

Hypertension Prevalence and Control at Trial Entry in the REPRIEVE Study Population: Results From a Secondary Analysis

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Background. We evaluated baseline hypertension prevalence and control and risk of major adverse cardiovascular events (MACEs) among people with HIV in REPRIEVE who had low to moderate traditional cardiovascular disease (CVD) risk.

Methods. Hypertension at baseline was defined by (1) a preexisting diagnosis regardless of antihypertensive treatment or (2) systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg without a prior diagnosis. We estimated the prevalence of the composite hypertension and control outcomes and calculated adjusted prevalence ratios controlling for traditional CVD risk factors using log binomial regression. We explored the relationship between hypertension and MACE using cause-specific Cox proportional hazards models.

Results. Of 7769 participants enrolled from 5 regions, the median age was 50 years, and 2419 (31%) were women. The prevalence of baseline hypertension was 36% ($n = 2780$) with geographic variation. Among these, 1911 (69%) individuals had a preexisting hypertension diagnosis; the remainder ($n = 869$, 31%) were undiagnosed. Region and traditional CVD risk factors were associated with hypertension prevalence, with obese and overweight body mass index having the highest adjusted prevalence ratios (1.80 [95% CI, 1.67–1.95] and 1.38 [95% CI, 1.28–1.49], respectively). Among those with preexisting hypertension, 40% were uncontrolled, with regional variation. Hypertension at baseline was associated with an increased hazard of MACE (hazard ratio, 2.00; 95% CI, 1.57–2.55) and key components of MACE, including myocardial infarction and stroke.

Conclusions. Approximately 1 in 3 REPRIEVE participants had hypertension at baseline. Hypertension was frequently suboptimally controlled. These findings highlight the need for improved screening and optimized treatment of hypertension in people with HIV.

Keywords. cardiovascular disease; HIV; hypertension; hypertension control.

With the success of antiretroviral therapy (ART), lifespan for people with HIV (PWH) has been extended to within a few years of the general population [1], and the burden of

noncommunicable diseases (NCDs) associated with aging is increasing [2]. Hypertension is among the most common NCDs diagnosed globally, including PWH [3], and is the leading cause of cardiovascular disease (CVD) and premature death globally [4]. Hypertension has been associated with a higher risk for CVD among PWH [5, 6], making the syndemic of HIV and hypertension a significant public health priority.

A large systematic review and meta-analysis prior to the widespread use of integrase-based ART estimated the prevalence of hypertension in PWH in the range of 24%, with a higher prevalence among those on ART (27% vs 17% in ART naive) [7]; however, differences in prevalence by region and risk factors for hypertension have been less well described from representative global cohorts on modern ART regimens. Additionally, rates of hypertension control among PWH

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indicate wide variation (range, 13%–60%) with better control in high-income countries [8–10], and there are limited data on how demographic factors such as sex, global region, and clinical factors affect control. Comparisons of hypertension prevalence and control rates across studies are difficult because of highly variable populations, study designs, and definitions used to define hypertension and hypertension control.

REPRIEVE was a randomized primary cardiovascular prevention trial of pitavastatin vs placebo in PWH aged 40 to 75 years with low to moderate CVD risk in 5 global regions, with a primary outcome of major adverse cardiovascular events (MACE; NCT02344290) [11]. MACE was reduced by 36% in the statin arm as compared with placebo, although there was evidence of heterogeneity of the statin effect by hypertension at baseline. In this analysis, we assess hypertension prevalence, risk factors, control, and differences by key participant characteristics at trial baseline. Additionally, we investigate (1) the relationship between baseline hypertension and MACE outcomes and (2) differences in the effect of statin on MACE by hypertension status and by blood pressure control. REPRIEVE provides an ideal opportunity to explore hypertension in a diverse global primary cardiovascular prevention population of PWH with low to moderate CVD risk.

METHODS

Participants were enrolled in REPRIEVE from 26 March 2015 to 31 July 2019. All primary outcomes have been published with detailed methods and Consolidated Standards of Reporting Trials diagrams (protocol article and primary outcome article) [11, 12]. The hypertension analyses presented in this article align with prespecified exploratory objectives in the protocol.

Study Population and Procedures

Participants were enrolled from Botswana, Brazil, Canada, Haiti, India, Peru, Puerto Rico, South Africa, Spain, Thailand, Uganda, the United States, and Zimbabwe. Inclusion criteria included a diagnosis of HIV-1 infection, ages 40 to 75 years, receipt of ART for the last 180 days prior to enrollment with any plasma HIV-1 RNA level, CD4 cell count >100 cells/mm³, and meeting specific low-density lipoprotein and 2013 Pooled Cohort Risk Equation 10-year risk levels below thresholds typically associated with statin prescribing [13]. Those with a history of statin use within the previous 90 days and with known atherosclerotic CVD were excluded.

Risk factors for this analysis were obtained at either the screening or entry visit (henceforth, baseline) and included demographic characteristics (age, sex, region, smoking) and clinical data (blood pressure, body mass index [BMI], renal function, CD4 cell count at entry, ART regimen at entry by class, duration of ART, and viral load). Per the Division of AIDS grading table, blood pressure was based on a single reading unless the value was high (≥ 140 and/or ≥ 90 mm Hg), in

which case a second reading was performed and the lower of the 2 readings was recorded. BMI was calculated by weight and height. Race-specific BMI categories were based on World Health Organization recommendations [14].

Participants were categorized geographically by Global Burden of Disease (GBD) super regions, which have been developed based on cause-of-death patterns [15]. Countries represented in REPRIEVE were grouped as follows: high income, Latin America and the Caribbean, sub-Saharan Africa, Southeast Asia/East Asia, and South Asia. We used the 2021 CKD-EPI equation (Chronic Kidney Disease Epidemiology Collaboration) for estimated glomerular filtration rate, which excludes race in its calculation.

Outcomes and Outcome Definitions

Preexisting hypertension was defined as having a diagnosis of hypertension prior to the REPRIEVE baseline assessment regardless of antihypertensive medication use at the time. The diagnosis was made by self-report or medical records. Undiagnosed hypertension was defined as no known prior diagnosis and systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg at baseline.

Analyses examining baseline hypertension and hypertension control used a composite hypertension outcome that comprised 3 mutually exclusive subsets of participants: preexisting hypertension with antihypertensive medication; preexisting hypertension without antihypertensive medications, including 29 participants off medications at study baseline with treatment initiated at that visit; and undiagnosed hypertension.

For the primary analysis of hypertension control at baseline, “uncontrolled” was defined as systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mm Hg based on World Health Organization guidelines [16]. We secondarily analyzed blood pressure control by stage of hypertension using 2 guidelines: “global thresholds” based on guidelines from several African countries, including Kenya [17] and South Africa [18], and thresholds as defined by the American College of Cardiology/American Heart Association (ACC/AHA) in the 2017 guidelines [19], which were unchanged in the 2025 update [20]. Table 1 shows the thresholds used for these analyses.

Various MACE outcomes were assessed as time from entry to the first qualifying event as previously described [11]. Qualifying MACE included cardiac ischemia or myocardial infarction, stroke or transient ischemic attack, cardiovascular death, cardiac catheterization or revascularization, peripheral arterial revascularization, peripheral arterial ischemia, or death of undetermined cause.

Statistical Analyses

We summarized participant demographic and clinical characteristics by the baseline composite hypertension subgroups vs no hypertension as number and percentage for categorical

Table 1. Thresholds Used in the Analysis of Blood Pressure Control

ACC/AHA [19]	SBP, mm Hg		DBP, mm Hg	Global [17, 18]	SBP, mm Hg		DBP, mm Hg
Normal	<120	and	<80	Normal	<130	and	<80
Elevated	120–129	and	<80	Elevated	130–139	or	80–89
Stage 1	130–139	or	80–89	Stage 1	140–159	or	90–99
Stage 2	140–179	or	90–119	Stage 2	160–179	or	100–109
Hypertensive crisis	≥180	or	≥120	Stage 3	≥180	or	≥110

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; DBP, diastolic blood pressure; SBP, systolic blood pressure.

variables and median with lower and upper quartiles (Q1, Q3) for continuous variables. We estimated the prevalence of the composite hypertension outcome and, separately, the control outcome overall and by demographic and clinical characteristics with 95% Wald CIs. An additional analysis was performed to estimate prevalence and control ratios adjusted for all traditional CVD risk factors and GBD super region using log binomial regression.

Secondarily, we characterized stages of hypertension using global thresholds comparing the distributions overall and by GBD super region, sex, and age strata (40–49, 50–59, ≥60 years) for participants with preexisting hypertension. We repeated this analysis using current ACC/AHA thresholds [20].

We estimated incidence of MACE and its individual components [11] by hypertension status at baseline using Poisson distributions. Hazard ratios and 95% CIs were estimated with “no hypertension” as the reference group from individual cause-specific Cox proportional hazards models unadjusted and adjusted for known MACE risk factors [6], including age, geographic region and race, sex, BMI, and smoking status. Across all analyses, person-years of follow-up were truncated at the date of event or last contact, whichever was earlier.

We used Cox models to explore differences in the effect of statin on the primary MACE outcome by baseline hypertension categories (no hypertension, preexisting by antihypertensive medication status, and undiagnosed) and by levels of hypertension control. Models contained main effects for treatment, hypertension status, and an interaction between the two. Estimated hazard ratios (HRs) and 95% CIs of the interaction effect by factor levels were assessed. Since the focus of these analyses was the randomized statin effect, additional adjustment was not performed.

Patient Consent Statement and Trial Ethics

REPRIEVE was approved by the institutional review board at Mass General Brigham and at each site. All participants provided written informed consent.

RESULTS

Trial Population

From 26 March 2015 to 31 July 2019, 7769 participants were enrolled in REPRIEVE. Baseline characteristics of the

REPRIEVE trial have been published [11]. In brief, the median age was 50 years (IQR, 45–55), 5065 participants (65%) were non-White, and 2419 (31%) were women. The median screening low-density lipoprotein cholesterol level was 106 mg/dL (IQR, 86–128), and the median CD4 count was 621 cells/mm³ (IQR, 448–827). The median 10-year atherosclerotic CVD risk score was 4.5% (IQR, 2.1%–7.0%). The HIV viral load was below the lower limit of quantification in 88% of participants (range, <40 to <400 copies/mL).

Hypertension Prevalence and Subgroup Differences

The prevalence of the composite hypertension outcome at REPRIEVE trial baseline was 36% (2780/7769; 95% CI, 35%–37%). Among these, 1911 (69%) individuals had preexisting hypertension, of whom 1549 were taking antihypertensive medications and 362 were not. The remainder (n = 869, 31%) were undiagnosed. Table 2 shows baseline characteristics of the hypertension subtypes as compared with those without hypertension. Undiagnosed hypertension was more likely in the Latin America/Caribbean and South Asian regions and less likely in the high-income region relative to the proportion of participants with preexisting hypertension across regions. Among those with undiagnosed hypertension, 76% were male and 24% female, while among those with preexisting hypertension on antihypertensive medications, 59% were male and 41% were female.

Prevalence of Hypertension and Clinical and Demographic Variables

Overall, the composite hypertension outcome was more common among those with traditional risk factors, including older age, Black or African American race in the high-income region, higher BMI, and reduced renal function, with minimal differences by HIV characteristics (Figure 1). There was limited regional variability in hypertension with overlapping confidence intervals, with the exception of Southeast/East Asia, which had a lower prevalence (24%; 95% CI, 20%–27%) as compared with other regions. Hypertension was more common in women than men; however, after adjustment for other traditional CVD risk factors, sex differences were no longer apparent (Supplementary Figure 1). Obese and overweight BMI remained strongly associated with hypertension in the adjusted

Table 2. Baseline Characteristics by Prior Diagnosis of Hypertension and Use of Antihypertensives

	Analysis HTN Type, No. (%) or Median (IQR)			
	No HTN (n = 4989)	Undiagnosed HTN (n = 869)	Preexisting HTN Without Medication (n = 362)	Preexisting HTN With Medication (n = 1549)
Age, y	49 (45–54)	50 (46–54)	51 (47–55)	52 (47–56)
40–49	2586 (52)	410 (47)	144 (40)	590 (38)
50–59	2008 (40)	394 (45)	188 (52)	771 (50)
≥60	395 (8)	65 (7)	30 (8)	188 (12)
Natal sex				
Female	1464 (29)	208 (24)	118 (33)	629 (41)
Male	3525 (71)	661 (76)	244 (67)	920 (59)
GBD super region				
High income	2553 (51)	386 (44)	217 (60)	939 (61)
Latin America and Caribbean	899 (18)	211 (24)	42 (12)	271 (17)
Southeast/East Asia	449 (9)	31 (4)	23 (6)	87 (6)
South Asia	339 (7)	120 (14)	12 (3)	33 (2)
Sub-Saharan Africa	749 (15)	121 (14)	68 (19)	219 (14)
Race				
White	1826 (37)	275 (32)	115 (32)	488 (32)
Black or African American	1861 (37)	326 (38)	185 (51)	836 (54)
Asian	821 (16)	156 (18)	36 (10)	125 (8)
Other	481 (10)	112 (13)	26 (7)	100 (6)
Race within HIC				
White	3888 (78)	693 (80)	247 (68)	1000 (65)
Black or African American	910 (18)	148 (17)	100 (28)	517 (33)
Other	191 (4)	28 (3)	15 (4)	32 (2)
Smoking status				
Never	2497 (50)	443 (51)	186 (52)	796 (51)
Former	1161 (23)	206 (24)	96 (27)	442 (29)
Current	1324 (27)	220 (25)	79 (22)	310 (20)
ASCVD risk score, %	3.6 (1.6–6.2)	5.2 (2.9–7.9)	5.4 (3.1–7.6)	6.6 (3.9–9.2)
BMI: race specific				
Low/normal	2335 (47)	336 (39)	101 (28)	401 (26)
Overweight	1774 (36)	335 (39)	140 (39)	565 (37)
Obese	876 (18)	198 (23)	120 (33)	581 (38)
eGFR by CKD-EPI, mL/min/1.73 mm ²				
<90	2058 (41)	347 (40)	189 (52)	839 (54)
≥90	2930 (59)	522 (60)	173 (48)	709 (46)
PREVENT Heart Failure risk score ^a	1.1 (0.6–1.9)	1.7 (1.0–2.5)	1.7 (1.1–2.6)	2.3 (1.5–3.4)

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; GBD, Global Burden of Disease; HIC, High Income Countries; HTN, hypertension.

^aThe PREVENT Heart Failure risk score (percentage) is computed for only those participants not missing any components.

analysis with prevalence ratios of 1.80 (95% CI, 1.67–1.95) and 1.38 (95% CI, 1.28–1.49), respectively.

A subanalysis stratified by GBD super region exhibited similar trends, with traditional risk factors more common among those with hypertension vs without in all regions ([Supplementary Table 1](#)).

Hypertension Control and Associated Factors

A total of 1911 participants with preexisting hypertension were included in the analysis of hypertension control. Overall, 40% (95% CI, 38%–42%) of this group had uncontrolled hypertension. Uncontrolled hypertension was more common in

younger individuals, women, and participants from South Asia (84%; 95% CI, 74%–95%) and least common in the high-income region (32%; 95% CI, 29%–34%; [Figure 2](#)). There was a higher prevalence of uncontrolled hypertension among those not prescribed antihypertensive medications (180/362, 50% [95% CI, 45%–55%]) as compared with those taking medications (583/1549, 38% [95% CI, 35%–40%]; [Table 3](#)). Prevalence of hypertension control among all participants and by region is shown in [Supplementary Figure 2](#).

Adjusted analysis suggests that regional differences are associated with control ([Supplementary Figure 3](#)). Additionally, after adjustment, the trend toward a higher prevalence of

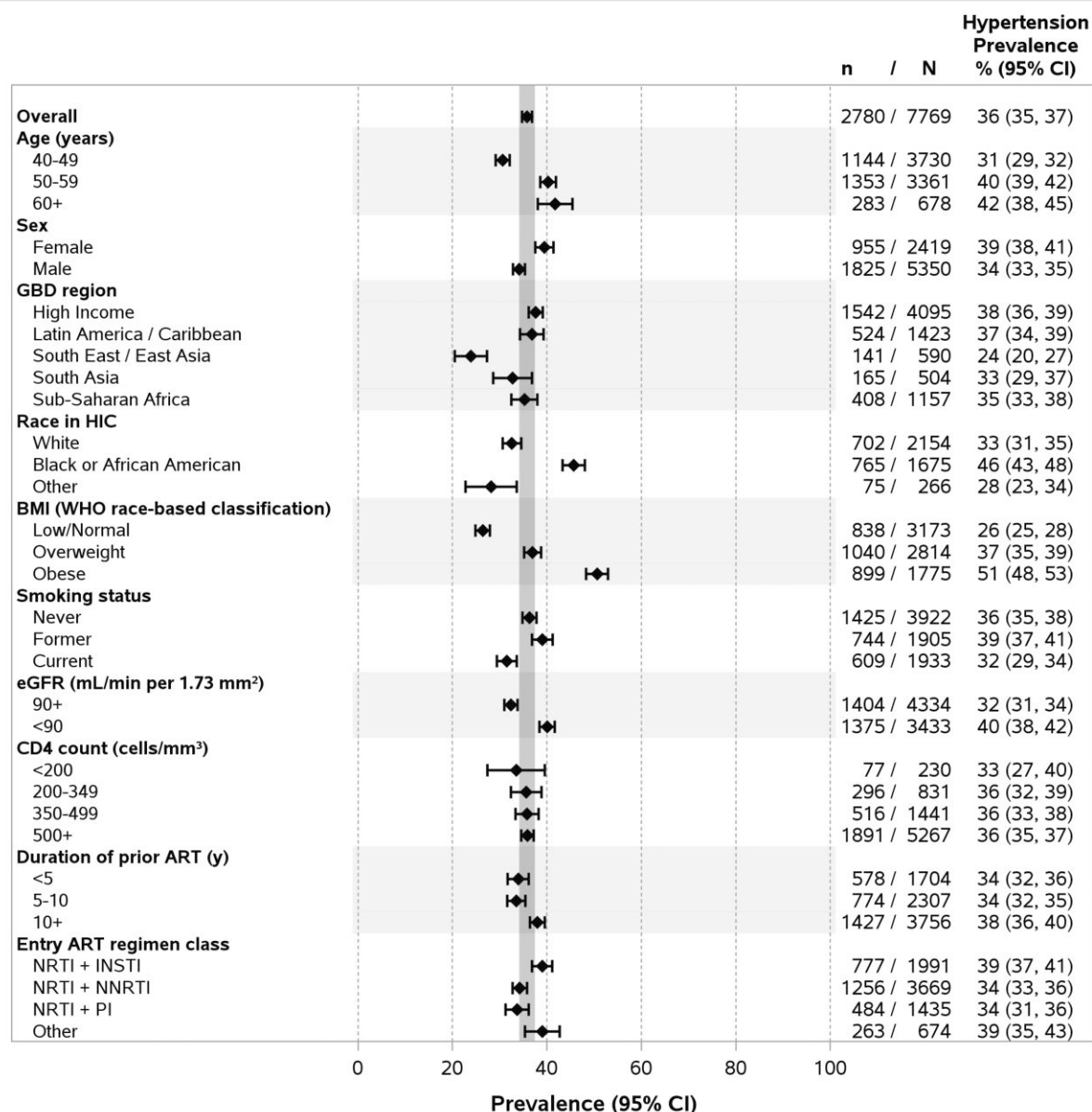


Figure 1. Prevalence of preexisting hypertension in REPRIEVE (N = 7769). n = number of participants with hypertension at entry; N = all REPRIEVE participants. Gray column indicates the width of the 95% CI of the overall hypertension prevalence. ART, antiretroviral therapy; BMI, body mass index; eGFR, estimated glomerular filtration rate; GBD, Global Burden of Disease; HIC, High Income Countries; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; WHO, World Health Organization.

uncontrolled hypertension in women vs men persisted (adjusted prevalence ratio, 1.11; 95% CI, 0.99–1.24).

Hypertension Control by Global Hypertension Stages

According to global hypertension stages, 22% (n = 427) of participants with hypertension had normal blood pressure, 38% (n = 721) had elevated blood pressure, and 31% (n = 584) had stage 1 hypertension, with a higher frequency of stage 1 hypertension among those not prescribed antihypertensive medications vs those with medications (40% vs

28%, respectively; Table 3, top). Stage 2 and 3 hypertension was uncommon.

Hypertension Control by ACC/AHA Blood Pressure Stages

Applying ACC/AHA thresholds to the same population, stage 1 and 2 hypertension was the most common and occurred with equal frequency (38% and 39%, respectively; Table 3, bottom). Only 15% (n = 280) of REPRIEVE participants were categorized as having normal blood pressure based on ACC/AHA guidelines.

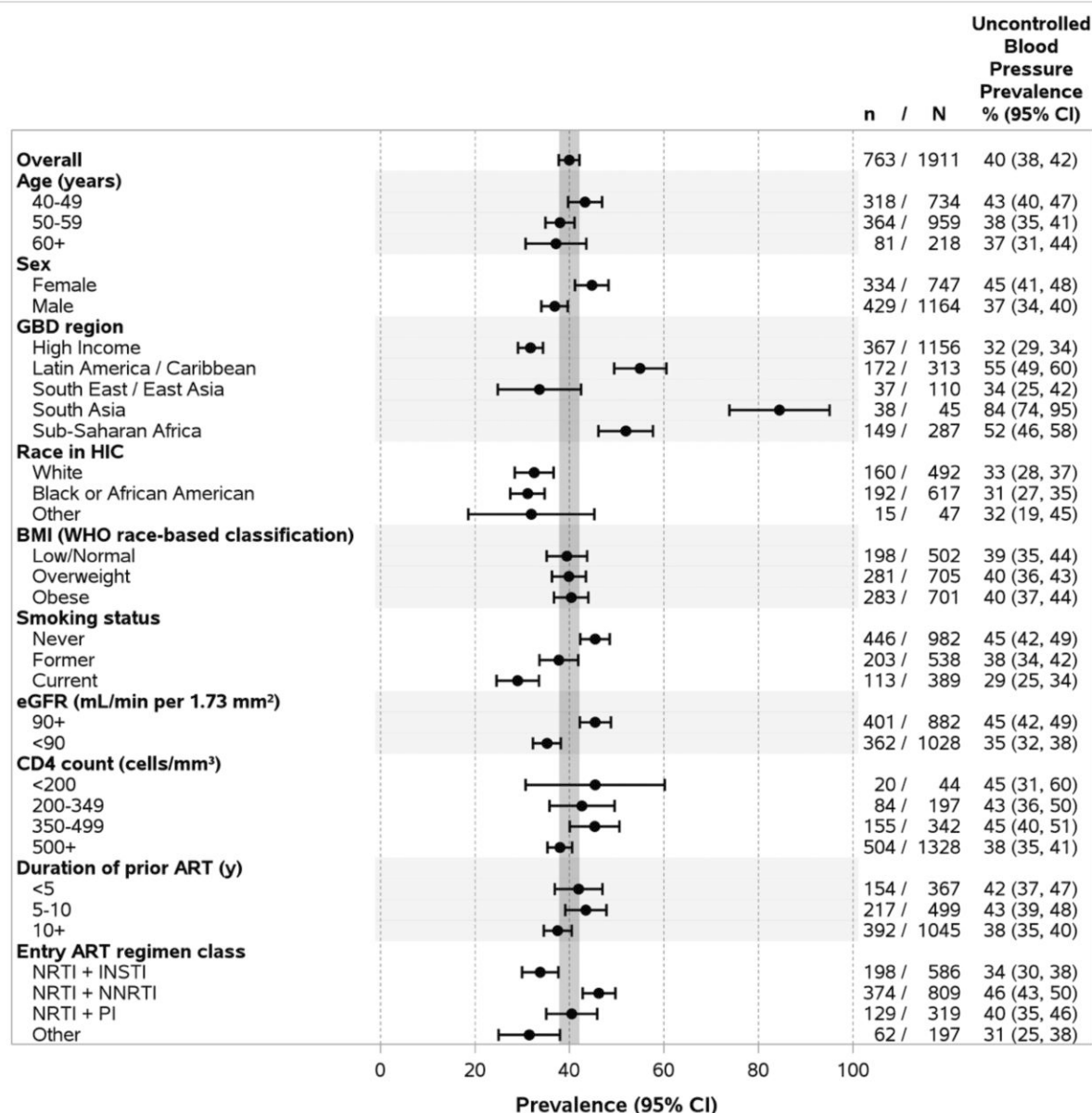


Figure 2. Blood pressure control (<140/90 mm Hg) among participants with preexisting hypertension. Prevalences are computed among all participants with a preexisting hypertension diagnosis who did not start antihypertensive medication at study entry ($n = 1911$). Abbreviations: n = number of participants with uncontrolled blood pressure; N = number of participants with a preexisting hypertension diagnosis who did not start antihypertensive medication at study entry. Gray column indicates the width of the 95% CI of the hypertension control prevalence. ART, antiretroviral therapy; BMI, body mass index; eGFR, estimated glomerular filtration rate; GBD, Global Burden of Disease; HIC, High Income Countries; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; WHO, World Health Organization.

Hypertension Control by GBD Super Region, Sex, and Age Using Global and ACC/AHA Stages

Figure 3A shows hypertension control at baseline by region, sex, and age using global hypertension stages among those taking antihypertensive medications. Although numbers were small ($n = 33$), participants in South Asia had the highest rate of uncontrolled blood pressure. Women were less likely than men to have normal blood pressure and more

likely to have stage 1 and 2 hypertension. Patterns were similar for participants with preexisting hypertension not prescribed antihypertensive medications at baseline, with worse control in the South Asia region (Figure 3B). Applying ACC/AHA thresholds produced a shift toward higher stages of hypertension, as expected, given more stringent cutoffs (Supplementary Figure 4).

Table 3. Stages of Hypertension by Global vs ACC/AHA Thresholds Among Participants With Preexisting Hypertension Overall and by Antihypertensive Medication Status (n = 1911)

Baseline Blood Pressure Status	Preexisting Hypertension at Baseline					
	Total (n = 1911)		With Antihypertensives (n = 1549)		Without Antihypertensives (n = 362) ^a	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Single-value threshold						
Controlled: <140/90	1148	60 (58–62)	966	62 (60–65)	182	50 (45–55)
Uncontrolled: ≥140/90	763	40 (38–42)	583	38 (35–40)	180	50 (45–55)
Global thresholds						
Normal: SBP <130 and DBP <80	427	22 (20–24)	357	23 (21–25)	70	19 (15–23)
Elevated: SBP 130–139 or DBP 80–89	721	38 (36–40)	609	39 (37–42)	112	31 (26–36)
Stage 1: SBP 140–159 or DBP 90–99	584	31 (28–33)	441	28 (26–31)	143	40 (34–45)
Stage 2: SBP 160–179 or DBP 100–109	143	7 (6–9)	116	7 (6–9)	27	7 (5–10)
Stage 3: SBP ≥180 or DBP ≥110	36	2 (1–2)	26	2 (1–2)	10	3 (1–4)
ACC/AHA thresholds						
Normal: SBP <120 and DBP <80	280	15 (13–16)	241	16 (14–17)	39	11 (8–14)
Elevated: SBP 120–129 and DBP 80–89	147	8 (6–9)	116	7 (6–9)	31	9 (6–11)
Stage 1: SBP 130–139 or DBP 80–89	721	38 (36–40)	609	39 (37–42)	112	31 (26–36)
Stage 2: SBP 140–179 or DBP 90–119	745	39 (37–41)	571	37 (34–39)	174	48 (43–53)
Hypertensive crisis: SBP ≥180 or DBP ≥120	18	1 (1–1)	12	1 (0–1)	6	2 (0–3)

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; DBP, diastolic blood pressure; SBP, systolic blood pressure.

^a29 participants who started antihypertensive medications at baseline were included as having preexisting HTN without medication.

Hypertension Status at Baseline and MACE Outcomes

Baseline hypertension was associated with an increased risk of all MACE outcomes (Figure 4). After adjustment for region and traditional risk factors, baseline hypertension was associated with a 1.8-fold higher hazard of primary MACE (95% CI, 1.4–2.3), a 2-fold higher hazard of hard MACE (myocardial infarction, stroke, or cardiovascular death; 95% CI, 1.5–2.8), and a 2.5-fold higher hazard of stroke (95% CI, 1.5–4.1).

Effect Modification of Statin on Primary MACE by Baseline Hypertension and Hypertension Control

As previously reported, the effect of statin on primary MACE was attenuated among those with hypertension at baseline as compared with those without (HR, 0.88 vs 0.45) [11]. Additionally, attenuation of statin effect was apparent across all hypertension subgroups ($P = .06$) but with wide confidence intervals given the relatively small sample sizes across groups (Figure 5). Evidence of effect modification was less apparent in exploratory analyses stratified by levels of blood pressure control, although the largest statin benefit was estimated among those with hypertension control ($P > .20$), with similar point estimates for control at <140/90 mm Hg (HR, 0.59; 95% CI, .44–.79) as compared with <130/80 mm Hg (HR, 0.52; 95% CI, .34–.80).

DISCUSSION

In this analysis leveraging the REPRIEVE trial, we demonstrate a high prevalence of hypertension in a global population of PWH without known atherosclerotic CVD and low to

moderate traditional CVD risk. The prevalence of hypertension varied by GBD super region. Moreover, a high percentage of PWH with hypertension were suboptimally controlled, again varying by region, highlighting the urgent need to prevent, diagnose, and control hypertension as a key contributing factor to MACE in PWH. Moreover, exploratory analyses suggest that, despite low to moderate CVD risk, the presence of hypertension in this population is associated with risk of MACE and individual components of MACE, including stroke and myocardial infarction.

The prevalence of hypertension at baseline in REPRIEVE (36%) aligns closely with data from a systemic review and meta-analysis of hypertension in PWH (49 studies: 25 from the United States, 13 from Europe, 10 from Africa, and 1 from Asia), which reported a prevalence of 35% (95% CI, 27%–43%) in ART-experienced adults [3]. We found regional variability in hypertension prevalence, with highest rates in the high-income region and lowest in Southeast/East Asia. This is consistent with data reported from a global systematic review and meta-analysis of 59 cross-sectional studies of hypertension in PWH vs the general population [21]. The authors found a higher relative risk (RR) of hypertension among PWH in North America (RR, 1.12) and lower RRs in Africa (0.75) and Asia (0.77). Our prevalence in the sub-Saharan African region is substantially higher (35%) than the ~20% rate reported from 2 recent systematic reviews and meta-analyses of PWH from Africa [2, 9]. This may be attributed, in part, to the focus on people aged ≥40 years in REPRIEVE.

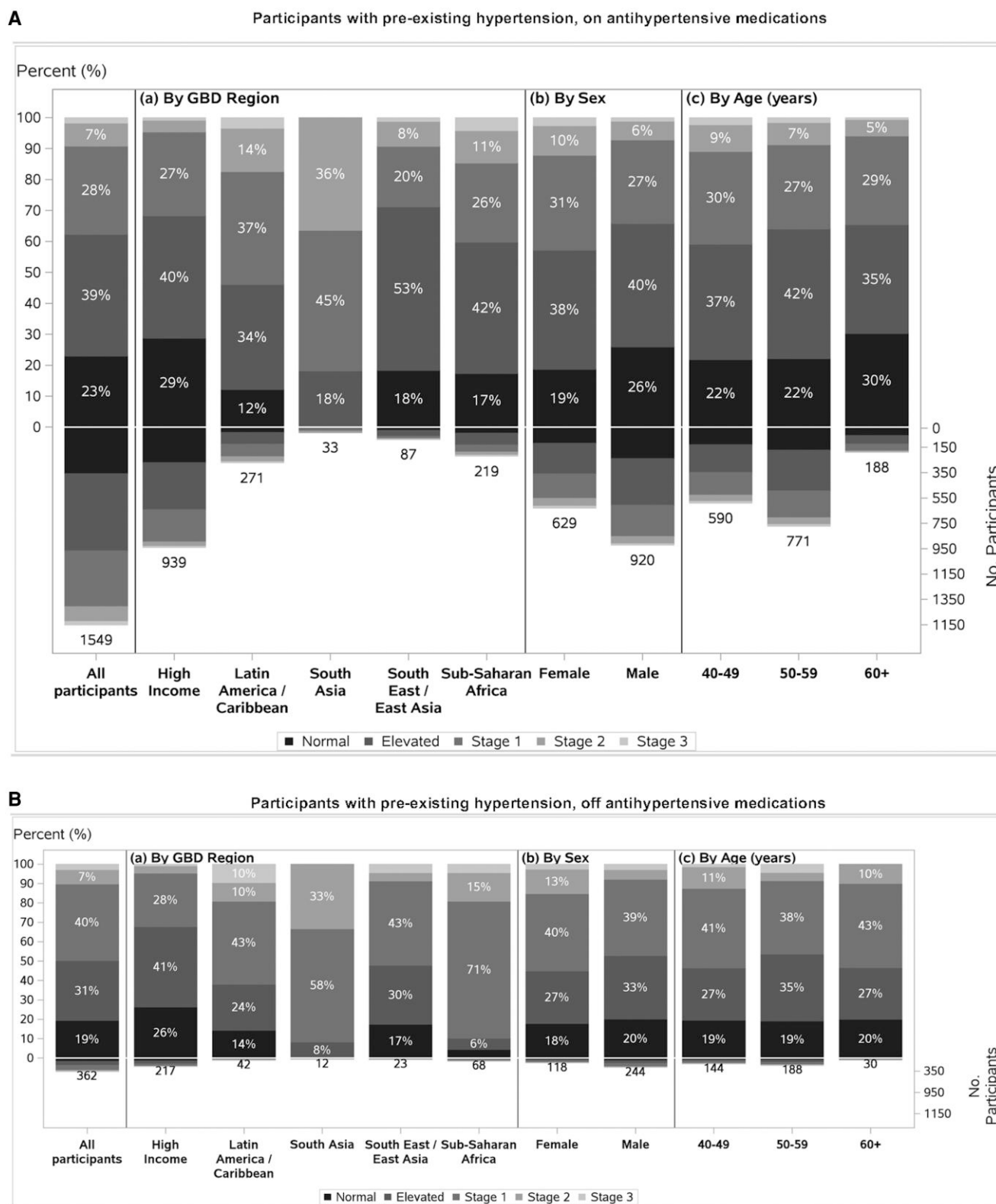


Figure 3. Hypertension control at baseline by stage among participants with preexisting hypertension, based on global thresholds. *A*, Participants with preexisting hypertension prescribed antihypertensive medications. *B*, Participants with preexisting hypertension without antihypertensive medications. Normal: SBP <130, DBP <80. Elevated: SBP, 130–139; DBP, 80–89. Stage 1: SBP, 140–159; DBP, 90–99. Stage 2: SBP, 160–179; DBP, 100–109. Stage 3: SBP ≥180, DBP ≥110. Abbreviations: DBP, diastolic blood pressure; GBD, Global Burden of Disease; SBP, systolic blood pressure.

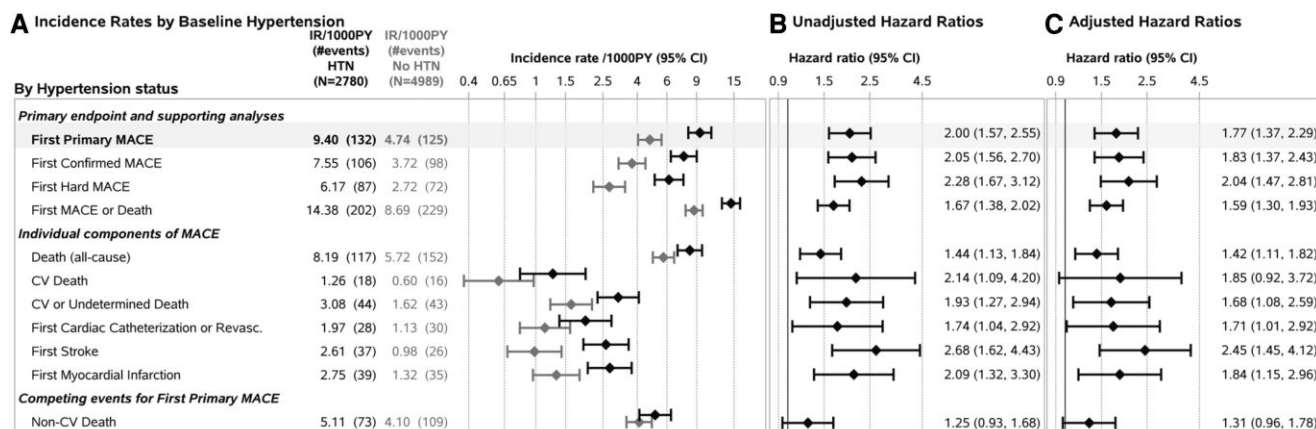


Figure 4. Incidence of primary MACE and components of MACE by baseline hypertension status (N = 7769): *A*, incidence rates by baseline hypertension; *B*, unadjusted hazard ratios; *C*, adjusted hazard ratios. CV, cardiovascular; HTN, hypertension; IR, incidence rate; MACE, major adverse cardiovascular event; PY, person-year.

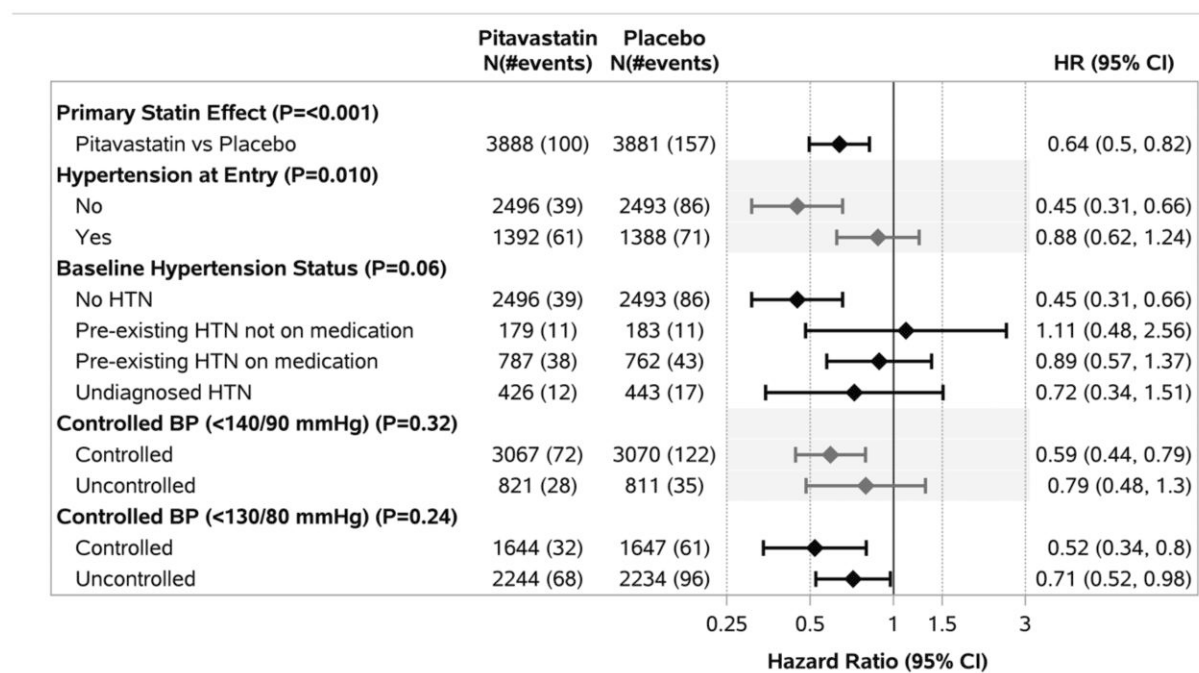


Figure 5. Effect modification of statin effect on MACE outcomes by baseline hypertension status and control (N = 7769). BP, blood pressure; HR, hazard ratio; HTN, hypertension; MACE, major adverse cardiovascular event.

Baseline hypertension was more common in REPRIEVE participants with traditional risk factors, including older age, higher BMI, Black or African American race in the high-income region, and estimated glomerular filtration rate <90 mL/min/1.73m². BMI >25 kg/m² has emerged as an important risk factor for hypertension in other studies of PWH [9], and the importance of weight gain in HIV has garnered increased attention in the era of integrase strand transfer inhibitor-based

first line regimens, which are associated with weight gain, particularly in Black African and African American women [22]. In our unadjusted analysis, women had a higher prevalence of hypertension than men, but this finding did not hold in the adjusted analysis, which demonstrated that overweight and obese BMI (which was more common in women) was strongly driving hypertension prevalence. We are unable to disentangle contributions of ART vs weight to hypertension

in this analysis. Finally, reduced renal function based on estimated glomerular filtration rate <90 mL/min/1.73 m² emerged as more common among those with hypertension. This is notable because REPRIEVE excluded people with renal disease (GFR ≤ 60 mL/min/1.73m²); however, this finding is consistent with the known association of hypertension and cardiovascular-kidney-metabolic syndrome [23]. Overall, findings from this REPRIEVE analysis highlight that traditional risk factors for hypertension (particularly overweight and obese BMI) are important in PWH, and modifiable factors should be routinely addressed as part of routine HIV care. These data add to those from another recently published analysis from REPRIEVE showing a 13% incidence of hypertension over the study follow-up period, with traditional risk factors associated with developing hypertension and a protective effect of pitavastatin (17% RR reduction in incident hypertension) [24].

Blood pressure control ($<140/90$ mm Hg) among people in REPRIEVE with preexisting hypertension (60%) is similar to the general population in high-income countries (range 50–72%) [10]. Our control rates are higher than data reported in PWH from low- and middle-income countries, which range from as low as 13% to 20% [8, 9] and as high as 42% in Botswana [3]. We found considerable variability in hypertension control by region, with lower levels of control in South Asia regardless of antihypertensive medication and in the sub-Saharan Africa region among those not taking antihypertensive medications. These data are limited by the small enrollment from some regions, including South Asia. Further research is needed to disentangle contributions of clinical, lifestyle, and health system factors that may contribute to regional variability in hypertension control. We found a signal for lower rates of hypertension control in women even after adjustment for traditional risk factors, which diverges from reports in the general population [10]. This finding requires further exploration and confirmation.

We found that hypertension at baseline in REPRIEVE was associated with a 1.8- to 2.5-fold hazard for primary and hard MACE and key components of the MACE outcome, including myocardial infarction and stroke, which persisted even when adjusted for other traditional CVD risk factors. Of note, a similar finding was reported for the association between incident hypertension during REPRIEVE follow-up and MACE (HR, 2.16; 95% CI, 1.32–3.52), highlighting the importance of preventing hypertension to protect cardiovascular health [24]. Additionally, we expand on previous data from REPRIEVE that showed that the statin effect was attenuated for those with hypertension at baseline [11]. While limited by small sample size, we see similar effect modification of statin on MACE across our hypertension subgroups. Additionally, the statin effect was attenuated less in those with blood pressure control at the $<140/90$ and $<130/80$ thresholds but with wide and overlapping confidence intervals, limiting our ability to draw conclusions about stronger benefit in the more stringent control category. At the time when

REPRIEVE started enrolling in 2015, ACC/AHA guidelines utilized 140/90 mm Hg as the threshold for a confirmed hypertension diagnosis [25]. The ACC/AHA updated its guidelines in 2017 to define stage 1 hypertension as $<130/80$ mm Hg based on data suggesting a gradient of risk for CVD as blood pressure increases from $<120/80$ to 130–139/85–89 mm Hg [26, 27], and the recent 2025 update has retained the same thresholds [20]. Our small sample size across subgroups precludes confirmation of a gradient. Further research is needed to characterize the degree to which more stringent blood pressure control may reduce MACE and other hypertension-related complications.

Limitations

This analysis was performed in a population specifically enrolled with low to moderate CVD risk and cannot be generalized to PWH in higher-risk categories. Our “undiagnosed” subgroup was categorized by only a single blood pressure measurement. Current guidelines require >1 elevated blood pressure for diagnosis unless the value exceeds a threshold indicating hypertensive urgency/emergency. This group could encompass people with “white coat” hypertension, those with a spurious reading, or those in whom blood pressure was assessed with an incorrectly sized blood pressure cuff. Furthermore, our subgroups classifying blood pressure control were based on a single blood pressure reading and thus likely misclassified some participants. Our analyses of statin effect modification by baseline hypertension subgroup lacked precision given the relatively small sample sizes within each group. Finally, significant heterogeneity in prevalence and control data likely reflects differences in health care access and social and behavioral factors that influence antihypertensive medication adherence as well as the ability to implement lifestyle changes for improving control. An evaluation of these factors is beyond the scope of this analysis and is important for future studies.

CONCLUSIONS

Despite being enrolled with low to moderate traditional CVD risk, approximately 1 in 3 participants in REPRIEVE had hypertension at baseline. Hypertension was associated with traditional risk factors and was frequently suboptimally controlled. We identified regional differences that may have implications for screening and treatment programs tailored to the local context. Our exploratory analyses bring attention to unanswered questions about the relationship between hypertension, hypertension control, and MACE in PWH. These findings highlight the urgent need for improved screening and treatment of hypertension as part of HIV care, as well as further research on optimal hypertension control thresholds for PWH.

Supplementary Data

Supplementary materials are available at [Open Forum Infectious Diseases](#) online. Consisting of data provided by the authors to benefit the reader,

the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Data-sharing statement. Data are available from the REPRIEVE Trial (mghreprieve-trial@mgb.org) upon reasonable request. In this case, shared data may include individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices). To gain access, data requestors will need to sign a data access agreement. The study protocol is available on clinicaltrials.gov. Data will be available following publication, pending approval by the parent study data-sharing committee and the ACTG.

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