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Hypertension and one-year risk of all-cause mortality among women with treated HIV in the United States

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Abstract

Objective: Hypertension is a critical cause of cardiovascular disease, and women with HIV have a higher prevalence of hypertension compared to women without HIV. The relationship between hypertension and mortality has not been well characterized in women with treated HIV. Here, we estimate the effect of hypertension on one-year risk of all-cause mortality among women with HIV on antiretroviral therapy (ART) in the United States.

Design: An analysis of multicenter, observational cohort data from the Women's Interagency HIV Study (WIHS) collected between 1995 and 2019.

Methods: We included women with HIV who reported ever using ART. We used parametric g-computation to estimate the effect of hypertension (systolic blood pressure ≥ 140 [mmHg], diastolic blood pressure ≥ 90 , or use of hypertensive medication) on all-cause mortality within one year of a WIHS visit.

Results: Among 2,929 unique women, we included 57,034 visits with a median age of 45 (interquartile range: 39, 52). Women had hypertension at 34.5% of visits, and 641 deaths occurred within one year of a study visit. Comparing women at visits with hypertension to women at visits without hypertension, the standardized one-year risk ratio (RR) for mortality was 1.16 (95% confidence interval [CI]: 1.01, 1.33). The risk ratios were higher in Hispanic (RR: 1.23, 95% CI: 0.86, 1.77) and non-Hispanic Black women (RR: 1.19, 95% CI: 1.04, 1.37) and lower in non-Hispanic white women (RR: 0.93, 95% CI: 0.58, 1.48).

Conclusion: Among women with treated HIV, those with hypertension, compared to those without, had an increased one-year risk of all-cause mortality.

Keywords

HIV; hypertension; mortality; epidemiology; antiretroviral therapy; chronic comorbidities; cohort study

Introduction

People with HIV are surviving longer due to the efficacy and uptake of antiretroviral therapy (ART).[1–3] Aging of people with HIV has resulted in a larger burden of chronic conditions and comorbidities in this population.[4] As deaths from AIDS-related causes have declined in the era of modern ART, the leading causes of death have shifted to chronic conditions such as cardiovascular disease.[3,5–7] HIV has been recognized as a risk factor for cardiovascular disease, as people with HIV are at higher risk than people without HIV for cardiovascular disease and events.[8–12] Moreover, women with HIV have a higher burden of non-AIDS comorbidities than men with HIV.[13,14] The impact of cardiovascular disease and chronic conditions on women with HIV, compared to men with HIV, is less well understood due to under-representation of women in HIV research and lack of sex-stratified analyses.[15–17]

Hypertension is a leading cause of myocardial infarction, sudden cardiac death, and stroke, [18–20] and is more common in women with HIV than HIV seronegative women. In 2011-2014, the estimated prevalence of hypertension among women with HIV was

46.3%[21] while the prevalence among HIV seronegative women was 28.1%.[22] The higher prevalence in women with HIV may be due to immune activation, altered hormone production, and health behaviors.[16] The effect of hypertension on all-cause mortality is not well characterized among women with HIV.[23]

Among women with HIV, disparities exist in the prevalence of hypertension. Black women with HIV have a higher prevalence of hypertension than white women with HIV,[24] likely due to social determinants of health, exposure to structural racism, and poorer access to healthcare.[25] Women with HIV with insurance coverage interruptions have an increased risk of loss of hypertensive control.[26] Yet, few studies have assessed whether these disparities influence the relationship between hypertension and health outcomes, including mortality.

We estimated the effect of hypertension on one-year risk of all-cause mortality among women with HIV in the Women's Interagency HIV Study (WIHS, now the MACS/WIHS Combined Cohort Study, MWCCS), and whether the estimated effect varied by racial-ethnic categories, age, and health insurance.

Methods

Data.

We analyzed data from the WIHS.[27] Since starting recruitment in 1994, the WIHS expanded from 6 to 10 sites including Brooklyn, NY; the Bronx/Manhattan, NY, Washington, DC; Chicago, IL; San Francisco, CA; Los Angeles, CA; Chapel Hill, NC; Atlanta, GA; Birmingham, AL/Jackson, MS; and Miami, FL. Additional recruitment waves occurred in 2001-02, 2011-12, and 2013-15. Eligibility criteria remained similar throughout the study. WIHS enrollees participated in study visits approximately every 6 months that consisted of laboratory testing, clinical evaluation, and structured interviews. Social, behavioral, clinical, and medication use information was collected at each visit. All participants provided informed consent, and each study site's institutional review board approved study protocols.

Eligible participants for this study had 1) HIV infection at WIHS enrollment or seroconverted (n=21) before the one-year follow-up period and 2) reported ever receiving triple combination ART before the one-year follow-up period. Upon reported use of ART, women contributed attended visits thereafter. We excluded 90 women who did not have visits after reported use of triple combination ART.

Exposure definition.

At each visit, women were categorized as hypertensive if they had at least one of the following: 1) systolic blood pressure (SBP) \geq 140 (millimeters of mercury, mmHg), 2) diastolic blood pressure (DBP) \geq 90 (mmHg), or 3) reported use of hypertensive medication over the past 6 months. Guidelines recommend the threshold for hypertension be \geq 130 SBP or \geq 80 DBP, though pharmacological treatment is typically administered at \geq 140 SBP or \geq 90 DBP.[28]

Prior to 2001, blood pressure was measured and recorded once at each visit. Between 2001 to 2004, blood pressure was measured twice per visit. The higher measurement was recorded if SBP or DBP measurements differed by more than 80 and 45 mmHg, respectively; otherwise, the second measurement was recorded. Starting in 2004, three blood pressure measurements were taken at each visit, and the average of the second and third measurement was recorded. Study staff collected blood pressure from the seated participant's right arm at one-minute intervals by an oscillometric automated blood pressure monitor (DinaMap ProCare Series; GE Medical Systems, Chicago, IL). Between each measurement, study staff raised the participant's arm for five seconds.[29]

Outcome definition.

The outcome was all-cause mortality within one year of a WIHS visit. The one year follow up period employed the 6-month WIHS visit interval and allows hypertensive status to vary over follow up. Dates of death were determined by matching to the National Death Index, reviewing death certificates and medical records, and contacting next of kin following participants' missed visits.[30] Women who died within one year of their visit were classified as experiencing the outcome.

Covariates.

We constructed a causal diagram to identify potential confounders.[31,32] To ensure that confounders temporally preceded hypertension, we used values taken at the preceding visit for select variables that may affect hypertension with delay. Figure 1 illustrates measurement timing of analysis variables with V_t (center) as the visit of interest. We specified the following continuous covariates as restricted quadratic splines with knots placed at the 5th, 35th, 65th, and 95th percentiles:[33] age, body mass index (kg/m^2), previous visit CD4 cell count (cells/mm^3), and previous visit kidney function (estimated glomerular filtration rate). [34]

We used binary indicator variables for categorical covariates: alcohol use in past 6 months (abstainer, 0-7 drinks per week, >7-12 drinks per week, >12 drinks per week); annual household income (<\$6,000, \$6,001-\$12,000, >\$12,000-\$18,000, >\$18,000); ART drug classes used in past 6 months (nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors, entry inhibitors, and integrase inhibitors); health insurance (insured or uninsured); self-reported mutually exclusive racial-ethnic category (Hispanic Black, non-Hispanic Black, Hispanic white, non-Hispanic white, Hispanic other, or non-Hispanic other); history of hypertension (hypertension at any of previous four visits); smoking status (never, former, current); self-reported use of non-injection drugs (e.g., marijuana, hallucinogens, PCP, club drugs, methamphetamines) within past six months; self-reported injection of any illicit drug within past six months; diabetes at previous visit (when non-pregnant, self-reported anti-diabetic medication, two fasting glucose measurements ≥ 126 mg/dL, or concurrent measurements of hemoglobin A1c $\geq 6.5\%$ and fasting glucose ≥ 126 mg/dL, or not); nadir CD4 cell count (<200 cells/mm^3 , or not); previous visit low-density lipoprotein (LDL, >130 mg/dL or not); and previous visit HIV viral suppression (<80 copies/mL, or not). For 21 visits where HIV viral load was undetectable using tests with a lower limit of detection >80 copies/mL, we assumed viral

load was <80 copies/mL. We adjusted for calendar time (WIHS visit) to account for secular trends in hypertension and mortality not captured by other covariates.

Missing data.

We used Markov chain Monte Carlo multivariate normal multiple imputation to impute missing values.[35,36] We imputed 30 datasets. While we had complete data on mortality, blood pressure measurement was missing at 7.8% of visits. The alternative hypertension definition (controlled or uncontrolled) had more missing data (17.4%), due to additional missingness on medication use. Most variables had less than 10% of missing data across visits; however, LDL was missing at 30.4% of visits due to annual measurement of cholesterol in the WIHS. Using published guidance,[37] our imputation model included hypertension, mortality, covariates, and interaction terms included in analysis models.[36]

Statistical analysis.

We estimated marginal risks, risk differences (RDs), and risk ratios (RRs) using parametric g-computation, a model-based form of standardization.[38–41] Parametric g-computation removes measured confounding by standardizing the study sample with hypertension and study sample without hypertension to the covariate distributions of the combined study sample. Under certain necessary assumptions (see Discussion),[38] estimated risks can represent a causal effect.[39]

We used the following steps, adapted from Snowden et al.,[39] to obtain estimates using parametric g-computation. First, we copied each visit twice to create a g-computation analysis dataset that contained the original visit (with observed exposure and outcome), a visit copy with exposure assigned to “hypertensive” and a missing mortality outcome, and another copy with exposure assigned to “not hypertensive” and a missing mortality outcome. All visits (original and copied) maintained observed covariate values. We fit a logistic regression model, with covariates identified from our causal diagram, on the combined copied and observed data. Using this model, we predicted the probability of all-cause mortality within one year for visit copies with assigned hypertension exposure. We averaged predicted probabilities among those assigned to “hypertensive,” and then those assigned to “not hypertensive,” to obtain estimated marginal one-year risks of all-cause mortality under each level of hypertension. Those marginal risks were used to estimate RDs and RRs. We evaluated effect modification by calculating contrasts within strata of age (<40, 40–<55, or 55 years), racial-ethnic category (non-Hispanic Black, non-Hispanic White, or Hispanic; “other” race not assessed due to small cell counts), and health insurance coverage (insured or uninsured).

We checked for adequate parametric g-computation model specification by comparing main effects, marginal estimates of the RD and RR to those from an inverse-probability-of-treatment-weighted (IPTW) model[41,42] (steps in Supplementary Digital Content). Upon confirming similar estimates from g-computation and the IPTW model, we used AIC to select interaction terms for a more flexible parametric g-computation model. We included interaction terms between hypertension and 1) CD4 cell count, 2) suppression of HIV viral load, 3) racial-ethnic category, 4) health insurance, and 5) continuous age.

We calculated Wald 95% confidence intervals (CIs) by employing nonparametric bootstrap methods.[43] Bootstrapping must accommodate lack of independence between observations due to multiple visits per woman; thus, bootstrap samples selected (with replacement) unique women from the study sample.[43] If a woman was selected for the bootstrap sample, she contributed all eligible visits to the sample. Each bootstrap sample applied the steps outlined for g-computation (and IPTW) to obtain risk estimates for that sample.[40,44] After repeating this process 200 times, we obtained the standard deviation of the 200 risks and contrast estimates, which served as the estimated standard errors for Wald 95% CIs.

Sensitivity analyses.

We performed sensitivity analyses using an alternative definition of hypertension, as mortality may differ by controlled or uncontrolled hypertension.[45,46] The alternative exposure definition used three hypertension categories. *Normotensive* women had no indications of hypertension; women with *controlled hypertension* had SBP <140, DBP <90, and reported hypertensive medication use; and women with *uncontrolled hypertension* had SBP ≥ 140 or DBP ≥ 90 with or without reported use of hypertensive medication. We performed an additional sensitivity analysis for mortality events that occurred within 18 months of the last attended visit, which included 23 additional mortality events. Further, we restricted the analysis to 2000-2019 to evaluate whether results were robust to potential increases in ART efficacy during later years of the study.

Results

The analysis sample contained 2,929 unique women and 57,034 study visits from 1995-2019, with 42.7% of visits occurring from 2010 to 2019. The median number of visits contributed by each woman was 16 (IQR: 10, 32). The median age at analysis baseline was 39 years (IQR: 33, 46) while the median age over all visits was 45 (IQR: 39, 52; range: 18-89) (Table 1). The median age at visits with hypertension (50, IQR: 44, 56) was higher than at visits without (42, IQR: 36, 49). Most visits were attended by non-Hispanic Black women (59.4%), followed by Hispanic women (23.7%) and non-Hispanic white women (13.6%). Women reported having insurance coverage at 86.7% of visits. Current smoking (40.9% vs. 39.8%) and heavy alcohol use (>7 drinks per week) (7.9% vs 7.7%) were similar at hypertensive and normotensive visits. Obesity (50.2% vs. 34.0%) and diabetes (24.5% vs. 7.7%) were more common at hypertensive visits (Table 1).

The prevalence of hypertension was 26.6% at analysis baseline, and women were hypertensive at 34.5% of all visits (Table 1). Non-Hispanic Black women had hypertension at 41.7% of visits. Non-Hispanic white women and Hispanic women had hypertension at 25.2% and 22.6% of visits, respectively. Among women 40-49, 40-49 <55, and ≥ 55 years of age, the proportions of visits with hypertension were 14.9%, 36.2%, and 60.5%, respectively. Among visits with non-missing insurance data, more women had hypertension at visits with reported health insurance (38.1%) than without health insurance (25.6%).

Within one year of a visit, 641 women experienced death from any cause. The crude RR comparing the one-year risk of death among women at visits with hypertension to those without was 1.63 (95% CI: 1.48, 1.80), and the crude RD was 1.0% (95% CI: 0.7%, 1.2%).

Main analysis.

The covariate standardized one-year RR and RD estimated from the parametric g-computation main effects model were similar to the IPTW estimates, indicating adequate model specification for the parametric g-computation model (data not shown). Upon including interaction terms in the parametric g-computation model, the estimated one-year risks of mortality for women with hypertension and without hypertension at their visit, respectively, were 2.0% (95% CI: 1.8%, 2.3%) and 1.8% (95% CI: 1.6%, 1.9%). The RR comparing women with hypertension at their visit to women without was 1.16 (95% CI: 1.01, 1.33), and the RD was 0.3% (95% CI: 0.0%, 0.6%) (Table 2).

Analysis of health disparities.

RDs and RRs modestly varied by racial-ethnic categories, age, and health insurance coverage (Table 2). Hispanic women with hypertension at their visit had 1.23 (95% CI: 0.86, 1.77) times the one-year risk of all-cause mortality than Hispanic women without hypertension. The RR for non-Hispanic Black women was 1.19 (95% CI: 1.04, 1.37). Among non-Hispanic white women, those with hypertension at their visit had 0.93 (95% CI: 0.58, 1.48) times the risk for all-cause mortality than those without hypertension. The RRs and RDs did not linearly increase or decrease with age (Table 2). The estimated RRs and RDs comparing women with hypertension to those without was greatest among women who were 40 years of age at their visit (RR: 1.64, 95% CI: 1.19, 2.26).

Insurance status did not modify the estimates of hypertension and one-year risk of all-cause mortality. At visits where women reported no health insurance, the RR was 0.97 (95% CI: 0.60, 1.56), which was slightly lower than visits with health insurance (RR: 1.17, 95% CI: 1.03, 1.34).

Sensitivity analyses.

Using the alternate exposure definition for hypertension, 69.8% of women were normotensive, 21.4% had controlled hypertension, and 8.8% had uncontrolled hypertension. The RR comparing the risk of all-cause mortality for controlled hypertension to the risk for no hypertension was 1.22 (95% CI: 0.89, 1.66) (Table S1, Supplementary Digital Content). The RR comparing the mortality risk for uncontrolled hypertension to the risk for no hypertension was 1.13 (95% CI: 0.83, 1.54) (Table S2, Supplementary Digital Content). We saw no qualitative differences in our estimates when extending the risk window from 12 to 18 months (Table S3, Supplementary Digital Content). Restricting the analysis to the years 2000-2019 yielded qualitatively similar results as the main analysis (data not shown).

Discussion

We assessed the relationship between hypertension and one-year risk of all-cause mortality among women with HIV with a reported history of triple combination ART in the WIHS. Women with hypertension, compared to those without, had an increased one-year risk of death among women with treated HIV. The RDs and RRs varied slightly by age and racial-ethnic category. While variations were modest, they were consistent with current knowledge

about disparities in the prevalence, incidence, and control of hypertension, as well as the incidence of cardiovascular events.[13,24,47–50]

The higher RRs for non-Hispanic Black and Hispanic women reflect racial-ethnic disparities in the relationship between hypertension and mortality. Results may help clinicians target subgroups of women with treated HIV who may benefit from prioritizing hypertensive treatment. This disparity aligns with racial disparities that exist in the prevalence of hypertension and incidence of cardiovascular events.[24,48] It is important to note racial-ethnic categories do not fully capture exposure to racism and structural racism, which are known to negatively impact health, including cardiovascular health.[25,51]

The prevalence of hypertension at analysis baseline (26.6%) and included visits (34.5%) were lower than a recent estimate among people with HIV engaged in care (42.4%),[21] but were within the range of prevalence estimates among people with HIV globally.[47] Further, we observed disparities in the prevalence of hypertension: Non-Hispanic Black women were hypertensive at 41.7% of their visits, compared to 25.2% of non-Hispanic white women and 22.6% of Hispanic women. Older women were more likely than younger women to have hypertension at their visit. The proportion of current smoking did not substantially differ by hypertensive status, a phenomenon that has been previously observed in HIV cohorts.[52] However, women who were never smokers were slightly more likely to be normotensive at their visit.

Access to health care, partially reflected by health insurance coverage, is associated with improved management of chronic diseases, such as hypertension,[51] but loss of health insurance can increase the risk of loss of hypertension control.[26] Health insurance status in the WIHS cohort is mostly stable, as most do not experience insurance interruptions, though change of insurance type is fairly common.[26,53] Estimated RRs and RDs were slightly higher among insured women than uninsured women, though confidence intervals were wide. This seemingly paradoxical finding is common in mortality studies among people with HIV as people with severe disease or risk of death are more likely to be insured.[54,55] Further, less than 10% of visits were attended by women without insurance, resulting in underpowered stratified analyses.

People with controlled hypertension have improved mortality and cardiovascular disease outcomes compared to those who have uncontrolled hypertension.[45,46] However, our sensitivity analysis using the controlled, uncontrolled, and no hypertension definition revealed minimal differences in the risk contrasts for visits with controlled and uncontrolled hypertension, compared to visits without hypertension. The estimates for visits with controlled and uncontrolled hypertension agreed with the binary definition of hypertension in the main analysis, though confidence intervals were less precise due to decreased sample sizes in the uncontrolled and controlled hypertension groups.

Hypertension increases the risk for adverse health outcomes, leading to decreased quality of life or chronic illnesses, not only cardiovascular events or deaths.[56] While the WIHS cohort ascertains cause of death among participants using death certificates and the NDI, determining primary cause of death is challenging and often misclassified on

death certificates.[57] The most common cause of death in the WIHS was AIDS until 2002 and non-AIDS causes thereafter, which included non-AIDS malignancies and liver- and cardiovascular-related deaths.[30,58] Our time-restricted sensitivity analysis indicated our results were not sensitive to including visits prior to the modern ART era, likely because most study visits occurred after 1999 and analysis inclusion criteria required at least triple combination ART.

We applied a novel method (i.e., parametric g-computation) to answer our research question; but this analysis presents some limitations. Parametric g-computation estimates the causal RR and RD assuming no uncontrolled confounding, causal consistency of the exposure, no measurement error, and correct model specification.[38,39,42] Blood pressure, a continuous measure, was used to create a binary hypertension variable. Within levels of the binary exposure, blood pressure has varying levels of severity, as very high and very low blood pressure have a strong relationship with mortality.[28,59] Nevertheless, this threshold aligns with clinical practice guidelines for pharmacologic treatment of hypertension.[28] Despite including several covariates in models to account for confounding, unobserved confounding remains a threat in observational research. Possible unmeasured confounders include diet, exercise, and other lifestyle factors; these data were not collected routinely during follow-up.[45,46] Lastly, results may not be generalizable to all ART-treated women with HIV in the United States. Most women in the WIHS were engaged in HIV care and regularly attended study visits; therefore, they may be different than women with HIV not engaged in care. Despite limitations, this analysis builds upon previous research[6,21,24,26] and presents an application of parametric g-computation to estimate the effect of hypertension on one-year risk of mortality, rather than estimating conditional, associational measures from ordinary regression models.

The small increase in the one-year RD for all-cause mortality among women with hypertension, compared to women without, was not surprising given the short risk period. However, the increase in the one-year risk of death in the RR is notable. While we did not evaluate an intervention for hypertension (e.g., blood pressure lowering medication), evidence supports efficacy of lifestyle modification and pharmaceuticals to lower blood pressure.[28] The largest estimated RRs and RDs for mortality comparing women with hypertension to women without were among non-Hispanic Black women, Hispanic women, and women <40 years of age. Clinicians providing care to women of color with HIV or young women with HIV may want to prioritize reducing blood pressure through lifestyle modification or hypertensive medication. More attention is needed to understand disparities in the relationship between hypertension and mortality.

Women with HIV on ART had hypertension at over a third of their visits. Given the high prevalence in this population, this analysis underscores how even a moderate relative increase in risk of death can be clinically important. While hypertension may not have been the direct cause of death for women with treated HIV, improvements in population health can result from intervening on a condition with a modest to moderate association that is highly prevalent in the population, rather than a rare exposure with a strong association.[60] Thus, hypertension is a promising target for intervention to improve population health for women with treated HIV in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of interest:

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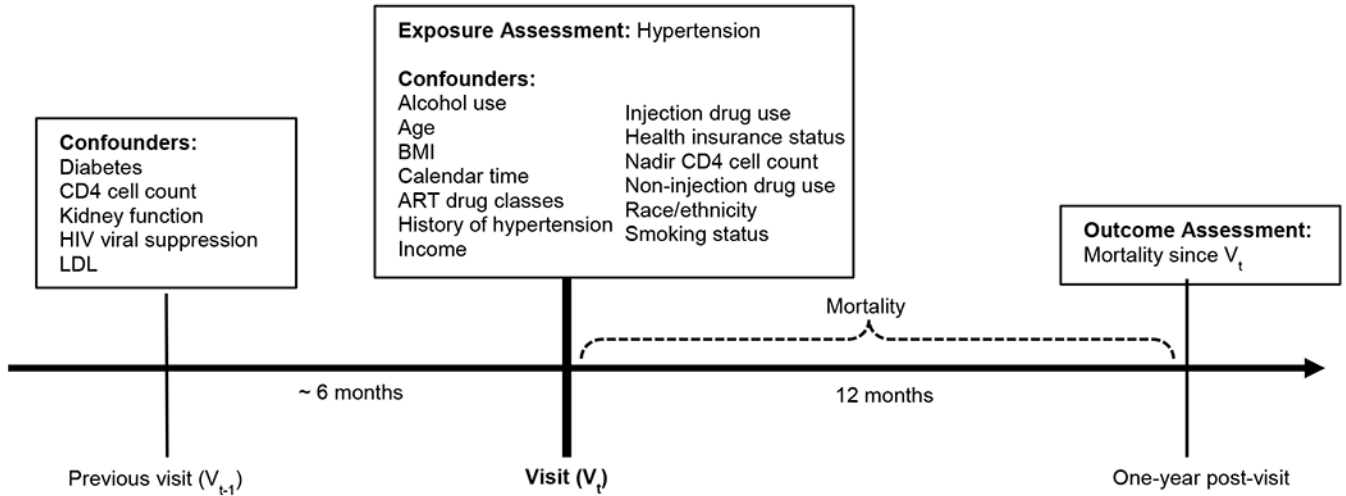


Figure 1: Measurement timing of key variables in the relationship between hypertension and mortality in the WIHS

V_t (center) is the visit of interest. Values for diabetes, CD4 cell count, kidney function, HIV viral suppression, and high LDL are from the previously attended visit (V_{t-1}) which was approximately six months prior to V_t . Values used from V_t includes alcohol use, age, BMI, ART drug classes, history of hypertension, income, injection drug use, health insurance status, nadir CD4 cell count, non-injection drug use, race/ethnicity, and smoking status. The outcome, mortality, is measured one year after V_t . BMI, body mass index; ART, antiretroviral therapy; LDL, low-density lipoprotein.

Table 1:

Characteristics at analysis baseline and at study visits among women with HIV in the Women's Interagency HIV Study, by hypertension status, 1995-2019

	Total women (n=2,929)	Women with hypertension at baseline (n=780)	Women with no hypertension at baseline (n=2,039)	Total visits (n=57,034)	Visits with hypertension (n=19,674)	Visits with no hypertension (n=32,895)
Year of visit						
1995-1999	1,050 (35.9)	210 (26.9)	817 (40.1)	4,186 (7.3)	835 (4.2)	3,225 (9.8)
2000-2009	1,006 (34.3)	187 (24.0)	754 (37.0)	28,493 (50.0)	7,957 (40.4)	18,096 (55.0)
2010-2019	873 (29.8)	383 (49.1)	468 (22.9)	24,355 (42.7)	10,882 (55.3)	11,574 (35.2)
Age in years, median (IQR)	39 (33, 46)	45 (39, 52)	37 (32, 43)	45 (39, 52)	50 (44, 56)	42 (36, 49)
<40 years	1,505 (51.4)	207 (26.5)	1,245 (61.1)	15,914 (27.9)	2,370 (12.0)	12,503 (38.0)
40 to <55 years	1,239 (42.3)	452 (57.9)	740 (36.3)	31,222 (54.7)	11,315 (57.5)	17,389 (52.9)
55 years	185 (6.3)	121 (15.5)	54 (2.6)	9,898 (17.4)	5,989 (30.4)	3,003 (9.1)
Race and Ethnicity						
Non-Hispanic Black	1,827 (62.4)	612 (78.5)	1,153 (56.5)	33,900 (59.4)	14,137 (71.9)	17,537 (53.3)
Non-Hispanic white	379 (12.9)	68 (8.7)	294 (14.4)	7,734 (13.6)	1,949 (9.9)	4,787 (14.6)
Hispanic	637 (21.7)	87 (11.2)	522 (25.6)	13,512 (23.7)	3,058 (15.5)	9,397 (28.6)
Other	86 (2.9)	13 (1.7)	70 (3.4)	1888 (3.3)	530 (2.7)	1,174 (3.6)
Annual household income						
<\$6,000	610 (24.2)	172 (24.4)	427 (24.0)	7,797 (16.4)	2,565 (14.6)	4,975 (17.3)
\$6,001-\$12,000	980 (38.9)	283 (40.1)	677 (38.1)	18,944 (39.7)	7,824 (44.6)	10,560 (36.8)
\$12,001-\$18,000	418 (16.6)	114 (16.2)	299 (16.8)	7,707 (16.2)	2,872 (16.4)	4,606 (16.1)
>\$18,000	513 (20.3)	136 (19.3)	373 (21.0)	13,223 (27.7)	4,268 (24.3)	8,548 (29.8)
Missing	408	75	263	9363	2,145	4,206
Health insurance coverage						
Insured	2,292 (78.4)	620 (79.6)	1,587 (78.0)	46,988 (86.7)	16,478 (90.6)	26,744 (84.3)
Uninsured	632 (21.6)	159 (20.4)	448 (22.0)	7216 (13.3)	1,710 (9.4)	4,963 (15.7)
Missing	5	1	4	2,830	1,486	1,188
CD4 cell count, cells/mm ³ , median (IQR)	408 (245, 610)	435 (282, 655)	397 (236, 592)	495 (301, 716)	539 (334, 776)	472 (286, 682)

	Total women (n=2,929)	Women with hypertension at baseline (n=780)	Women with no hypertension at baseline (n=2,039)	Total visits (n=57,034)	Visits with hypertension (n=19,674)	Visits with no hypertension (n=32,895)
Missing	282	50	201	5261	1,304	2,561
HIV viral load <80 copies/mL	695 (25.5)	307 (40.8)	371 (19.7)	22,394 (41.0)	9,772 (51.0)	10,776 (34.0)
Missing	202	27	151	2,429	502	1,208
BMI (kg/m ²), median (IQR)	27.8 (23.9, 33.4)	31 (25.5, 38.6)	26.8 (23.4, 31.6)	28.1 (24.0, 33.5)	30 (25.0, 36.1)	27.1 (23.6, 32.0)
30 kg/m ²	1,082 (38.7)	424 (55.0)	649 (32.3)	21,064 (40.1)	9,737 (50.2)	11,081 (34.0)
Missing	130	9	30	4,455	262	286
eGFR (ml/min/1.73 m ²), median (IQR)	102.6 (85.2, 118.4)	95.7 (76.4, 112.0)	105.8 (89.3, 120.2)	96.7 (78.8, 112.9)	87.9 (69.6, 106.4)	101.7 (85.0, 116.0)
Missing	689	150	516	7,140	1,671	4,145
LDL cholesterol >130 mg/dL	264 (19.0)	93 (20.4)	162 (18.1)	7,189 (18.1)	2,751 (18.3)	4,131 (18.0)
Missing	1,543	325	1,144	17,320	4,612	9,970
Diabetes	162 (5.5)	103 (13.2)	54 (2.6)	7,961 (14.0)	4,820 (24.5)	2,525 (7.7)
Smoking status						
Current	1,334 (46.6)	375 (48.1)	932 (45.9)	21,726 (40.1)	8,030 (40.9)	13,055 (39.8)
Former	547 (19.1)	159 (20.4)	378 (18.6)	15,415 (28.4)	6,196 (31.6)	8,642 (26.4)
Never	980 (34.3)	245 (31.5)	721 (35.5)	17,045 (31.5)	5,408 (27.5)	11,090 (33.8)
Missing	68	0	8	2,848	40	108
Alcohol use >7 drinks per week	272 (9.6)	97 (12.5)	168 (8.3)	4,162 (7.7)	1,549 (7.9)	2,504 (7.7)
Missing	89	6	22	3164	143	244

Observed data (before multiple imputation) are shown. Data are presented as column n (%) unless otherwise noted. Categories without a row for missing did not have any missing values. Hypertension status was missing for 110 women at baseline and at 4,465 visits; therefore "total" columns may not be the sum of hypertension and no hypertension. Hypertension was defined as systolic blood pressure 140 mmHg, diastolic blood pressure 90 mmHg, or reported use of any hypertensive medication

BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LDL, low-density lipoprotein.

Table 2:

Estimates of marginal, counterfactual risks and contrasts of hypertension on one-year risk of all-cause mortality, Women’s Interagency HIV Study (WIHS), 1995–2019

	Risk, no hypertension	Risk, hypertension	RD (hypertension vs. no hypertension)	RR (hypertension vs. no hypertension)
Overall	1.8% (1.6%, 1.9%)	2.0% (1.8%, 2.3%)	0.3% (0.0%, 0.6%)	1.16 (1.01, 1.33)
Race and Ethnicity				
Non-Hispanic Black	2.0% (1.7%, 2.2%)	2.3% (2.0%, 2.6%)	0.4% (0.1%, 0.7%)	1.19 (1.04, 1.37)
Non-Hispanic white	1.5% (1.1%, 1.9%)	1.4% (0.9%, 1.9%)	-0.1% (-0.8%, 0.6%)	0.93 (0.58, 1.48)
Hispanic	1.5% (1.2%, 1.7%)	1.8% (1.2%, 2.4%)	0.3% (-0.3%, 1.0%)	1.23 (0.86, 1.77)
Age				
<40 years	1.1% (1.0%, 1.3%)	1.9% (1.3%, 2.4%)	0.7% (0.1%, 1.3%)	1.64 (1.19, 2.26)
40–<55 years	1.9% (1.8%, 2.1%)	1.9% (1.2%, 2.4%)	-0.1% (-0.4%, 0.3%)	0.97 (0.83, 1.14)
55 years	2.2% (1.7%, 2.7%)	2.8% (2.5%, 3.1%)	0.6% (-0.1%, 1.3%)	1.28 (0.96, 1.71)
Health insurance coverage				
Insured	1.9% (1.7%, 2.1%)	2.2% (1.9%, 2.5%)	0.3% (0.0%, 0.6%)	1.17 (1.03, 1.34)
Uninsured	0.8% (0.6%, 1.0%)	0.8% (0.5%, 1.1%)	0.0% (-0.4%, 0.3%)	0.97 (0.60, 1.56)
HIV viral load				
<80 copies/mL	1.1% (0.9%, 1.3%)	1.4% (1.2%, 1.6%)	0.3% (0.0%, 0.6%)	1.30 (1.03, 1.63)
80 copies/mL	2.2% (2.0%, 2.4%)	2.5% (2.1%, 2.9%)	0.3% (-0.2%, 0.7%)	1.11 (0.94, 1.32)

Estimates presented as risk % (95% CI). RRs and RDs may differ from presented marginal risks due to post-calculation rounding. Adjusted model included continuous variables as restricted quadratic splines and categorical covariates as indicator variables. Estimates adjusted for age (continuous), alcohol use in past 6 months (abstainer, 0–7 drinks per week, >7–12 drinks per week, >12 drinks per week), annual household income (<\$6,000, \$6,001–\$12,000, \$12,001–\$18,000, >\$18,000), BMI (continuous), race/ethnicity (Hispanic Black, non-Hispanic Black, Hispanic white, non-Hispanic white, Hispanic other, or non-Hispanic other), ART drug classes used since last visit (nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors, entry inhibitors, integrase inhibitors), health insurance coverage (insured or uninsured), history of hypertension (hypertension at any previous 4 visits), smoking status (current, former, never), diabetes status (binary), self-reported injection drug use (binary), self-reported non-injection drug use (binary), CD4 cell count (<200 cells/mm³ (binary), HIV viral load <80 copies/mL (binary), LDL cholesterol >130 mg/dL (binary), and eGFR (continuous).

ART, antiretroviral therapy; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LDL, low-density lipoprotein; RD, risk difference; RR, risk ratio.