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Treatment of prehypertension among adults with HIV

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Objective: Elevated blood pressure (BP), even at prehypertensive levels, increases cardiovascular disease risk among people with HIV (PWH); yet international guidelines in low-income countries recommend treatment initiation at BP at least 140/90 mmHg. We determined the efficacy, feasibility, and acceptability of treating prehypertension in PWH in Haiti.

Design: An unblinded randomized clinical trial (enrolled April 2021–March 2022) with 12-month follow-up.

Setting: GHESKIO Centres, Port-au-Prince, Haiti.

Participants: Two hundred fifty adults with HIV with prehypertension (SBP 120–138 or DBP 80–89) not on medication, aged 18–65 years, virally suppressed, and without pregnancy, diabetes, or kidney disease.

Intervention: Participants were randomized to treatment (amlodipine 5 mg) or control (no amlodipine unless two BP $\geq$140/90 mmHg).

Main outcome measure: Primary outcome was mean change in SBP between intervention versus control groups from enrollment to 12 months.

Results: Among 250 adults, median age was 49 years, 40.8% were women. Baseline median BP was 129/78 mmHg intervention versus 128/77 mmHg control. After 12 months, the difference in mean change between study groups for SBP was -5.9 mmHg [95% confidence interval (95% CI) -8.8 to -3.0] and for DBP was -5.5 mmHg (95% CI -7.9 to -3.2). At 12 months, 5.6% intervention and 23.0% control participants developed incident hypertension (hazard ratio 0.18; 95% CI 0.07–0.47). There were no differences in viral load suppression at 12 months or drug-related serious adverse events. Intervention acceptability was high among providers and participants in qualitative interviews.

Conclusion: In PWH in a resource-poor setting, prehypertension treatment was feasible, acceptable, and effective in reducing mean SBP and incident hypertension.

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Introduction

The leading modifiable cardiovascular disease (CVD) risk factor among people with HIV (PWH) worldwide is elevated blood pressure (BP), raising it as a potential pragmatic target for CVD prevention [1,2]. PWH are at a higher risk for elevated BP, and two-fold greater risk for CVD compared to the general population [3]. The dual burden of HIV and CVD is highest in low and middle-income countries (LMICs), where over 31 million PWH are living longer from ART advances, underscoring the need for CVD prevention [1,3,4].

Currently, the WHO and national guidelines recommend PWH initiate antihypertension medication at SBP/ DBP at least140/90 mmHg, the same threshold as the general population [5]. In contrast, the guidelines have lowered the BP threshold for other inflammatory diseases with increased CVD risk, including diabetes and kidney disease [5]. Treatment of prehypertension in PWH may reduce CVD events, similar to what has been shown for people with diabetes, chronic kidney disease, and nonobstructive coronary disease [6–9].

Haiti has the highest HIV prevalence in the Western hemisphere [10], and CVD is the leading cause of death among adults with elevated BP the most common risk factor [11,12]. Hypertension at time of ART initiation is associated with an adjusted mortality hazard ratio of 2.47 among a cohort of PWH in Haiti [13]. As a first step to evaluate the effect of earlier treatment of elevated BP among PWH, we conducted an unblinded randomized clinical trial to determine if initiation of antihypertensive treatment among PWH with prehypertension is feasible, acceptable, and can decrease BP in the low-resource setting of Haiti.

Materials and methods

Design overview

This unblinded randomized clinical trial was conducted at Groupe Haitien d'Etude du Sarcome de Kaposi et des Infections Opportunistes Centers (GHESKIO) in Port-au-Prince, Haiti. GHESKIO is a medical nonprofit organization that has operated continuously over four decades in Haiti to provide clinical care and conduct research on infectious and chronic diseases.

Participant recruitment occurred at the GHESKIO Adult HIV clinic as well as through a review of the electronic medical record to preidentify PWH who met inclusion criteria. Two BP measurements in clinic, on different days, in the range of SBP 120–139 mmHg or DBP 80–89 mmHg were needed to qualify for the study. Per 2017 American Heart Association guidelines, this traditional prehypertensive range has been redefined to elevated BP (systolic 120–129, diastolic < 80) and hypertension stage 1 (systolic 130–139, diastolic 80–89) [14]. The prior terminology and definition of prehypertension was chosen because these values are still considered below the antihypertensive treatment threshold for the general population including PWH, in WHO guidelines and in Haiti's national guidelines, which are similar to many other low-middle income countries [15]. Eligible participants were introduced to the study, provided written informed consent in Creole, and underwent screening procedures, including screening laboratories for pregnancy, diabetes, and chronic kidney disease. Those without evidence of pregnancy, diabetes, or renal disease proceeded with randomization.

Data were collected at an enrollment visit, and follow-up visits in the clinic and community. Additional information on study procedures and data collection have been published previously [16] and can be found in the Supplement. For all visits, BP measurements were taken following American Heart Association and WHO guidelines [14,17] using automated oscillometric machines (OMRON 742–5 series in the community, OMRON HEM 907 in clinic). After resting for 5 min, the participant had three BPs measured, separated by 1-min intervals. The average of the three BPs is the BP for the study visit. These are the same procedures as used in the SPRINT trial [6].

The trial was designed by the principal investigators and funded by the National Institutes of Health. The funder played no role in the study design, study administration, conduct of analyses, or drafting the manuscript. The study protocol and ethical consent forms were approved by Weill Cornell Medicine and GHESKIO institutional review boards (WCM protocol number 20–03021735). Individuals selected for the study provided written informed consent in Creole before enrollment. An independent data and safety monitoring board appointed by the principal investigator reviewed the trial every 6 months.

Participants

We enrolled 250 PWH, aged 18–65 years, on ART at least 1 year, and viral suppression defined as plasma HIV-1 RNA viral load less than 1000 copies/ml within the past

12 months. All participants had prehypertension as defined by the WHO [17] as SBP 120–139 mmHg or DBP 80–89 mmHg, and were not on antihypertensive medication. Exclusion criteria included pregnancy, kidney disease, diabetes, advanced illness with limited life expectancy, plans to move within the next year, and clinician determination of unstable ART regimen (Table S1, http://links.lww.com/QAD/D373).

Randomization, masking, and intervention

Participants were randomly assigned by a computer in a 1 : 1 ratio, under block randomization with 10 participants at a time, to receive prehypertension treatment (intervention group) versus standard of care (control group) without blinding. Participants randomized to intervention were started on amlodipine 5 mg at enrollment, which was increased to 10 mg if SBP at any follow-up visit was at least 130 mmHg. Amlodipine is a first-line antihypertensive medication recommended by the Haitian Ministry of Health, selected for efficacy in black populations, cost, and ease of use without need for laboratory monitoring [18,19]. Participants randomized to the control arm were not started on any medication at study start. If control participants had two visits with SBP at least 140 mmHg or DBP at least 90 mmHg, they were recommended per national guidelines to initiate amlodipine 5 mg. Treatment in the intervention group was continued for 12 months, loss to follow-up, or death. All participants in both arms received lifestyle counseling on diet, physical activity, and medication adherence.

Outcomes

The primary outcome was the difference in mean change in SBP between study groups from enrollment to 12 months. Secondary outcomes per protocol included: mean change in DBP between study groups; difference in proportion with BP control less than 120/80 mmHg at 12 months; incident hypertension defined as two follow-up visits with BP at least 140/90 with at least one being a clinic visit, or one follow-up visit with BP at least 160/100 mmHg; difference in viral suppression at 12 months between groups; ART medication adherence defined as missing only 0–1 days during the week and never on the weekend per a validated ACTG questionnaire [20]; cardiovascular risk profile defined as high alcohol intake, smoking, low physical activity, low fruit/vegetable intake, mean change in BMI; and serious adverse events (grade 3–5), including dizziness, hypotension, peripheral edema, or other according to the Division of AIDS table for grading of severity of adverse events. Feasibility was defined as proportion of eligible participants participating in trial, and participant retention in all visits. Intervention acceptability was based on qualitative interviews with a random subset of participants and providers (see Supplement for details). In the main analysis, outcomes at 12 months were assessed for all participants with 12-month data, excluding deaths (Figure S1, http://links.lww.com/QAD/D373).

Statistical analysis

We determined enrollment of 250 participants and 6 time points for BP measurements would provide the trial with 80% power to detect at least 4 mmHg difference in mean change in SBP between intervention and control groups, from enrollment to 12 months, assuming consistent differences across time and a conservative correlation of 0.95 among BP measurements for the same individual [21].

We compared the difference in mean change in SBP and DBP using a linear mixed-effects model including time and intervention as fixed effects, and accounting for repeated measures and correlations within subjects by including patient as a random effect. The time*treatment interaction terms serve as the primary parameter. For the primary outcome, our main analysis used intention to treat, and we conducted a prespecified sensitivity analysis restricted to participants who reported high adherence to study drug (never missing medication based on Hill-Bone questionnaire) at least 80% visits [22]. In the main analysis, missing BP values were implicitly handled by using the mixed model for repeated measures under the assumption of missing at random. As a sensitivity analyses for missing BP values, we used last observed value carried forward to impute missing BP in a linear mixed-effects model.

Difference in proportion with BP control was analyzed using Poisson mixed-effects models, accounting for repeated measures and correlations within subjects. We calculated incidence of hypertension using Kaplan–Meier methods, and calculated an unadjusted hazard ratio using Cox proportional hazards after confirming proportional hazards assumptions. We calculated difference in viral suppression and HIV medication adherence using Fischer's exact test. For remaining secondary outcomes, we present descriptive statistics.

For qualitative interviews, audio recordings were translated and transcribed from Creole into English as needed. Thematic content analysis of transcripts was conducted using Grounded Theory, an inductive approach where themes are drawn directly from the data and responses, in NVIVO.

Data analysis was conducted using R version 4.2.3 (R Foundation for Statistical Computing). The primary analysis was computed using lme4 package version 1.1.34.

Results

Participant characteristics

From March 25, 2021, to March 30, 2022, a total of 678 PWH were approached for study screening in the GHESKIO HIV clinic based on review of electronic medical records (Fig S1, http://links.lww.com/QAD/D373). A total of 310 were eligible for study screening

and 279 screened eligible with laboratory assessments and BP criteria. Among those, a total of 250 participants were interested and enrolled (124 in intervention group, 126 in control group). The median age was 49 years (interquartile range, 42–55), 40.8% were women, all identified race as Haitian Black (Table 1). The participants' characteristics were well balanced between the two treatment groups at baseline (Table 1). For HIV care, median time on ART at study enrollment was 2.45 years (interquartile range 2.17–2.67). All participants were on a dolutegravir-based regimen.

Cardiovascular risk factors were also well balanced between the two groups, except for higher obesity in the intervention group. Median SBP was 129.0 mmHg (interquartile range 126.0–132.0), and median DBP was 78.5 mmHg (interquartile range 73.4–82.6). Few participants drank alcohol, currently smoked, had low physical activity, or consumed 5 servings of fruits or vegetables daily. High 10-year risk of major cardiovascular event was 21.0% in intervention and 12.1% in control.

Median follow-up was 12 months. A total of 122 participants (98.4%) in intervention group and 120 participants (95.2%) in control group remained in the study until 12 months (Table S2, http://links.lww.com/QAD/D373).

Primary outcome

The difference in mean change in SBP from enrollment to 12 months between study groups was -5.88 mmHg (95% CI -8.77 to -3.01) (Table 2) in intention to treat. Figure 1 shows the SBP and DBP trend across study visits, between study groups.

Among participants who reported high adherence (56/124 intervention group), mean change in SBP between study groups was greater, at -9.21 mmHg (95% CI -13.03 to -5.38) (Table S3, http://links.lww.com/QAD/D373, Figure S2, http://links.lww.com/QAD/D373). Across all nine study visits, the intervention group had 12.6% missing BP measurements (141/1116), while the control group had 16.8% missing BP measurements (191/1134) (Table S2, http://links.lww.com/QAD/D373). After imputation of missing data, mean SBP change between study groups was similar at -5.99 mmHg (95% CI -8.84 to -3.13) (Table S3, http://links.lww.com/QAD/D373).

Secondary outcomes

The difference in mean change in DBP was -5.54 mmHg (95% CI -7.92 to -3.16) in intention to treat. BP control was higher in the intervention versus control with an incidence rate ratio (IRR) of 1.59 (95% CI 1.07–2.37) under intention to treat (Table 2), with similar findings among adherent participants and after imputation of missing data (Table S3, http://links.lww.com/QAD/D373).

By 12 months, 7/124 (5.6%) intervention participants and 29/126 (23.0%) control participants developed incident hypertension (Table 2, Fig. 2), with a hazard ratio between intervention versus control of 0.18 (95% CI 0.07–0.47).

The intervention group had higher percentage of HIV medication adherence (89.5 versus 78.6%, $P = 0.05$) (Table 2). Both groups had similar percentages of viral load suppression, and lifestyle behaviors related to cardiovascular risk.

Adverse events

There were a total of 26 adverse events (21.0%), with the majority occurring by the 1 month follow-up visit (17/21) (Table S5, http://links.lww.com/QAD/D373, Table S6, http://links.lww.com/QAD/D373). The most common were dizziness (13) and edema (5). There were three serious adverse events including two deaths, neither of which were drug related. One participated died of a gunshot wound on the way to work, and the other died due to tuberculosis complications. The remaining serious adverse event was weakness due to newly diagnosed diabetes mellitus.

Feasibility and acceptability

About 89.6% (250/279) of individuals who were eligible for randomization agreed to participate in the trial. Follow-up visit attendance varied from 79.8 to 98.4% in the intervention group and from 72.2 to 95.2% in the control group, with retention at 12 months 98.3 and 95.2% (Table S2, http://links.lww.com/QAD/D373). At 12 months, 99.2% (121/122) intervention participants not lost to follow-up were on any dose of amlodipine, with 8.9% on amlodipine 10 mg and 0.8% on amlodipine and hydrochlorothiazide (Table S4, http://links.lww.com/QAD/D373). At 12 months, in the control group, 4.8% were on amlodipine 5 mg and 0.8% on amlodipine and hydrochlorothiazide (Table S4, http://links.lww.com/QAD/D373). There were no cases of sustained treatment discontinuation in either study group.

In qualitative interviews, participants reported taking amlodipine was acceptable. Providers had initial concerns about participants becoming hypotensive and symptomatic with amlodipine initiation, but as the study proceeded without frequent hypotensive events, they became more comfortable. Participants did not express this same concern. Participants expressed interest in continuing the medication, denied major side effects, denied feeling the additional pill was burdensome, and reported feeling better and calmer taking the medication.

Discussion

The results of this randomized controlled trial show that the initiation of antihypertensive medication in PWH with prehypertension in a resource-poor setting was

Table 1. Participant characteristics at study enrollment ($n = 250$).

	Intervention group $N = 124$	Control group $N = 126$
SOCIODEMOGRAPHICS		
Age		
Median [Q1, Q3] – year	50.0 [43.8, 55.3]	47.5 [41.3, 55.0]
Distribution – no. (%)		
18–29	2 (1.6)	4 (3.2)
30–39	21 (16.9)	16 (12.7)
40–49	35 (28.2)	50 (39.7)
50–59	50 (40.3)	46 (36.5)
60+	16 (12.9)	10 (7.9)
Female sex – no. (%)	48 (38.7)	54 (42.9)
Race Black Haitian	124 (100)	126 (100)
Education – no. (%)		
Primary or lower	57 (46.0)	68 (54.0)
Secondary or higher	59 (47.6)	51 (40.5)
Missing	8 (6.5)	7 (5.6)
Occupation – no. (%)		
Merchant owns business	47 (37.9)	46 (36.5)
Employed	25 (20.2)	26 (20.6)
Homemaker/Retired	2 (1.6)	0 (0)
Not working	50 (40.3)	54 (42.9)
Marital status – no. (%)		
Married/Living together	52 (41.9)	51 (40.5)
Single/Widowed/Divorced/Separated	72 (58.1)	75 (59.5)
Daily Income – no. (%)		
Less than or equal to 1 USD	51 (41.1)	54 (42.9)
1–10 USD	26 (21.0)	28 (22.2)
More than 10 USD	39 (31.5)	36 (28.6)
Missing	8 (6.5)	8 (6.3)
HIV CARE		
WHO HIV/AIDS Stage at time of ART initiation– no. (%)		
Stage 1	11 (8.9)	18 (14.3)
Stage 2	23 (18.5)	14 (11.1)
Stage 3	48 (38.7)	45 (35.7)
Stage 4	42 (33.9)	49 (38.9)
Time on ART		
Median [Q1, Q3] – yr	2.49 [2.19, 2.66]	2.41 [2.16, 2.68]
Current ART Regimen – no. (%)		
TDF-3TC-DTG	121 (97.6)	123 (97.6)
AZT-3TC-DTG	2 (1.6)	3 (0.02)
ABC-3TC-DTG	1 (0.8)	0 (0)
CARDIOVASCULAR DISEASE RISK FACTORS		
SBP	129.0 [126.0, 132.0]	128.0 [126.0, 133.0]
Median [Q1, Q3] – mmHg		
DBP	78.5 [73.4, 82.6]	77.5 [73.6, 81.0]
Median [Q1, Q3] – mmHg		
BMI, Median [Q1, Q3] – kg/m2	27.1 [23.3, 30.9]	25.3 [22.6, 28.9]
BMI $\geq$30 kg/m^2 – no. (%)	40 (32.3)	29 (23.0)
Total cholesterol, Median [Q1, Q3] – mg/dl	167 [144, 192]	166 [146, 193]
Low-density lipoprotein, Median [Q1, Q3] – mg/dl	98.0 [79.0, 116]	94.5 [79.0, 122]
Hyperlipidemia– no. (%)	11 (8.9)	8 (6.3)
Alcohol intake $\geq$ 1 drink/day – no. (%)	4 (3.2)	1 (0.8)
Smoking current – no. (%)	3 (2.4)	9 (7.1)
Physical activity $\leq$150 min/week – no. (%)	21 (16.9)	21 (16.7)
Fruit/Vegetable intake <5 servings/day – no. (%)	121 (97.6)	120 (95.2)
ASCVD 10-year risk if age >40 – no. (%)	$N = 100$	$N = 99$
Low	49 (49.0)	61 (61.6)
Intermediate	30 (30.0)	26 (26.3)
High	21 (21.0)	12 (12.1)

Hyperlipidemia defined as taking total cholesterol $\geq$240 mg/dl, LDL $\geq$160 mg/dl, or taking statin.

feasible, acceptable, and effective in reducing mean SBP by 5.88 mmHg more than the control group at 12 months. Additionally, treatment of prehypertension reduced incident hypertension with a hazard ratio of 0.18 (95% CI 0.07–0.47). Importantly, there were no drug-related serious adverse events and no impact on viral suppression.

This study provides clinical trial data specific to PWH on the potential impact of lowering BP treatment thresholds

Table 2. Primary and secondary outcomes at 12 months.

	Intervention group $N=124$	Control group $N=126$	β or incidence rate ratio	*P*
	N (%)	*N* (%)	Estimate (95% CI)	
PRIMARY OUTCOME: INTENTION TO TREAT				
SBP change, Mean (95% CI) – mmHg	-10.52 (-12.55, -8.48)	-4.63 (-6.67, -2.59)	-5.88 (-8.77, -3.01)	<0.001
SECONDARY OUTCOMES				
BP OUTCOMES				
DBP change, Mean (95% CI) – mmHg	-8.87 (-10.55, -7.19)	-3.33 (-5.01, -1.65)	-5.54 (-7.92, -3.16)	<0.001
BP control <120/80 – no. (%)	70/122 (57.4)	44/120 (36.7)	1.59 (1.07, 2.37)	0.02
Incidence of hypertension – no. (%)	7/124 (5.6)	29/126 (23.0)	0.18 (0.07, 0.47)	<0.001
HIV OUTCOMES				
HIV-1 RNA viral load < 1000 copies/ml – no. (%)	115 (92.7)	114 (90.5)	N/A	1.0*
High HIV medication adherence – no. (%)	111 (89.5)	99 (78.6)	N/A	0.05*
CARDIOVASCULAR RISK PROFILE				
Alcohol intake ≥ 1 drink/day – no. (%)	3 (2.4)	5 (4.0)	N/A	†
Smoking current – no. (%)	5 (4.0)	8 (6.3)	N/A	†
Physical Activity ≤150 min/week – no. (%)	23 (18.5)	18 (14.3)	N/A	†
Fruit/Vegetable intake <5 servings/day – no. (%)	121 (97.6)	119 (94.4)	N/A	†
Mean change in BMI Mean (SD) – kg/m^2	-0.44 (1.41)	-0.43 (1.10)	N/A	†

*Fischer's exact test.
†No prespecified testing for statistical significance to avoid multiple hypothesis testing.

in this high-risk population that has traditionally been excluded from earlier studies. Previous observational and clinical trial data in the general population without HIV show that any elevated BP more than 120/80 mmHg is associated with an increased risk of CVD [23]. Observational data from the UK and the US found a stepwise increase in CVD risk starting as low as SBP 115 mmHg across outcomes of myocardial infarction,

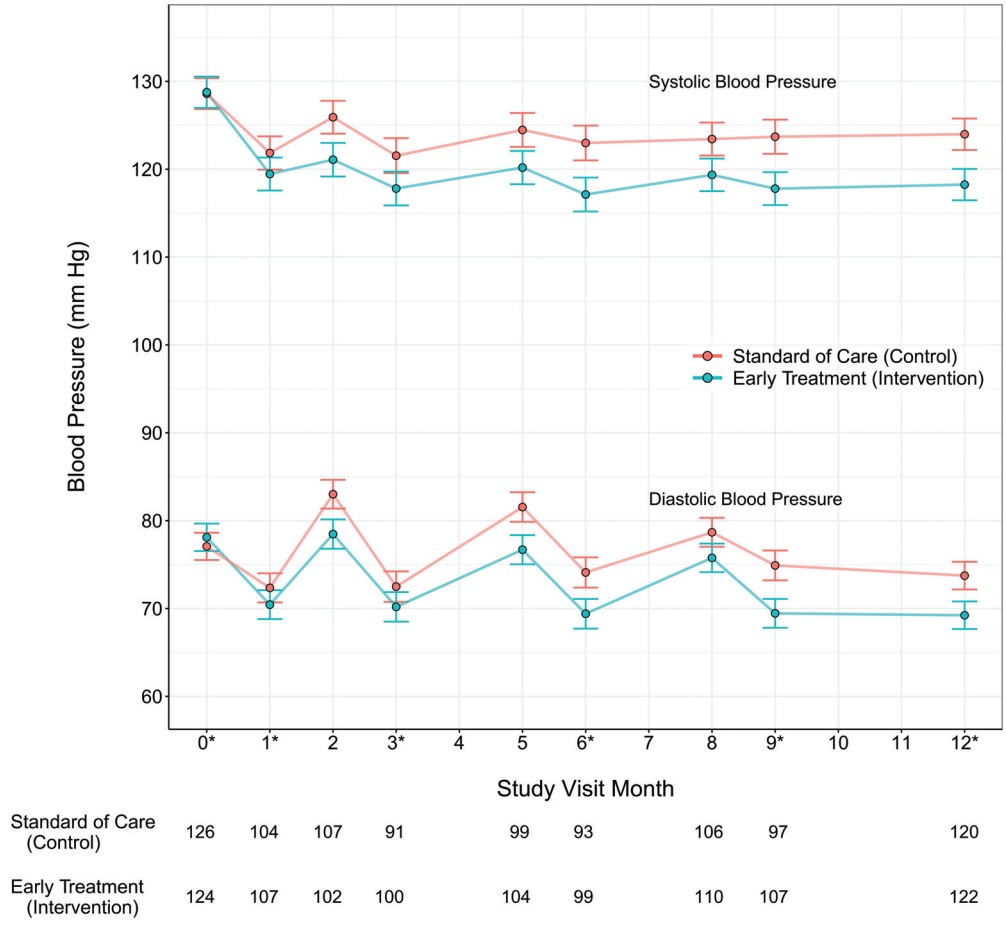

Fig. 1. Blood pressure trends in intervention versus control groups. [a]Clinic visits, remainder of study visits were community visits.

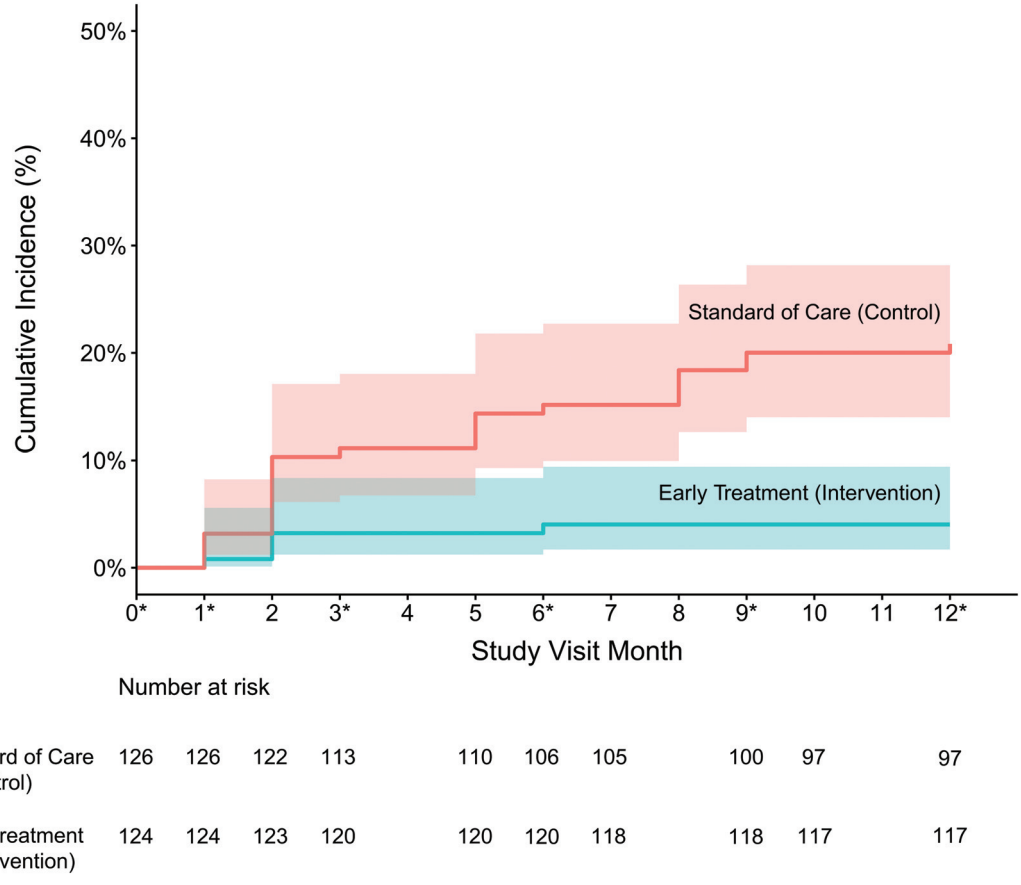

Fig. 2. Incident hypertension over 12 months. Incident hypertension defined as two follow-up visits with BP ≥140/90 mmHg or one follow-up visit with BP ≥160/100 mmHg.

hemorrhagic and ischemic strokes, and heart failure [23,24]. Clinical trial data on lowering BP using antihypertensive medication, including SPRINT, demonstrate achieving SBP control less than 120 mmHg in patients at a high risk for cardiovascular events, including chronic kidney disease, lowers rates of fatal and nonfatal CVD and death [6]. A meta-analysis of 48 randomized clinical trials of BP-lowering medications versus placebo showed more than 10% reductions of CVD events at a 5 mmHg reduction of SBP, regardless of previous CVD history and even at normal BP with SBP less than 120 mmHg [21].

Collectively, these data have led to guideline changes that lowered the BP threshold for initiation of antihypertensive medications to less than 130/80 mmHg first for high-risk groups, including people with diabetes and chronic kidney disease [8,9], and subsequently for the general population in the US and Europe [14,25]. While the WHO and many LMICs, including Haiti, have lowered the BP threshold to less than 130/80 mmHg for people with diabetes and chronic kidney disease, they have yet to classify PWH as a similarly high-risk group who may benefit from earlier BP treatment [5]. Our trial demonstrates initiating antihypertensive medications for PWH at lower BP thresholds is effective, feasible, and acceptable with potential broad generalizability to low-middle income countries where 80% of PWH live. This includes initiating antihypertensive medications for the BP range defined by the American Heart Association as elevated BP (SBP 120–129 mmHg) [14], which is currently below the antihypertensive medication treatment threshold in high-income countries as well. This study provides the first clinical trial data toward considering changing BP treatment guidelines for PWH living in LMICs.

Importantly, our data demonstrate that acceleration of prehypertension to hypertension among PWH in Haiti appears strikingly high across 12 months, suggesting earlier treatment of elevated BP may be particularly beneficial in PWH. Our rates of incident hypertension may be higher than studies conducted in the general population without HIV; however, direct comparison is difficult given varying follow-up periods. For example, the TROPHY trial at 2 years reported incident hypertension in 40.4% of the control group and 13.6% of the intervention candesartan group, with a 66% risk

reduction [26]. In addition, the PREVER-Prevention trial in Brazil at 1.5 years showed incident hypertension in 4.5% of the control group and 8.6% of the intervention chlorthalidone plus amiloride group, with a 44% risk reduction [27], while the PHARAO study in Germany at 3 years showed incident hypertension in 42.9% of their control group and 30.7% in their intervention ramipril group, with a 34% risk reduction [28].

Interventions to prevent or delay the onset of CVD are critical for PWH, given HIV-associated CVD has tripled over the past two decades as the success of ART has resulted in over 37.5 million aging adults with HIV worldwide [3]. The leading modifiable CVD risk factor among PWH worldwide is elevated BP, raising it as a potential pragmatic target for CVD prevention [1,2]. Recently, the REPRIEVE study showed initiation of pitavastatin for CVD prevention among PWH with low-to-moderate risk of 10-year atherosclerotic CVD less than 15% was effective at reducing CVD events [29]. Our work in Haiti among PWH on ART more than 10 years found hypertension was the most prevalent modifiable CVD risk factor (58% hypertension compared to 43% dyslipidemia) [30]. Furthermore, we found elevated BP at time of ART initiation was a significant predictor of 10-year mortality, with one-third of deaths due to stroke [13]. Thus, just as REPRIEVE targeted a group of PWH historically considered low risk with statins and showed improved health outcomes, so too could targeting PWH with BP historically considered low risk with anti-hypertensives be a pragmatic target for CVD prevention. Given our PWH were on stable ART regimens and had low-intermediate traditional ASCVD risk with significant reductions in BP, the effects may be even greater for higher risk groups of PWH.

Additional research may be needed to identify optimal antihypertensive regimens for PWH to minimize drug-drug interactions with ART, the absolute risk benefit of earlier treatment of elevated BP on both preclinical and clinical CVD events among PWH, and implementation strategies for dissemination and sustainability. The medical care and medications were free in this trial which may limit external validity, and future studies are needed for costing analyses for health system planning. A larger, definitive multisite trial is needed to explore some of these issues and to validate findings especially in LMICs.

Strengths of this study include data from an understudied black PWH population living in extreme poverty, and inclusion of women. This study was not blinded, without placebo, and conducted at a single site, which may limit generalizability. The majority of participants had systolic prehypertension, with few having isolated diastolic prehypertension. The 12-month follow-up time is relatively short for assessing long-term outcomes and medication adherence. We assumed BP values were missing at random in main analysis, but found similar results with sensitivity analyses that did not assume BP missing at random.

In conclusion, there is an urgent need to prevent hypertension among PWH with elevated BP, who have an alarmingly high risk of incident CVD events and mortality. Initiation of antihypertensive medications for prehypertension in a low-resource setting was feasible, acceptable, and effective in reducing BP and preventing incident hypertension.

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Data Sharing Statement:

Researchers who provide a methodologically sound proposal may have access to a subset of deidentified participant data, with specific variables based on the proposal. Proposals should be directed to the principal investigator at mam9365@med.cornell.edu. To gain access, data requestors will need to sign a data access agreement. Data are available following publications through 3 years after publication and will be provided directly from the PI.

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Conflicts of interest

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