# Factors associated with advanced HIV in the Tshwane District drainage area: A protocol for a cross-sectional analytical study

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**Background.** HIV continues to be a global pandemic. Despite significant achievements in reaching the global 95-95-95 targets, advanced HIV disease (AHD) continues to contribute to substantial morbidity and mortality, with 600 000 deaths worldwide in 2022 including 51 000 in South Africa (SA). The patient demographic has shifted from antiretroviral therapy (ART)-naïve individuals to those facing treatment interruptions or non-adherence.

**Objective.** To explore the factors associated with AHD in patients within the Tshwane District drainage area, SA, where high treatment coverage has not fully curbed mortality rates.

**Method.** This cross-sectional analytical study employs both quantitative and qualitative methods, utilising structured questionnaires and blood samples to assess ART levels, specifically dolutegravir. A minimum of 10 participants will undergo semi-structured interviews to explore their treatment experiences. Quantitative data will be analysed using descriptive and inferential statistics, while qualitative data will be examined through thematic analysis.

**Conclusion.** This research aims to enhance the understanding of AHD-related factors to inform effective interventions and policies for HIV care.

**Keywords.** advanced HIV; Tshwane District; treatment coverage; mortality rates.

HIV continues to be a global pandemic, claiming over 40 million lives by the end of 2022. Currently, as of 2024, 39 million people are living with HIV, including an estimated 26 million in the World Health Organization (WHO) African Region.[1] In 2022, there were 1.3 million new infections and over 600 000 AIDS-related deaths globally.[2] South Africa (SA) had an HIV prevalence of 13.5% in 2022, with 8 million people living with HIV, 51 000 AIDS-related deaths and a significant number presenting with advanced HIV disease (AHD).[3] To end the epidemic by 2030, Sustainable Development Goal 3.3 and the 95-95-95 targets were established, aiming for 95% of HIV-positive people to be diagnosed, 95% to be on antiretroviral therapy (ART) and 95% to achieve viral suppression.[1] However, current global and SA rates fall short of these targets. Many people, including those previously on ART, present with AHD, highlighting the need for targeted interventions to reduce AHD-related morbidity and mortality.[1-3]

## Objectives

This study aims to explore the factors associated with AHD in patients presenting to healthcare facilities in the Tshwane District drainage area, SA. The specific objectives include determining the sociodemographic, behavioural and clinical characteristics of patients with AHD; assessing ART exposure levels and understanding health system factors and patient perceptions related to AHD.

## Methods

This cross-sectional study will employ a mixed-methods approach, combining quantitative and qualitative analyses. The study will be conducted from 1 July 2024 to 30 December 2024, across three hospitals in the Tshwane District drainage area: Tshwane District Hospital, Steve Biko Academic Hospital and Tembisa Provincial Tertiary Hospital. The study population includes patients presenting with advanced HIV disease, defined as having a CD4 count <200 cells/mm³ in the last 6 months. Eligible participants must be HIV-positive, aged 18 years or older and oriented to time, place and person.

For the quantitative component, a sample size of 115 participants will be recruited through purposive sampling. A structured questionnaire adapted from validated tools such as the Simplified Medication Adherence Questionnaire (SMAQ) and the Human Sciences Research Council (HSRC) South African National HIV Survey,

**Table 1. Variables that will be collected per objective**

| Objective | Variables |
|---|---|
| 1. To determine sociodemographic factors of participants presenting with advanced HIV disease in a hospital setting. | *Sociodemographic factors:* <br> Age, biological sex, ethnicity, relationship status, level of education and employment status. |
| 2. To determine the behavioural factors of participants presenting with advanced HIV in a hospital setting. | *Behavioural factors:* <br> Drug use in the past 3 months, alcohol use, circumcision, age of first sexual debut, number of lifetime partners, disclosure of status to family and social support structures. |
| 3. To determine the clinical factors of participants presenting with advanced HIV in a hospital setting. | *Clinical factors:* <br> CD4 count, viral load, previous/current TB, previous/current cryptococcal meningitis, history of other opportunistic infection, other chronic condition and reason for admission (if admitted). |
| 4. To determine the prevalence of ART coverage in participants with advanced HIV in a hospital setting. <br> a. To determine self-reported ART coverage <br> b. To determine the proportion of ART-naïve and ART-exposed participants <br> c. To determine the biochemical coverage of ART using ART drug-level testing. | *ART coverage factors:* <br> Ever exposed to ART, currently on ART, length of time on ART, adherence to ART, length of defaulted ART, reasons for stopping ART and reasons for not initiating ART. <br> Qualitative antiretroviral drug level testing results. |
| 5. To explore health system factors that contribute to the development of AHD. | *Access to health services:* <br> Accessibility, affordability, accommodation availability, acceptability, access to medication (drug stockouts). |

TB = tuberculosis; ART = antiretroviral therapy; AHD = advanced HIV disease.

will be administered electronically via the research electronic data capture (REDCap) tool.[4-7] In cases of technical issues, paper-based questionnaires will be used. ART exposure will be assessed further through qualitative drug-level testing, to determine exposure to dolutegravir. A subset of 10 participants, selected for the qualitative component, will undergo semi-structured interviews to explore their perceptions of HIV and ART, with data collection continuing until thematic saturation is achieved.

## Data collection procedures

Data collection involves recruiting participants at the study sites, screening them for eligibility and obtaining informed consent. The quantitative questionnaire will take 10 - 15 minutes, and blood samples for ART drug-level testing will require an additional 15 minutes. The qualitative interviews, lasting 30 minutes, will explore patients' perceptions of HIV and ART. Data collection will conclude once the target sample size is reached. All data will be securely stored in electronic and paper formats, and blood samples will be couriered to the contracted laboratory for analysis.

## Data analysis

Quantitative data will be analysed using descriptive and inferential statistics. Continuous variables will be summarised as means or medians, while categorical variables will be expressed as counts and percentages. Tests of association will be performed using $\chi^2$ and T-tests, with a *p*-value<0.05 considered significant. Logistic regression models will be used to identify predictors of ART exposure. Qualitative data will undergo thematic analysis to identify key themes and patterns. Data triangulation will integrate quantitative and qualitative findings to provide a comprehensive understanding of the factors associated with AHD. Table 1 details the variables that will be assessed against the outcome variable of ART exposure.

## Discussion

This study will provide critical insights into the factors contributing to the development of AHD among patients in the Tshwane district drainage area. Understanding these factors is essential for developing targeted strategies and evidence-based policies to reduce AHD-related morbidity and mortality, ultimately improving patient care and advancing toward the goal of ending the HIV epidemic by 2030.

## Conclusion

This comprehensive analysis will aid public health stakeholders in designing interventions to improve the care and outcomes of people living with advanced HIV.

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