivery system redesign (increased follow-up visits, preappointment phone texts), self-management support (patient report card, post-clinic follow-up phone texts, waiting room educational video), and clinical information systems (patient report card as part of medical chart, hospital registry). The intervention was applied over a period of one-year after enrollment.

1. Preappointment phone text: Asking patients to arrive an hour early for their appointment.
2. In-clinic educational video: While in the waiting room the patients were asked to watch a stroke awareness educational video containing dramatized stroke scenarios, educational messages, and questions on the material taught. The content was structured to be consistent with the content and sequence of material in checklist form on the patient report card. It was developed based on understanding of the barriers and facilitators of stroke prevention in the qualitative phase as well as contributions from opinion leaders in the society and transdisciplinary team of health personnel and administrators.[12,13] The video ran repeatedly for every 30 to 45 minutes throughout the clinic.
3. Patient report card: When the patient met with the physician the material of the video was briefly discussed. The physician then showed the patient the customized report card (Appendix 1 in the Data Supplement) and went over the patient's current versus optimal control of key stroke risk factors (including BP). After the discussion, the patient or caregiver signed the report card, and a copy was given to the patient and another placed in the medical chart. If this was a return visit, progress since the last visit was queried, and specific difficulties in optimizing per-guideline risk factor control[14] discussed with a plan of action.
4. Post-clinic phone text: At the end of given THRIVES clinic, the physician who saw the patient prescribed a brief structured telephone text which was sent to the patient's mobile (cell) phone emphasizing the areas requiring better risk factor control.
5. Outpatient stroke registry: Each patient was tracked in an electronic registry. The registry contained data written on the report cards. It also contained contact information on how the subject can be notified for care coordination telephone texts.

Control Group

The control group (CG) received a standardized version of the usual care delivered at each hospital. This consisted of risk factor identification and control without the additional interventions introduced in this trial. We expected some variation in the standard care practices among hospitals and addressed this in the study design by stratifying randomization by recruiting hospital.

In addition to the usual care, the control subjects were provided with the name and contact information of a phone contact.

All Participants

To maximize retention, all participants were contacted by phone every month simply to remind them of study participation and appointments. All participants were sent regular study updates by bulk phone-based text messages and received modest financial incentives of $30 per encounter for being in the trial.

Masking and Minimizing Contamination

The subjects and the assessors were not aware of the treatment group to which individual subjects belonged. (The subjects were not told which intervention was the test or control).

The report card was only issued to and discussed with THRIVES intervention patients. Treatment-specific phone texts were only sent to intervention patients. Group video therapy was applied only to the intervention patients on their clinic days in a closed room. We ensured that control patients were not scheduled to come to the clinic on the same day as intervention patients, and control patients were scheduled to see other noninvestigator neurologists/doctors by the research coordinator. Outcome assessments were performed by blinded adjudicators on nonclinic days.

Primary Outcome Measure

The primary outcome is mean change in SBP at one-year. SBP was specifically chosen given its relatively stronger relationship with vascular risk (versus diastolic BP [DBP]) and more reliable measurements.[15,16]

Outcome Assessment

Trained research coordinators (blinded assessors) who are blinded to the randomization arm (and with no contact with THRIVES clinical team) collected study outcomes on all participants. Assessments were conducted in person at baseline, 1 month, 3 months, 6 months, and 12 months. At each in person assessment, 2 BP measurements were obtained and averaged from each subject with use of the Omron HEM-907XL26 according to a standardized protocol provided by the manufacturer about cuff size, cuff application, body position, and time intervals when taking a measurement.

Subject Accrual and Retention

We enrolled study participants from September 2014 to September 2016 and completed follow-up in September 2017.

We chose a one-year primary time point for follow-up to balance maximizing study follow-up with studying a clinically useful time period of compliance. Strategies for participants retention included regular telephone contacts; in the CGs these did not include material regarding stroke-related health care issues.

Fidelity

To address intervention fidelity, we developed defined manuals/protocols/algorithms that explicitly spelt out the THRIVES study purpose, goals/objectives, and essential or critical elements and all the content that must be covered.

Adverse Events and Data Safety Monitoring

No negative health effect of the intervention was recorded. A task force monitored the trial with quarterly meetings conducted throughout the trial.

Standard Protocol Approvals, Registrations, and Patient Consents

Ethical approval was obtained and renewed periodically to cover the entire treatment period from the Institutional Review Boards of the participating institutions. Trial participants gave written informed consent before enrollment. The trial was registered at http://www.clinicaltrials.gov.

Sample Size and Statistical Power

The sample size calculation and power analyses were based on the primary outcome of change in SBP. A change in BP is defined as the difference between the BP at month 12 and baseline. Sample size calculations were based on a 2-sided, 2-sample *t* test to compare mean 12-month change in SBP between the THRIVES intervention and the CG management groups. Based on data from University College Hospital Ibadan, the mean SBP for persons with a history of stroke whose SBP is above 120 mm Hg is 153.1 mm Hg, and the SD is 22.7 mm Hg. Given a type I error of 0.05, a type II error of 0.1 (or power of 0.9), a 2-sided test, a SD of 22.7 mm Hg at baseline in the control arm, and assuming a 12-month

change in SBP in the control arm of 0 mm Hg and a correlation between the baseline and 12-month SBP of 0.7, 108 subjects in each treatment arm (or 216 subjects in total) will permit detection of a difference of 7 mm Hg in SBP, which corresponds to an effect size of 0.4 between the 2 treatment arms. The minimum sample size in the trial was based on the need to power the trial based on the ability to detect the smallest clinically meaningful difference in treatment effect between the 2 intervention groups. This difference of 7 mm Hg in SBP between the 2 treatments is smaller than the 10 mm Hg clinically meaningful threshold recommended in Secondary Prevention guidelines,[14] and thus we have sufficient statistical power with the estimated sample size to detect a clinically relevant benefit in the full sample but not in the subgroup analysis. In fact, we do have more than sufficient power for the BP outcomes using linear mixed model and generalized estimating equations.[17] The 1-year all-cause death rate after stroke is about 30% in this population. As such applying a conservative estimate of a 54% retention rate to account for attrition factors, the target number for enrolment was 400.

Statistical Analysis

Analysis incorporated the intent-to-treat principle, namely, all randomized participants were included in the analysis according to their intervention assigned at baseline. More details about the study design and analysis are given in the published study protocol.[17] All results are reported as point estimates (proportions or mean differences between intervention groups, as appropriate) and 2-sided *P* values denoting statistical significance. As stipulated in CONSORT 2010,[18] we report both baseline covariate adjusted and unadjusted analysis. Distributions of baseline characteristics between the THRIVES intervention and CGs were compared using a 2-sample *t* test for continuous measures and χ^2 test for categorical measures. We used a mixed-effects regression model to determine if the THRIVES intervention produced a greater decrease in SBP from baseline compared with the CG at months 1, 3, 6 and 12 of the intervention period (with the primary outcome being the comparison between the 2 groups in the baseline to month 12 difference). This model included intervention arm, baseline age, time and time by intervention interaction as fixed-effects. We used auto-regressive (AR[1]) correlation structure to account for the correlation among the repeated measures of SBP.[17] This mixed ANCOVA model addresses both the ANCOVA type analysis (unadjusted) and adjusted for the correlation due to repeated measurements of BP. In addition, based on CONSORT 2010 and arguments given in several publications,[19,20] any covariate of interest that were unbalanced at baseline (eg, age and baseline stroke levity scale SLS score) were included in the mixed-effects model. Prespecified covariates of interest include the stratification factors (site, stroke subtype, time from qualifying stroke occurrence) and other known vascular risk factors. In exploratory analyses, additional comparisons of the 2 treatment arms were also made based on a subset by level of prerandomization (SBP/DBP >140/90). We also compared the 2 arms in terms of the proportion of subjects with controlled SBP (SBP/DBP <140/90) over time using logistic regression models where the odds ratio and corresponding 95% CI are estimated using general estimating equations with empirical SE.[17] We used auto-regressive (AR[1]) correlation structure to account for the correlation among the repeated measures of SBP.[17] Similar approaches were used for comparing the 2 arms with respect to DBP and for estimating changes in patient report card scores over time in the THRIVES arm. Results were reported under the assumption of missing at random after checking that there were no evidence supporting differences in baseline BP and other baseline characteristics between those who dropped out and those who did not using a logistic regression model.[17] SAS version 9.4 was used for all analysis.

RESULTS

Baseline Characteristics

The study sample comprised 200 subjects in each treatment arm with 36% females and a mean baseline age of 57.2 (SD 11.7) years overall (Table 1). Most of the study subjects had some form of education. About 45% had higher education or more with about 30% in skilled/professional occupations. Clinically, 72% of the subjects had ischemic stroke. Most of the subjects had mild stroke (mean National Institutes of Health Stroke Scale =4.0; and SLS =12.2). There was no significant difference between those who completed the study and those who did not (Table I in the Data Supplement). There was no significant difference between the treatment arms in sex, stroke severity (National Institutes of Health Stroke Scale), pre-enrollment hypertension, and diabetes mellitus. Similarly, there was no difference in preadmission and in-hospital medication (Table II in the Data Supplement). However, the CG was significantly younger (Table 1). We, therefore, adjusted for age in the subsequent analyses.

Treatment Outcome

Mean SBP decreased from 138.6 to 136.5 mm Hg in the intervention group and from 138.1 mm Hg at baseline to 136.2 mm Hg at 12 months for the CG (Table 2 panel 1). The within-group analyses in intervention subjects with baseline BP >140/90 mm Hg (n=89) showed a significant decrease in mean SBP from 157.3 to 145.1 mm Hg, a mean decrease of 11.7 mm Hg from baseline to 12 months (Table 2 panel 3, Figure 2). Similarly, there

Table 1. Baseline Background and Clinical Characteristics of Participants in Both THRIVES and Control Group

	All Records				Subset>SBP/DBP 140/90 mm Hg		
	Total (n=400)	Control (n=200)	THRIVES (n=200)		Control (n=79)	THRIVES (n=89)	
	n (%) or Mean (SD)	n (%) or Mean (SD)	n (%) or Mean (SD)		n (%) or Mean (SD)	n (%) or Mean (SD)	
Study site				0.967			0.179
Blossom	20 (5.0%)	10 (5.0%)	10 (5.0%)		1 (1.3%)	6 (6.7%)	
FMC	113 (28.3%)	56 (28.0%)	57 (28.5%)		25 (31.6%)	22 (24.7%)	
Sacred Heart	51 (12.8%)	24 (12.0%)	27 (13.5%)		15 (19.0%)	12 (13.5%)	
UCH	216 (54.0%)	110 (55.0%)	106 (53.0%)		38 (48.1%)	49 (55.1%)	
Sex				0.299			0.905
Male	254 (63.5%)	132 (66.0%)	122 (61.0%)		49 (62.0%)	56 (62.9%)	
Female	146 (36.5%)	68 (34.0%)	78 (39.0%)		30 (38.0%)	33 (37.1%)	
Age, y	57.22 (11.73)	55.86 (11.84)	58.58 (11.49)	0.020	56.47 (11.42)	58.01 (10.50)	0.363
Stroke type				0.920			0.411
Ischemic	279 (72.3%)	134 (72.0%)	145 (72.5%)		52 (71.2%)	58 (65.2%)	
Hemorrhagic	107 (27.7%)	52 (28.0%)	55 (27.5%)		21 (28.8%)	31 (34.8%)	
NIHSS score	3.99 (3.50)	3.85 (3.53)	4.14 (3.46)	0.413	4.75 (3.72)	4.41 (3.23)	0.538
SLS score	12.23 (2.58)	12.62 (2.20)	11.85 (2.85)	0.026	12.50 (1.97)	11.47 (2.97)	0.049
Systolic BP, mm Hg	138.3 (23.6)	138.1 (24.5)	138.6 (22.9)	0.813	159.1 (23.8)	157.3 (19.6)	0.578
Diastolic BP, mm Hg	83.0 (15.2)	83.5 (14.9)	82.5 (15.4)	0.538	93. (15.8)	92.0 (15.5)	0.455
BMI, kg/m^2	26.20 (5.08)	26.27 (5.39)	26.12 (4.77)	0.788	26.54 (6.08)	26.31 (4.74)	0.801
Ever used tobacco	89 (22.3%)	40 (20.0%)	49 (24.6%)	0.267	17 (21.5%)	20 (22.7%)	0.851
Alcohol use				0.446			0.639
Former	176 (44.1%)	83 (41.5%)	93 (46.7%)		43 (54.4%)	42 (47.7%)	
Current	29 (7.3%)	17 (8.5%)	12 (6.0%)		3 (3.8%)	5 (5.7%)	
Never	194 (48.6%)	100 (50.0%)	94 (47.2%)		33 (41.8%)	41 (46.6%)	

BMI indicates body mass index; BP, blood pressure; DBP, diastolic BP; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic BP; SLS, Stroke Levity Scale; and THRIVES, Tailored Hospital-Based Risk Reduction to Impede Vascular Events After Stroke.

was a mean 11.2 mm Hg decrease in SBP in the above-target (BP >140/90 mm Hg) subgroup of the CG (Table 2 panel 3). Figure 2 showed decrease in SBPs in those with baseline SBP above 140mmHg, and optimization of SBPs in those with baseline SBP <140mmHg over 12 months.

Mean DBP decreased from 82.5 to 79.3 mm Hg in the intervention group and from 83.5 mm Hg at baseline to 80.7 mm Hg at 12 months for the CG (Table III, panel 1 in the Data Supplement). The within-group analyses in intervention subjects with baseline BP >140/90 mm Hg (n=88) showed a significant decrease in mean DBP from 92 to 84 mm Hg, a mean decrease of 8 mm Hg from baseline to 12 months (Table III, panel 3 in the Data Supplement, Figure 2). A similar decrease was also observed in the CG.

The proportions of patients with BP controlled improved from baseline to 12 months (Table IV in the Data Supplement).

In the intervention group, the mean percentage patient report card score increased significantly from 64% at baseline to 82% at 12 months in all intervention subjects; and from 62% at baseline to 80% in the subgroup with BP >140/90 at baseline (Figure 3).

Mixed Effect and Subgroup Analyses

In summary, in the unadjusted ANCOVA analysis, there was no interaction between baseline SBP and treatment arm (P=0.8050), and there was no difference between the 2 groups (mean difference =0.04, P=0.984). Similarly, there was no interaction between baseline DBP and treatment arm (P=0.3699), and there was no difference between the 2 groups (mean difference =0.52, P=0.675).

In the mixed (adjusted) ANCOVA analysis of the between group effects for SBP there was no significant interaction between the 2 arms at each time point (Table 3). Similarly, there was neither treatment effect (P=0.364) nor any significant difference between baseline and each follow-up time in both SBP and DBP.

DISCUSSION

Key Inferences

We successfully developed and tested a multipronged intervention that was designed to improve SBP control at 12 months after an index stroke in sub-Saharan Africa

Table 2. Mean SBP Comparisons and SBP Reduction Over Time, Mixed Effect Analysis

Month	Treatment Arm					
	Control			THRIVES		
	N	Mean (SD)	Within Group, *P* Value	N	Mean (SD)	Within Group, *P* Value
All records						
0	199	138.1 (24.5)	REF	199	138.6 (22.9)	REF
1	197	137.7 (23.2)	0.85	192	137.9 (21.6)	0.7445
3	193	137.4 (20.1)	0.81	190	138.2 (22.2)	0.71
6	194	136.8 (21.4)	0.51	189	138.6 (21.8)	0.8879
9	190	135.0 (22.4)	0.08	188	138.4 (20.8)	0.8823
12	188	136.2 (21.2)	0.17	186	136.5 (22.3)	0.0908
Baseline SBP/DBP >140/90 mm Hg						
0	79	159.1 (23.8)	REF	89	157.3 (19.6)	REF
1	79	151.6 (26.6)	0.03	86	149.9 (21.1)	0.0355
3	75	150.0 (21.9)	0.01	87	148.2 (21.5)	0.0042
6	77	147.5 (24.7)	0.00	87	147.2 (22.6)	0.0012
9	75	145.6 (27.3)	<.0001	85	147.1 (20.8)	0.0006
12	74	148.5 (22.8)	<.0001	84	145.1 (22.6)	<.0001
SBP Reduction from Baseline to Follow-up months						
Month	Control			THRIVES		
	N	Mean (95% CI)		N	Mean (95% CI)	Between Group *P* Value
All records						
1	197	0.56 (–1.97 to 3.09)		192	1.13 (–1.52 to 3.78)	0.9195
3	193	0.34 (–2.3 to 2.98)		190	1.31 (–1.8 to 4.42)	0.9290
6	194	1.38 (–1.56 to 4.32)		189	0.86 (–2.2 to 3.92)	0.7144
9	190	3.2 (–0.06 to 6.46)		188	0.55 (–2.51 to 3.61)	0.2575
12	188	2.01 (–0.87 to 4.89)		186	2.32 (–0.86 to 5.5)	0.8154
Baseline SBP/DBP >140/90 mm Hg						
1	79	7.53 (2.57 to 12.47)		86	7.57 (3.24 to 11.9)	0.9125
3	75	8.98 (3.85 to 14.11)		87	9.26 (4.47 to 14.05)	0.9978
6	77	11.82 (6.45 to 17.19)		87	10.05 (5.39 to 14.71)	0.6963
9	75	13.88 (7.1 to 20.66)		85	9.71 (5.08 to 14.34)	0.3666
12	74	11.18 (5.61 to 16.75)		84	11.71 (7.01 to 16.41)	0.7451

DBP indicates diastolic blood pressure; REF, reference; SBP, systolic blood pressure; and THRIVES, Tailored Hospital-Based Risk Reduction to Impede Vascular Events After Stroke.

even though the findings did not support our hypothesis. There have been few, if any, dedicated clinical trials seeking to address key research questions among patients with stroke in sub-Saharan Africa. While we observed progressive improvement in BP control in both intervention and CGs, there was no significant difference in lowering of systolic BP at 12 months in the 2 study groups.

It is not immediately clear why there was a discrepancy between seemingly positive global influences of the intervention and its neutral effects on systolic BP reduction. However, potential explanations may include: (1) the mean SBP/DBP in the overall groups was already below 140/90 mm Hg at baseline. Therefore, it was likely harder for us to achieve a significant difference in effect size in favor of the intervention between the 2 groups. Correspondingly it did appear that in the subset of trial participants with BP >140/90 mm Hg at baseline, in both treatment arms, optimization of systolic BP (Figure 2) to a safer band was achieved with those with SBP above 140 mm Hg at baseline dropping towards 140 mm Hg sharply in the first 3 months and plateauing, while those below 140 mm Hg at baseline remained the same. In both arms, in the subgroup with BP at baseline >140/90 mm Hg, the magnitude of reduction in SBP was >10 mm Hg, while the magnitude

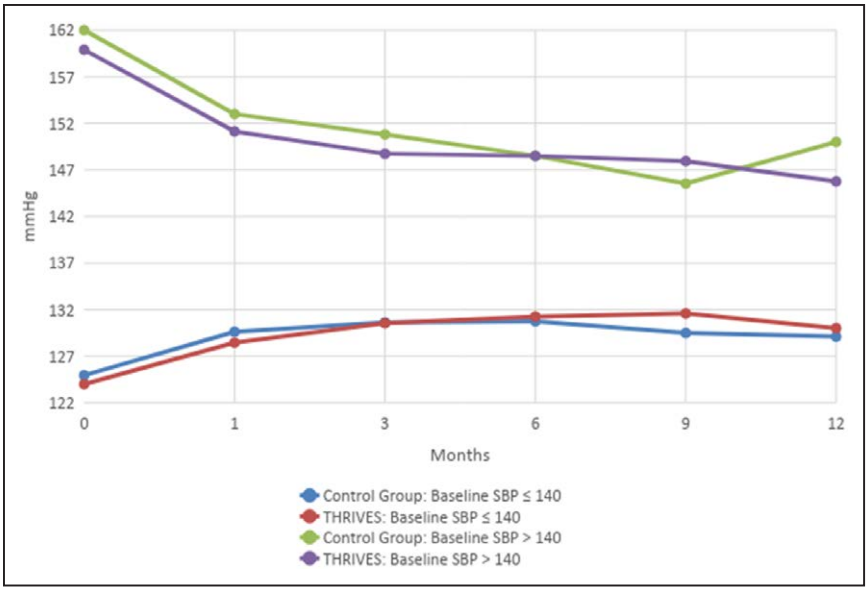

Figure 2. Mean systolic blood pressure (SBP) trend over 12 mo for standard care and Tailored Hospital-Based Risk Reduction to Impede Vascular Events After Stroke (THRIVES) intervention arms.

of reduction in DBP was >5 mm Hg. SBP decrease of 10 mm Hg and DBP of >5 mm Hg are the clinically meaningful thresholds recommended in Secondary Prevention guidelines.[14] Stroke risk is reduced by 60% with a SBP/DBP decrease of 10/5 mm Hg.[8] On the other hand, in both treatment groups with SBP already below 140 mm Hg (Figure 2), a net decrease in mean SBP was not observed. This is desirable because in stroke survivors, compared to a SBP of 131 to 141 mm Hg, a SBP of 120 mm Hg or less has been associated with a 61% greater risk of stroke, acute myocardial infarction and death.[9,21,22] (2) Standard of care after a stroke in Nigeria involves minimal follow-up or close scrutiny by the healthcare system. Since the only common elements between the intervention and CGs were text-messaging and a modest financial incentive to encourage retention, it is conceivable that the higher than usual attention given by the health system to the control patients (which varied from typical practice) may have minimized some of the advantage of the intervention group. These could have assisted the subjects to procure medications and keep clinic appointments better than usual. The issue of how usual is usual care in pragmatic intervention studies of this type continues to be an issue of discussion.[23]

Limitations, Lessons Learnt, and Future Directions

First, the CG also received some components of the intervention given to the THRIVES intervention group. These components were administered to the CG to reduce attrition but could also have enhanced adherence to BP medications. In subsequent investigation, a CG that is almost identical to the usual care, with no intervention, would be more appropriate.

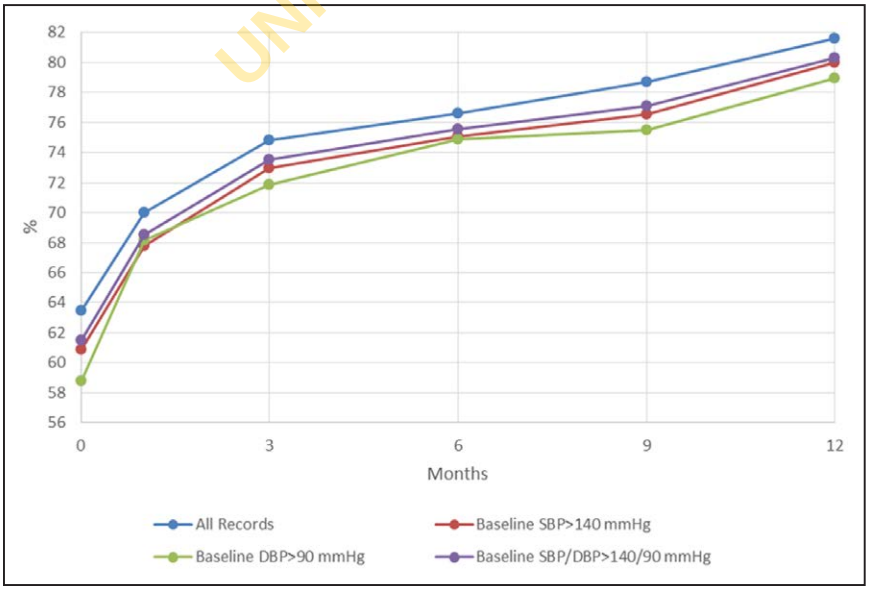

Figure 3. Mean patient report card total score percent over 12 mo. DBP indicates diastolic blood pressure; and SBP, systolic blood pressure.

Table 3. Comparison of Mean Baseline SBP With Each Follow-Up Mean (Months 1, 3, 6, 9 and 12) Between the THRIVES and Control arms for all Records and for Participants With BP >140/90 mm Hg Using Mixed-Effects Model

	All Records (n=400)				BP >140/90 mm Hg (n=168)			
	Mean Difference in Systolic BP (95% CI)				Mean Difference in Systolic BP (95% CI)			
	Unadjusted	*P* Value	Age Adjusted	*P* Value	Unadjusted	*P* Value	Age Adjusted	*P* Value
THRIVES vs control	0.55 (–3.82 to 4.92)	0.805	0.26 (–4.1 to 4.67)	0.8983	–1.87 (–8.79 to 5.05)	0.596	–1.82 (–8.73 to 5.09)	0.6043
Control (month 1)	–0.38 (–4.44 to 3.68)	0.8528	–0.38 (–4.44 to 3.68)	0.8538	–7.53 (–14.4 to –0.66)	0.0318	–7.53 (–14.4 to –0.66)	0.0318
Control (month 3)	–0.49 (–4.4 to 3.42)	0.8054	–0.49 (–4.4 to 3.42)	0.805	–9.27 (–16.01 to –2.53)	0.0072	–9.27 (–16.01 to –2.53)	0.0072
Control (month 6)	–1.23 (–4.89 to 2.43)	0.5095	–1.23 (–4.88 to 2.42)	0.5087	–11.78 (–18.19 to –5.37)	0.0003	–11.78 (–18.19 to –5.38)	0.0003
Control (month 9)	–2.91 (–6.17 to 0.35)	0.0796	–2.92 (–6.18 to 0.34)	0.0794	–13.39 (–19.24 to –7.54)	<0.0001	–13.98 (–15.33 to –11.47)	<0.0001
Control (month 12)	–1.77 (–4.3 to 0.76)	0.1701	–1.77 (–4.3 to 0.76)	0.1699	–10.67 (–15.36 to –5.98)	<0.0001	–10.67 (–15.36 to –5.99)	<0.0001
THRIVES (month 1)	–0.31 (–6.07 to 5.45)	0.9171	–0.3 (–6.05 to 5.46)	0.9195	0.54 (–8.92 to 10)	0.9118	0.54 (–8.93 to 10)	0.9125
THRIVES (month 3)	–0.26 (–5.8 to 5.28)	0.9271	–0.25 (–5.79 to 5.28)	0.929	0.0177 (–9.23 to 9.26)	0.997	0.02 (–9.23 to 9.26)	0.9978
THRIVES (month 6)	0.96 (–4.24 to 6.16)	0.7178	0.97 (–4.22 to 6.15)	0.7144	1.76 (–7.04 to 10.56)	0.6956	1.75 (–7.04 to 10.55)	0.6963
THRIVES (month 9)	2.66 (–1.96 to 7.28)	0.259	2.67 (–1.95 to 7.29)	0.2575	3.7 (–4.33 to 11.73)	0.3662	3.7 (–4.33 to 11.74)	0.3666
THRIVES (month 12)	–0.43 (–4.02 to 3.16)	0.8138	–0.43 (–4.02 to 3.17)	0.8154	–1.06 (–7.49 to 5.37)	0.7456	–1.07 (–7.5 to 5.37)	0.7451

Estimate shows mean differences in systolic BP (mm Hg) for each covariate category compared to the reference category. Arm: THRIVES versus control: 95% CI. Control, mean difference in systolic BP from baseline to respective months in the control group after adjusting for other covariates in the model. THRIVES, mean difference in systolic BP from baseline to respective months in the THRIVES and control group after adjusting for other covariates in the model. BP indicates blood pressure; and THRIVES, Tailored Hospital-Based Risk Reduction to Impede Vascular Events After Stroke.

Second, the trial could have focused solely on those subjects with BP >140/90 mm Hg with adequate sample size and power to demonstrate differential treatment effect, if any. However, the inclusion of those with BP <140/90 mm Hg enabled us to observe the optimization phenomenon whereby SBPs narrowed to a safe band over the treatment period. Third, it is desirable to determine the long-term effect of the intervention on other clinical outcomes, including recurrent stroke and cardiovascular events over 5 years.

Implications, Strengths, and Significance

Several aspects of the project are innovative: (1) The utilization of a multipronged intervention in the native low- and middle-income countries tongue consisting of stroke patient report card tool, mobile (cell) phone technology, and video therapy; (2) Randomized testing of the tailored intervention with regard to its efficacy in reducing the premier modifiable risk factor for stroke, elevated BP, among stroke survivors in a low-and middle-income country not typically familiar with clinical effectiveness trials. The need to improve stroke preventive care is particularly pressing in developing countries where resources are few, and the burden of stroke is disproportionately heavy.[1,6] In Africa, this is the first study conducted to design, implement, and evaluate intervention measures aimed at modifying stroke risk based on preliminarily identified barriers and facilitators for utilization of such measures.[12,13,24] Our study applied multipronged interventions with observed optimization of BP in individuals with recent stroke, although this was not statistically significantly better than the CG. As text-messaging and modest financial incentive for transportation to clinic appointment and drug procurement were the common elements between both treatment arms, further investigation is required to establish whether these measures alone can improve BP control among stroke survivors. This will require testing these interventions against a CG receiving none of these interventions.

Conclusions

In this rare stroke trial in sub-Saharan Africa, despite an improvement in global vascular risk factor control at one-year post-stroke, the THRIVES intervention did not significantly reduce SBP compared with controls. Both treatment arms had similar clinically significant decrease of BP (>10/5 mm Hg) only in the subgroup with BP >140/90 mm Hg at baseline. Further research will need to evaluate why the intervention did not have a more favorable impact on change in systolic BP after stroke and whether some aspects of the intervention worked better than others.

ARTICLE INFORMATION

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