# Stroke in Human Immunodeficiency Virus-infected Individuals in Sub-Saharan Africa (SSA): A Systematic Review

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*Background:* Human immunodeficiency virus (HIV) infection is associated with worse outcomes after stroke, but this association is less well-described in sub-Saharan Africa (SSA). We reviewed literature on stroke among people living with HIV (PLWH) in SSA. *Methods:* We systematically reviewed published literature for original clinical stroke studies conducted in SSA that included PLWH. We included studies that reported data on presenting characteristics, risk factors, and/or outcomes after stroke. *Results:* Seventeen studies (N = 478) met inclusion criteria. At the time of stroke presentation, PLWH had a median age ranging from 32 to 43 years. Subjects had low CD4 counts (median CD4, 108-225 cells/μl), and most were antiretroviral therapy-naïve. Fever, seizures, and concurrent opportunistic infections were common at presentation. Ischemic stroke accounted for up to 96% of strokes, which were mostly located in the anterior circulation territory. In studies comparing PLWH with HIV-uninfected individuals, PLWH had more frequent coagulopathy, greater stroke severity, (72% versus 36% National Institutes of Health Stroke Scale >13, $P = .02$), longer hospital length of stay (30.5 versus <10 days), and a higher 30-day mortality rate (23% versus 10.5%, $P = .007$). *Conclusion:* Stroke in PLWH in SSA occurs at a young age, in those with advanced disease, and is associated with worse outcomes than in HIV-uninfected comparators. Stroke in young individuals in the region should prompt HIV testing, and ongoing efforts to promote early antiretroviral therapy initiation might also help decrease stroke incidence, morbidity, and mortality in the region. **Key Words:** Stroke—HIV infection—risk factors—outcomes—sub-Saharan Africa.


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## Introduction

The widespread use of combined antiretroviral therapy (ART) has led to a decrease in morbidity and mortality from acquired immune deficiency syndrome (AIDS) and significantly increased the life expectancy for those infected.[1-3] Improvement in life expectancy has shifted health priorities for people living with HIV (PLWH) from treatment and prevention of opportunistic infections to include focus on non-AIDS related conditions.[4,5] Human immunodeficiency virus (HIV) infection has been demonstrated to significantly and independently increase the risk of stroke.[6-9] Several mechanisms for this relationship have been proposed, including HIV-related intra- and extracranial vasculopathy, HIV-induced cardiomyopathy, HIV-induced coagulopathy, and opportunistic infection-associated vasculitis.[10,11] Among PLWH on ART, both the inflammation and immune activation associated with chronic HIV-infection and direct effects of ART are hypothesized to contribute to stroke pathogenesis.[5,12]

Although over two-thirds of the world's population of PLWH lives in sub-Saharan Africa (SSA),[13,14] less is known about the contributions of HIV infection to stroke risk and stroke outcomes in the region. The impact of HIV on stroke risk in SSA is particularly important due to elevated stroke risk in the general population in this region.[15] Moreover, extrapolation of data from North America and Europe may not be valid due to differences in the environment, behaviors, and genetics between these populations. For example, intravenous drug abuse, which is prevalent among HIV-infected patients with stroke in the Western world, is rare in Africa.[16] Additionally, there are important differences in the healthcare infrastructure for stroke care in the developed world, and this is likely to affect stroke outcomes.[17-19]

This review sought to synthesize available literature on the risk factors, clinical presentation, and outcomes of stroke among PLWH in SSA. Our goals were to: (1) offer preliminary guidance to clinicians and public health programs in SSA on the evaluation and follow-up of PLWH with stroke and (2) identify gaps and make recommendations to inform research priorities for stroke prevention and treatment in PLWH.

## Methods

### *Search and Screening Strategy*

In this review, we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement as a guide. We searched the following electronic databases: PubMed, Scopus (MEDLINE and EMBASE), Google Scholar, Global Health, and The Cochrane Library for studies describing HIV and stroke in SSA. Full details of our search terms are available in the Supplementary Appendix. We searched without any language restrictions and our search was last updated on October 31, 2016. One manuscript was translated into English using Google Translate after we failed to get in touch with the author.[20] We screened abstracts of all returned articles for inclusion criteria. To promote reliability and validity of the screening process, the first 100 abstracts/papers were screened by 2 reviewers (A.A. and J.C.) and any discrepancies discussed. All further reviews were done independently by A.A. The study is registered with the International Prospective Register of Systematic Reviews (study no CRD42017050741).

### *Criteria for Selection*

Other than the case reports, we used the following inclusion criteria to identify studies for further review: (1) at least 10 participants (or 20% of the total participants) with both HIV infection and a stroke; (2) description of clinical presentation at the time of stroke, risk factors for, and/or outcomes after stroke among PLWH; (3) at least 50% of observed stroke in PLWH confirmed by brain imaging (computed tomography or magnetic resonance imaging); and (4) study subjects were 18 years old and above; and (4) the study included original data (i.e., not a review or opinion piece). Thus we also excluded incidence and prevalence studies that had no clear description of patient characteristics, risk factor, and/or outcomes.

### *Data Abstraction*

For each included study, we abstracted and summarized data for each of the following categories: (1) clinical characteristics; (2) traditional cardiovascular and HIV specific risk factors; and (3) outcomes (mortality and neurological function). Data were abstracted into a prespecified Microsoft Excel spreadsheet (Redmond, WA). We used standard data summarization techniques to record each of the characteristics in the 3 domains of interest.

### *Study Bias*

All studies meeting inclusion criteria were included in the systematic review. We used the Newcastle Ottawa Scale[21] to assess the quality of all studies included in the review, apart from the case reports (Table S6).

## Results

Our initial PubMed search yielded 140 papers. We excluded 118 papers after review of the abstracts and read the remaining 22 full-length manuscripts. We further excluded 8 studies after review of the manuscripts. Our final analysis included 14 manuscripts from the initial PubMed search and 3 additional, nonduplicative studies identified from the other databases following a similar search strategy (Fig 1). Most of the studies were conducted in South and West Africa (Table 1) and involved patients who were ART naïve (Table 2).