

Review Article

Global prevalence of hypertension among people living with HIV: a systematic review and meta-analysis



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Abstract

The purpose of this study was to estimate, through meta-analysis, the global prevalence of hypertension among people living with HIV (PLWH). A total of 49 studies published during 2011–2016 with 63,554 participants were included in analysis. These studies were conducted in America (25), Europe (13), Africa (10), and Asia (1) with data collected during 1996–2014. Prevalence of hypertension and confidence interval was estimated and stratified by participants' age, antiretroviral therapy (ART), and calendar-years using random effects modeling. The quality assessed using the Joanna Briggs Institute Prevalence Critical Appraisal Tool was high for all included studies. The estimated prevalence (95% confidence interval) of hypertension was 25.2% (21.2%, 29.6%) for the overall sample, 34.7% (27.4%, 42.8%) for ART-experienced, and 12.7% (7.4%, 20.8%) for ART-naïve participants. The estimated prevalence was found increased with age and in studies conducted after 2010. Hypertension among PLWH shows an increasing trend and is associated with receiving ART and older age. Findings of this study provide data for decision makers to incorporate blood pressure assessment in primary prevention and for researchers to further investigate factors and mechanisms related to hypertension among PLWH. *J Am Soc Hypertens* 2017;11(8):530–540. © 2017 American Society of Hypertension. All rights reserved.

Keywords: Antiretroviral therapy; high blood pressure; HIV-positive people.

Introduction

Globally, there are 34 million people living with HIV (PLWH).¹ The success of antiretroviral therapy (ART) has substantially increased the survivorship of PLWH.^{2,3} Along with rapid increases in life expectancy, PLWH face a new challenge: non-AIDS-related chronic diseases.⁴ Among various non-AIDS chronic diseases, hypertension is of particular significance.⁵ A number of influential factors may increase the risk of hypertension among PLWH. The proinflammatory effect induced by HIV infection on vascular endothelium may increase the risk of hypertension.^{6,7} Receiving ART represents another risk factor for

hypertension. Research has indicated that patients who received ART were more likely to have dysglycemia, hypertriglyceridemia, and lower levels of high-density lipoprotein cholesterol,^{8,9} increasing the risk for hypertension. Furthermore, PLWH are more likely than the general population to be exposed to conventional risk factors for hypertension, such as tobacco use,¹⁰ stress,¹¹ and kidney dysfunction.¹² Recent data from one longitudinal study showed a rapid increase in hypertension incidence among PLWH.¹³

Hypertension is a long-term chronic health condition and a significant risk factor for many other cardiovascular and cerebrovascular diseases. Hypertensive individuals, including PLWH, are at increased risk for cardiovascular events, including atherosclerosis, coronary disease, heart attack, heart failure, and peripheral artery disease,^{8,14,15} adding extra health burden. Hypertension is also one of the most significant predictors for many cerebrovascular diseases, particularly stroke.^{14,16} Finally, reported studies showed that among PLWH, elevated blood pressure was closely related to chronic

Conflict of interest: The authors declare that none of them has any competing interests associated with this study.

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kidney diseases and could aggravate renal dysfunction.¹⁷ HIV infection and treatment are themselves stressful and may significantly reduce the quality of life and well-being of PLWH,¹⁸ increasing the risk of developing hypertension. Having hypertension itself may add additional health burden.

The significance of hypertension among PLWH has long been recognized by researchers in clinical and public health communities. A number of published studies have reported data on hypertension among PLWH in different countries and regions across the globe. Typical studies include those conducted in North America,^{5,19} South America,²⁰ Europe,²¹ Asia,^{22,23} and Africa.^{24,25} The documented prevalence of hypertension among PLWH has differed by study population and time.^{26,27} Reported prevalence has varied from 4% in the United States from 1998 to 2008 to 50.8% in Serbia in 2010.^{26,27} Although these estimates provide useful data for clinicians and public health workers to treat and prevent hypertension locally, the global burden of hypertension among PLWH is still unknown.

Data regarding the prevalence of hypertension among PLWH in general are needed for evidence-based planning and decision-making to incorporate hypertension management into HIV/AIDS care. Two published review studies have described hypertension among PLWH^{28,29}; several meta-analyses reported elevated blood pressure–related HIV infection and ART exposure.^{30–32} However, no published study has investigated the global prevalence of hypertension among PLWH. The purpose of this study was to fill this data gap through a quantitative meta-analysis. We conducted this study capitalizing on the reported hypertension prevalence from numerous studies conducted in different countries and regions during different periods.

Methods

This study was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement.³³

Literature Search

Peer-reviewed articles on hypertension among PLWH and published between January 1, 2011, and December 31, 2016, were identified from two online sources: PubMed/Medline and Web of Science. Key phrases and combinations used in the literature search were (HIV-infected OR HIV-positive OR HIV-seropositive OR people living with HIV/AIDS OR AIDS OR Acquired Immunodeficiency Syndrome) AND (hypertension OR elevated blood pressure). As a complementary procedure, reference lists of relevant studies were manually checked for any citations missed by electronic database searching.

A total of 1884 articles published during 2011–2016 were identified and 226 articles were retained after removing 641 duplicates and 1017 articles that were reviews, case reports,

animal studies, non-English articles, and nonrelevant to review topic. Full-text of the 226 articles were downloaded and carefully reviewed according to our study's inclusion criteria. Eligibility criteria for inclusion were as follows: (1) cross-sectional or longitudinal study among PLWH aged ≥ 16 years, (2) data available regarding the prevalence of hypertension, and (3) hypertension was defined using the standard methods of Seventh Report of the Joint National Committee (JNC-7) with average blood pressure $>140/90$ mm Hg, or from medical records, or self-reported use of antihypertensive medication. Studies including only one specific study population, such as HIV-positive pregnant women or PLWH with chronic kidney disease were excluded. Finally, 49 articles were included in the meta-analysis. The article search and selection process are summarized in Figure 1.

Data Extraction and Quality Assessment

For each eligible study, data needed for this study were recorded manually by two of the authors of this article. The following data were extracted from the full-text of the individual 49 selected articles: authors, publication date, study design, study period and location, sample size, age (mean/median), sex (proportion of male and female), use of ART, prevalence of hypertension, and diagnosis method of hypertension. To ensure validity of data extraction, the two reviewers extracted the data independently first. Results from the two reviewers were then compared and differences were consolidated by consulting the original full-text article and having a small group discussion. Of the 49 articles included in this study, eight of them had inconsistent results and were rechecked.

To ensure quality of the included studies for meta-analysis, these studies were assessed using the Joanna Briggs Institute Prevalence Critical Appraisal Tool.^{34,35} The tool uses 10 items to examine the internal and external validity of included data for meta-analysis. Evaluation scores are in the range of 0–10 with <4 as “low quality,” 4–6 as “moderate quality,” and >6 as “high quality.” Among the 49 studies included, none were scored 4 or less, 2 (4.4%) scored 4–6, and the rest (95.6%) scored 7 or higher. Furthermore, among the total 49 studies, 24 (48.9%) scored 9 or high.

Statistical Analysis

Prevalence was estimated using random effects modeling method by combining prevalence estimates from individual studies.³⁶ The random effects method was used because the studies included in this analysis differed from each other substantially in a number of areas, including study design, study setting, and demographical characteristics of participants. In this case, fixed effects modeling method would not be adequate because this method assumes that differences among studies are simply due to random error; in contrast,

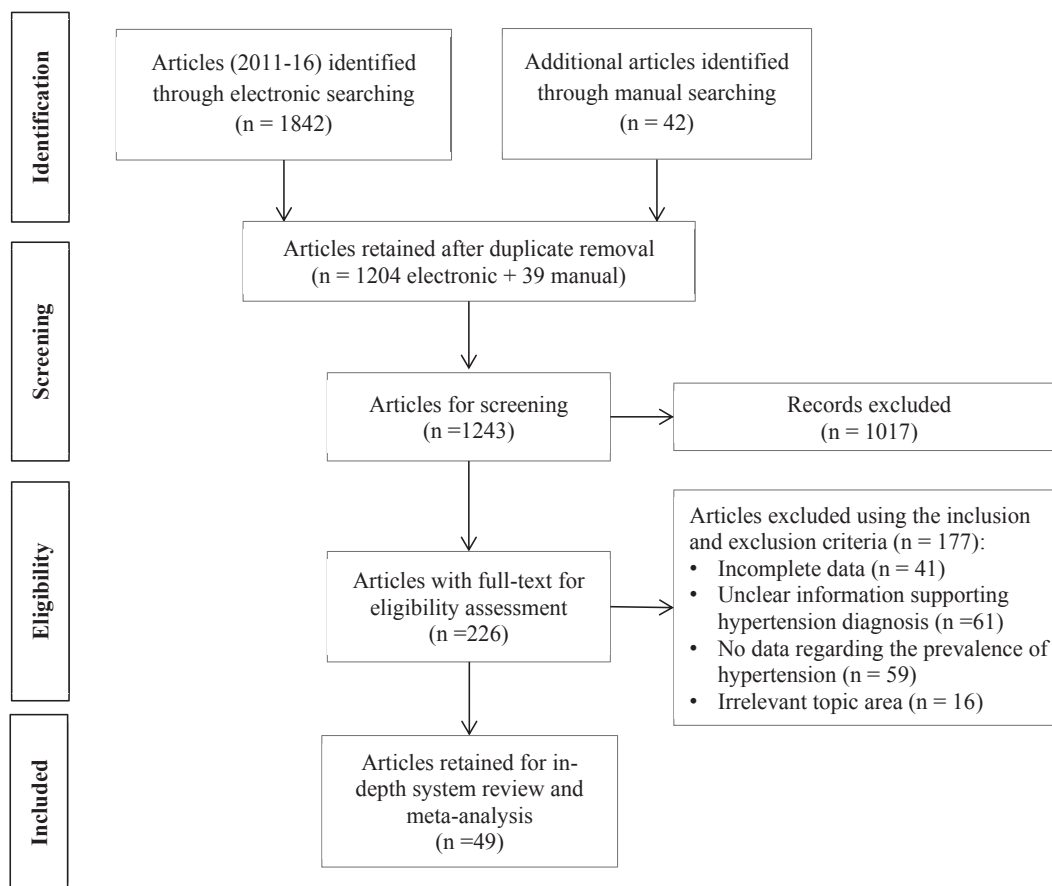


Figure 1. Prisma flow diagram of article selection for the meta-analysis.

differences in reported hypertension prevalence among the studies included in this meta-analysis may not be fully explained by random sampling. To support the application of the random effects modeling method, study heterogeneity was tested using both I^2 and the Q-statistic. $I^2 \geq 50\%$ and/or a Q-statistic $P < .05$ were used as evidence supporting the presence of heterogeneity.³⁷ All meta-analyses were performed using the “meta” package in R version 3.2.2.

Hypertension cases reported by cross-sectional study and at baseline of longitudinal study were used for analysis. Prevalence (95% confidence interval [CI]) was estimated for the overall sample and stratified by ART status (ART-naïve and ART-experienced), age group, and period. Studies with participants consisting of ART-experienced and ART-naïve were used to estimate overall prevalence. Prevalence for studies only including participants with ART-experienced and studies only including participants with ART-naïve was estimated separately. All the analyses were performed and stratified by the mean or median age extracted from the reported studies due to the lack of hypertension prevalence by single year of age. Period was defined based on the years when the data were collected and prevalence was estimated for two periods with 2010 as the cutoff year. Considering the lack of adequate

studies for ART-naïve group, meta-analysis by period was performed only for the overall participants and for ART-experienced participants.

Results

Characteristics of Selected Studies

The 49 selected studies were conducted in 18 countries, including 25 from America, 13 from Europe, 10 from Africa, and 1 from Asia. Data reported in these studies were collected during 1996–2014. These studies covered a total of 59 unique study populations with a total enrollment of 63,554 PLWH. Of these participants, 43,267 (68.1%) were from overall sample, 18,745 (29.5%) from ART-experienced sample, and 1542 (2.4%) from ART-naïve sample. The average reported age of subjects in different studies ranged from 28.8 to 63.0 years. Of the studies included, 36 (3.5%) were cross-sectional,^{5,19–21,23–25,27,38–65} and the rest were longitudinal (28.3%).^{26,66–77} The reported prevalence of hypertension varied from 4.0% to 67.0%. Table 1 lists the key characteristics of the included studies.

Table 1

List of the 49 included studies and their characteristics

First Author (y)	Study Design*	Period of Data Collection	Location	ART [†]	Sample Size	Age (y) (Mean/Median)	Sex (% Male)	Prevalence of Hypertension (%)	Diagnosis of Hypertension [‡]	JBIPCAT Quality Assessment
Antonello et al. (2015)	Cross-sectional	2008–2012	Brazil	B	1009	41.7	52.5	22.5	BP/MED	9
Baker et al. (2011)	Longitudinal (two samples)	2004 2006	United States United States	B B	389 389	42 44	77 77	33.0 46.0	BP/MED	9
Begovac et al. (2015)	Cross-sectional	2011	Serbia	Y	254	49	76	50.8	BP/MED	8
Bonjoch et al. (2014)	Cross-sectional	2011–2012	Spain	B	970	48	75.6	19.5	BP	9
Bryant et al. (2015)	Cross-sectional	No report	United States	Y	79	59	86	50.6	MED	6
Buchacz et al. (2013)	Cross-sectional	2006–2010	United States	Y	3166	47	79	54.4	MR	10
Calza et al. (2014)	Cross-sectional	2011	Italy	B	894	44.2	70.9	25.7	BP/MED	9
Cianflone et al. (2011)	Cross-sectional	2008 United States 2010	United States	B	223	43	96	30.0	MED	8
Diouf et al. (2012)	Cross-sectional	2009	Senegal	Y	242	46	42.1	28.1	BP/MED	8
Diaz et al. (2016)	Cross-sectional	2000–2010	Brazil	Y	2960	37	65	27	BP/MED/MR	9
Dimala et al. (2016)	Cross-sectional (three samples)	2013	Cameroon	B Y N	200 100 100	39.1 40.2 38	30 30 30	28.5 38 19	BP	8
Divala et al. (2016)	Cross-sectional	2014	Malawi	B	952	43	28.3	23.7	BP/MED	8
Fabbiani et al. (2013)	Cross-sectional	2010	Italy	B	245	46	75.5	15.1	BP/MED	8
Fuchs et al. (2013)	Longitudinal	2006–2011	Brazil	B	3529	39	59.1	28.8	BP/MED	10
Galli et al. (2012)	Cross-sectional	2007–2008	Italy	B	2345	45.7	76.4	24.8	BP/MED	9
Ganesan et al. (2013)	Longitudinal	2010	United States	B	3360	28.8	92.4	4.0	BP/MED	10
Greene et al. (2014)	Longitudinal	2008–2010	United States	B	89	63	94	43.0	MED	6
Hasse et al. (2015)	Longitudinal	2009–2011	Switzerland	B	3230	50	81	45.1	BP/MED	9
Ikeda et al. (2013)	Cross-sectional	2006–2008	Brazil	B	1240	39.1	50.6	19.4	BP/MED	10
Isasti et al. (2013)	Cross-sectional	2011	Spain	B	196	46.4	85.2	17.4	BP	8
Iwuala et al. (2015)	Cross-sectional	No report	Nigeria	Y	145	40.3	42.1	40.7	BP/MED	7
Krauskopf et al. (2013)	Longitudinal	1998–2011	United States	B	2390	43	80	22.2	BP/MED	10
Lichtenstein et al. (2013)	Longitudinal	2002–2009	United States	B	2005	42	76	51.7	BP/MED	10
Medina-Torne et al. (2012)	Cross-sectional	No report	United States	B	707	41	92.4	31.0	BP/MED	8
Menezes et al. (2011)	Cross-sectional	2009	Brazil	Y	213	45.6	51.6	20.7	BP	8
Metallidis et al. (2013)	Longitudinal (three samples)	1998–2008	Greece	N N N	455 558 103	32.8 37.4 57.7	81.8 81.5 80.6	5.1 10.2 33.0	MR	9
Mohammed et al. (2015)	Cross-sectional	2014	Ethiopia	B	393	37.9	33.1	34.4	BP/MED	9
Monteiro et al. (2012)	Cross-sectional	2009	Brazil	B	261	42	57.8	20.0	BP/MED	8
Muronya et al. (2011)	Cross-sectional	2010	Malawi	Y	174	40.8	38.5	45.6	BP/MED	7
Myerson et al. (2014)	Cross-sectional	2008–2011	United States	B	4133	46.1	74.7	43.0	BP/MED	9
Nery et al. (2013)	Cross-sectional	2009–2011	Brazil	B	294	36.8	76.9	20.0	BP	8
Nsagha et al. (2015)	Cross-sectional (three samples)	2014	Cameroon	B Y	215 160	43.2 44.7	25.1 22.5	25.6 29.4	BP	7

(continued)

Table 1 (continued)

First Author (y)	Study Design*	Period of Data Collection	Location	ART [†]	Sample Size	Age (y) (Mean/Median)	Sex (% Male)	Prevalence of Hypertension (%)	Diagnosis of Hypertension [‡]	JBIPCAT Quality Assessment
Ogunmola et al. (2014)	Cross-sectional (two samples)	No report	Nigeria	N	55	38.6	32.7	14.5		
				Y	130	38.6	33.1	12.3	BP	9
				N	120	36.5	42.5	15.8		
Olalla et al. (2013)	Cross-sectional	2009–2011	Spain	B	388	45.4	75.5	11.9	BP/MED	8
Overton et al. (2012)	Cross-sectional	2004–2006	United States	B	670	41	77	31.0	MR	9
Pacheco et al. (2015)	Cross-sectional	No report	Brazil	B	591	43.8	57.4	31.6	BP/MED	10
Parikh et al. (2015)	Cross-sectional	2011	United States	Y	150	52	88	67.0	MR	7
Patel et al. (2013)	Cross-sectional	2011	United States	B	454	51	71	42.5	MR	8
Peck et al. (2014)	Cross-sectional (two samples)	2012–2013	Tanzania	Y	150	40	23.3	28.7	BP	9
				N	151	37	41.1	5.3		
Rawlings et al. (2011)	Longitudinal	2003–2008	United States	Y	323	37.9	82	29.0	MR	8
Reinsch et al. (2011)	Cross-sectional	2004–2006	Germany	B	761	44.2	82	21.4	BP/MED	7
Santiago et al. (2014)	Longitudinal	2008	Brazil	B	1970	41.6	63.6	26.6	MED	10
Smit et al. (2015)	Longitudinal	1996–2010	Netherland	Y	10,278	44.5	84	23.0	BP	9
Sulyok et al. (2015)	Cross-sectional	2014	Hungary	B	136	44.5	97.8	21.3	MR	7
Tongma et al. (2013)	Cross-sectional	No report	United States	Y	111	52	86	33.0	MR	7
Tripathi et al. (2014)	Longitudinal	2004–2009	United States	B	6816	38	28.3	13.5	MED	9
Viskovic et al. (2013)	Cross-sectional	2009–2011	Croatia	Y	110	46.5	84.5	28.1	BP/MED	8
Wensink et al. (2015)	Longitudinal	2013	South Africa	B	903	40	31	23.0	BP/MED	9
Wu et al. (2014)	Cross-sectional (two samples)	2013	Taiwan	B	610	44.1	96.2	10.8	BP	10
				B	310	58.8	84.5	31.0		

ART, antiretroviral therapy.

* B: participants includes those received antiretroviral treatment (ART) and did not receive ART; Y: all participants received ART; and N: all participants did not receive ART.

[†] For longitudinal study, the prevalence reported at baseline was used for analysis.

[‡] Methods of hypertension diagnosis: BP, average blood pressure >140/90 mm Hg; MR, from medical records; MED, self-reported use of antihypertensive medication.

Table 2

Estimated prevalence of hypertension among people living with HIV, overall and stratified by average age of study population and ART use

Age (Mean/Median)	Number of Studies	Sample Size	Prevalence (%)	95% CI	I ² (P Value)
Overall					
Total	35	43,267	25.2	21.2–29.6	98.9 (<.0001)
<40 y	7	15,832	18.6	11.5–28.6	99.2 (<.0001)
40–49 y	24	23,352	25.2	21.3–29.6	98.2 (<.0001)
≥50 y	4	4083	40.3	34.2–46.8	86.8 (<.0001)
ART-experienced					
Total	17	18,745	34.7	27.4–42.8	98.7 (<.0001)
<40 y	3	3413	23.5	17.6–30.6	85.4 (.0011)
40–49 y	11	14,992	34.6	24.3–46.6	99.1 (<.0001)
≥50 y	3	340	50.6	30.4–70.5	93.0 (<.0001)
ART-naïve					
Total	7	1542	12.7	7.4–20.8	91.5 (<.0001)
<40 y	6	1439	10.5	6.8–15.8	83.1 (<.0001)
57.7 y	1	103	33.0	N/A	N/A

ART, antiretroviral therapy; CI, confidence interval; N/A, not available, only one study was included.

Estimated Prevalence of Hypertension

Table 2 summarizes the estimated prevalence (95% CI) of hypertension, overall and stratified by ART experiences and age groups. Overall, 25.2% (21.2%, 29.6%) of PLWH were diagnosed with hypertension. There was an increasing trend in hypertension prevalence with age. Estimated prevalence was 40.3% (34.2%, 46.8%) for participants with average age ≥50 years, significantly higher than 18.6% (11.5%, 28.6%), the prevalence for those with average <40 years, and also significantly higher than 25.2% (21.3%, 29.6%), the prevalence for those with average age 40–49 years. Forest plots of estimated hypertension prevalence for overall PLWH stratified by age were illustrated in Figure 1 of Appendix 1.

When stratified by ART status, estimated prevalence was 34.7% (27.4%, 42.8%) for the ART-experienced group (see forest plots in Figure 2 of Appendix 1), significantly higher than 12.7% (7.4%, 20.8%), the prevalence for the ART-naïve participants (see forest plots in Figure 3 of Appendix 1). After stratified by average age extracted from the reported studies, the estimated prevalence for each age group among ART-experiencing participants was higher than that from overall and ART-naïve sample (see Table 2).

Figure 2 presents estimated hypertension prevalence before and after 2010. Overall, the estimated prevalence was 24.4% (17.2%, 33.5%) before 2010 and 24.0% (19.5%, 29.1%) after 2010. The differences were not statistically significant. However, there were substantial differences in the estimated prevalence for the ART-experienced sample before and after 2010 although the difference was not statistically significant. Hypertension prevalence was 30.0% (23.6%–37.2%) before 2010, and it increased to 46.1% (30.8%–62.2%) after 2010. Forest plots

of estimated prevalence of hypertension stratified by time period are shown in Figures 4 and Figure 5 of Appendix 1.

Discussion and Conclusions

To the best of the authors' knowledge, this meta-analysis is the first study to estimate the prevalence of hypertension among PLWH with reported studies across the globe. Prevalence was estimated from a total of 49 quality studies conducted in 18 countries, covering 59 unique study samples, and a total of 63,554 PLWH. According to the findings of our analysis, overall 25.2% of PLWH were hypertensive. It is slightly lower than 30.8%, the reported worldwide prevalence for the general population.⁷⁸ Applying the estimated prevalence from our analysis to the 34 million PLWH worldwide, there are approximately 8.6 (7.1, 10.1)

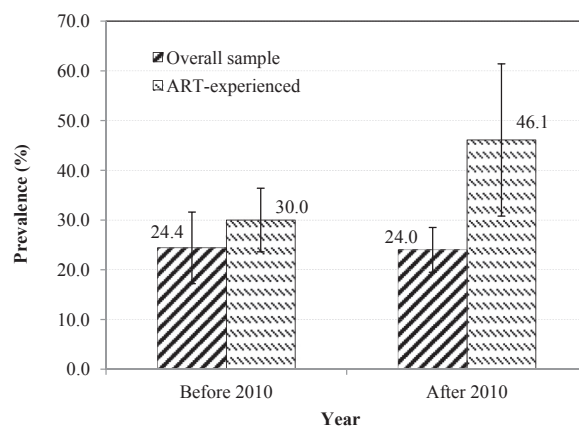


Figure 2. Estimated prevalence of hypertension among PLWH before and after 2010.

million PLWH are hypertensive. In addition to the overall study sample, prevalence was also estimated for ART-experienced and ART-naïve participants, for different distributions of age and for the periods before and after 2010.

Findings of our analysis show that ART-experiencing participants have heavier burden of hypertension compared with ART-naïve. Results of our meta-analysis indicate that among ART-naïve participants, 12.7% were hypertensive; whereas the prevalence among ART-experienced participants was almost three times higher (34.7%); the prevalence estimated for each age group among PLWH experiencing ART was also higher than ART-naïve. Therefore, the number of PLWH suffering from hypertension may continue to increase because more and more PLWH are now receiving ART⁷⁹ and the success of ART will continue to increase the survivorship of the PLWH.^{2,80} Furthermore, the difference was greater in more recent years. When analyzed by period, the estimated prevalence between the overall sample and ART-experienced was small (24.4% vs. 30.0%) before 2010, and the difference was not statistically significant. The difference was substantially increased (24.0% vs. 46.1%) after 2010. In addition to care providers, decision-makers in both public health and medicine fields must recognize the challenges of potential human and health care costs associated with the high prevalence of hypertension among PLWH. Additional resources, training, and research are needed to deal with this challenge.

This finding from our analysis is consistent with the positive and significant association between ART and hypertension reported in published studies.^{64,81–83} ART as a risk factor for hypertension can be supported by the fact that the side effects of certain antiretroviral drugs, including endothelial damage, were associated with early pathologic change in the development of hypertension.^{84,85} Findings from published studies also show that initiation of ART may alter various normal metabolic processes, leading to overweight and obesity.^{86–89} Weight gain has been recognized as one of the most important risk factors for hypertension.

Furthermore, our study shows that the prevalence of hypertension among PLWH increase with age regardless of their ART status, same as the increasing trend observed for HIV-negative people. Compared with study participants aged 40 years or younger, the prevalence of hypertension was 2.35 times higher for those aged ≥ 50 years. Meanwhile, HIV infection and ART may be associated with an early development of hypertension. Through a global estimate, about 5%–15% of HIV-negative adults aged <40 years had hypertension⁷⁸ while the prevalence reached to 18.6% for the overall PLWH through our results. In the same age group, the prevalence further increased to 23.5% for PLWH experiencing ART. The positive association between age and hypertension prevalence also implies a growing prevalence of hypertension among PLWH along with the growing use and success of ART.⁷⁹

Several limitations need to be acknowledged. First, numbers of studies for several strata are small, expanding the estimated 95% CI. Therefore, results do not show statistically significant difference although the differences among several subgroups are substantially large. In addition, heterogeneity due to individual-level difference must be considered (eg, duration of ART, therapeutic regimen, the use of other medicine, cigarettes smoking, physical activity, and BMI). In this study, we only considered age, ART, and period, other factors could not be considered because of data limitation. Third, because only the average age of participants in each study can be extracted, the changes in prevalence of hypertension with age cannot be estimated at individual level. Finally, selection bias could be an issue. Fewer studies from Asia than from other continents were included. Caution is needed when interpreting the findings from this study. Despite the limitations, this study is the first to provide data on the prevalence of hypertension among PLWH with data collected across the globe. The findings are significant for decision-making and for future research to support HIV/AIDS care.

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Authors' contributions: Y.X. designed the study, collected the articles, extracted and analyzed the data, and contributed the most to article development, including the first draft. X.C. conceived study, provided guidance, and participated in research design, data collection process and analysis, and article development. K.W. participated in research design, data collection and extraction, and article development.

Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.jash.2017.06.004>.

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