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# Cause of hospitalization and death in the antiretroviral era in Sub-Saharan Africa published 2008–2018

## A systematic review

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## Abstract

**Background:** Worldwide despite the availability of antiretroviral therapy, human immunodeficiency virus/acquired immunodeficiency syndrome still causes morbidity and mortality among patients. In Sub-Saharan Africa, human immunodeficiency virus/acquired immunodeficiency syndrome remains a major public health concern. The aim of this study was to identify the causes of morbidity and mortality in the modern antiretroviral therapy era in Sub-Saharan Africa.

**Methods:** We conducted a systematic review according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. We searched relevant studies from 3 databases which are Google Scholar, PubMed, and CINAHL. Two review authors independently screened titles, abstracts, and full-text articles in duplicate, extracted data, and assessed bias. Discrepancies were resolved by discussion or arbitration of a third review author. R software version 3.6.2 was used to analyze the data. Maximum values were used in order to show which disease was mostly spread out by looking at the highest prevalence reported. This systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO).

**Results:** A total of 409 articles were obtained from the database search, finally 12 articles met the inclusion criteria and were eligible for data extraction. Among them, 3 were conducted in Nigeria, 2 were conducted in Uganda, 3 were conducted in South Africa, 1 in Gabon, 1 in Ethiopia, 1 in Ghana, and 1 in Burkina Faso. In most of the included studies, tuberculosis was the leading cause of hospitalization which accounted for between 18% and 40.7% and it was also the leading cause of death and accounted for between 16% and 44.3%, except in 1 which reported anemia as the leading cause of hospitalization and in 2 which reported wasting syndrome and meningitis respectively as the leading causes of death. Opportunistic malignancies accounted between for 1.8% to 5% of hospitalization and 1.2% to 9.8% of deaths.

**Conclusions:** Tuberculosis is the commonest cause of hospitalization and death in Sub-Saharan Africa, but it is always followed by other infectious disease and other non-AIDS related causes.

**Abbreviations:** ART = antiretroviral therapy, CD4 = cluster of differentiation 4, HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome, Q2 = median, PICO = population, intervention, comparator and outcome, PLHIV = patients living with HIV, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, UKZN = University of KwaZulu-Natal.

**Keywords:** antiretroviral treatment, morbidity, mortality, Sub-Saharan Africa

## 1. Introduction

Worldwide, despite the availability of antiretroviral therapy (ART), human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) still causes morbidity and mortality among patients. Since the first outbreak of HIV in 1981, 39 million people have died due to HIV and related diseases.[1] In Sub-Saharan Africa, HIV/AIDS is a major public health concern. In 2009, 70% of the estimated 33 million people living with HIV (PLHIV), are in Sub-Saharan Africa.[2] This region is the most affected by HIV/AIDS with 68% of the world's patients living with HIV.[3] According to WHO (2013), 74% of HIV related deaths were in Sub-Saharan Africa.[4] In 2014 studies reported that 25.8 million people were estimated to be living with HIV.[5] According to UNAIDS (2018), Sub-Saharan Africa, particularly Eastern and Southern Africa remains the region most affected by the HIV epidemic accounting for 45% of the world's HIV infections and 53% of people living with HIV globally.[6] In this region in 2017, 19.6 million of adults and children were living with HIV, 800,000 of adults and children were newly infected with HIV and 380,000 of adults and children died due to

AIDS.[6] In the same year, in Western and Central Africa, 6.1 million of adults and children were living with HIV, with 370,000 adults and children newly infected with HIV, and 280,000 adults and children dying due to AIDS.[6] Tuberculosis remains the leading cause of death among people living with HIV, causing 1 in 3 AIDS-related deaths.[7] All included studies were aimed at assessing either cause of death or of hospitalization among PHLIV during the antiretroviral therapy era. In ART services in Sub-Saharan Africa the proportion of patients with tuberculosis is extremely variable, ranging between 5% and 40%.[8] Some studies from Africa reported that 10% to 20% of deaths among PLHIV are attributable to cryptococcal meningitis.[9,10] Recently, the global burden of cryptococcal meningitis has been re-estimated at 223,100 cases (162,500 cases in Sub-Saharan Africa) leading to 181,100 annual deaths (135,900 deaths in Sub-Saharan Africa). The highest annual incidence of cryptococcal meningitis has been found in Nigeria (27,100 cases), South Africa (21,400 cases), Mozambique (18,600 cases), India (18,300 cases), Uganda (12,200 cases), Ethiopia (9600 cases), Kenya (9000 cases), and Zambia (5000 cases).[5] Anemia is the most common hematological manifestation of HIV disease and is frequent among patients living with HIV on ART in Sub-Saharan Africa, with a prevalence ranging from 45% to 87%.[11] Among PLHIV, chronic kidney disease (CKD) has been observed as one of the main complications, with a prevalence ranging from 3.5% to 48.5% in Sub-Saharan Africa.[12] Antiretroviral therapy has improved the life expectancy of patients living with HIV/AIDS.[13] Maximal and durable suppression of viral replication, restoration of immunologic function, reduction of HIV-related morbidity and mortality, improvement of quality of life, and prolonging survival are the major goals of ART.[14] The fast growth in ART coverage represents one of the great public health success stories in the recent history of HIV care that led to reduction of mortality and improvement of quality of life of people living with HIV/AIDS.[14] However, despite the availability of ART, a substantial proportion of PLHIV have continued to be hospitalized and die from both AIDS-related and non-AIDS-related causes.[15] This study is therefore aimed at identifying the determinants of morbidity and specific causes of mortality in the modern ART era in Sub-Saharan Africa.

## 2. Methods

We followed the Preferred Reporting Items for the Systematic Reviews and Meta-analysis Protocols (PRISMA-P) 2015 guideline.[16] The protocol of this study is registered in PROSPERO with registration number: CRD42019141933. We searched Observational studies reporting on morbidity and mortality in the ART era in Sub-Saharan Africa.

### 2.1. Eligibility criteria
### 2.1.1. Inclusion criteria.

- Studies reporting on causes of hospitalization and causes of death in the antiretroviral era in Sub-Saharan Africa.
- Studies published in the period of 2008 to 2018.
- Studies reporting on PLHIV and those on ART.
- Studies reporting on adult men or women aged 18 years or older.
- Peer-reviewed English language publications.
- Observational studies published in Sub-Saharan Africa.

### 2.1.2. Exclusion criteria.

- Studies reporting on morbidity or mortality on non HIV patients.
- Studies reporting on adult men or women under the age of 18 years.

### 2.2. Search strategy for identifying relevant studies

To identify relevant studies, we searched in the following database: Google Scholar, Pub Med, and CINAHL. Studies published in English from January 2008 to December 2018, conducted in Sub-Saharan Africa. The main search strategy conducted in PubMed/Medline was as follows: "(((Morbidity OR Opportunistic infection related HIV) [MeSH Terms]) AND ((Mortality OR Death) [MeSH Terms]) AND ((ART OR Antiretroviral therapy) [MeSH Terms]) AND ((Sub-Saharan Africa) [MeSH Terms])). We adapted this search strategy for a possible extension to other databases and we also contacted experts in the field to identify additional eligible studies and we manually searched reference lists from relevant studies.

### 2.3. Data collection, analysis, and synthesis

Two reviewers followed independently inclusion criteria for selecting studies, articles were identified and screened by their titles and abstracts for eligibility. The full texts of articles were retrieved. The process of literature selection and reasons for exclusion and inclusion were documented by a Preferred Reporting Items for Systematic Review and Meta-Analysis flow diagram (Fig. 1).[17] The information about the most causes of hospitalization and death related to HIV in the antiretroviral treatment was captured into a spreadsheet, and analyzed using R statistical computing software of the R Core Team, 2020, version 3.6.2. The count and percentages were summarized in the form of quartiles (Q1, Q2, and Q3). The proportions were further graphically visualized in the form of a multiple bar chart for ease of comparison. Maximum values were used in order to show which disease was mostly spread out by looking at the highest prevalence reported. This review was based on publish data, it did not involve contact with participants, therefore no ethical approval was required for it to be conducted. However, the present review was part of a large study approved by the University of KwaZulu-Natal/Biomedical Research Ethics Committee (UKZN/BREC) under reference number BE 345/19.

## 3. Results

For the initial search, a total of 409 articles were retained, the number of studies was reduced to 12 after applying the exclusion criteria (Fig. 1).

### 3.1. Characteristics of included studies

Out of 22 reviewed articles, 12 articles were eligible for data extraction (Table 1). All 12 studies included were published between 2008 and 2018 in English and they were conducted in Sub-Saharan Africa. Of these, 3[18–20] were conducted in Nigeria, 2[21,22] were conducted in Uganda, 3 were conducted in South Africa,[23–25] 1 in Gabon,[26] 1 in Ethiopia,[27] 1 in Ghana,[28] and 1 in Burkina Faso.[29] The total sample size of 12 studies was 14,619 participants, predominantly women. According to the
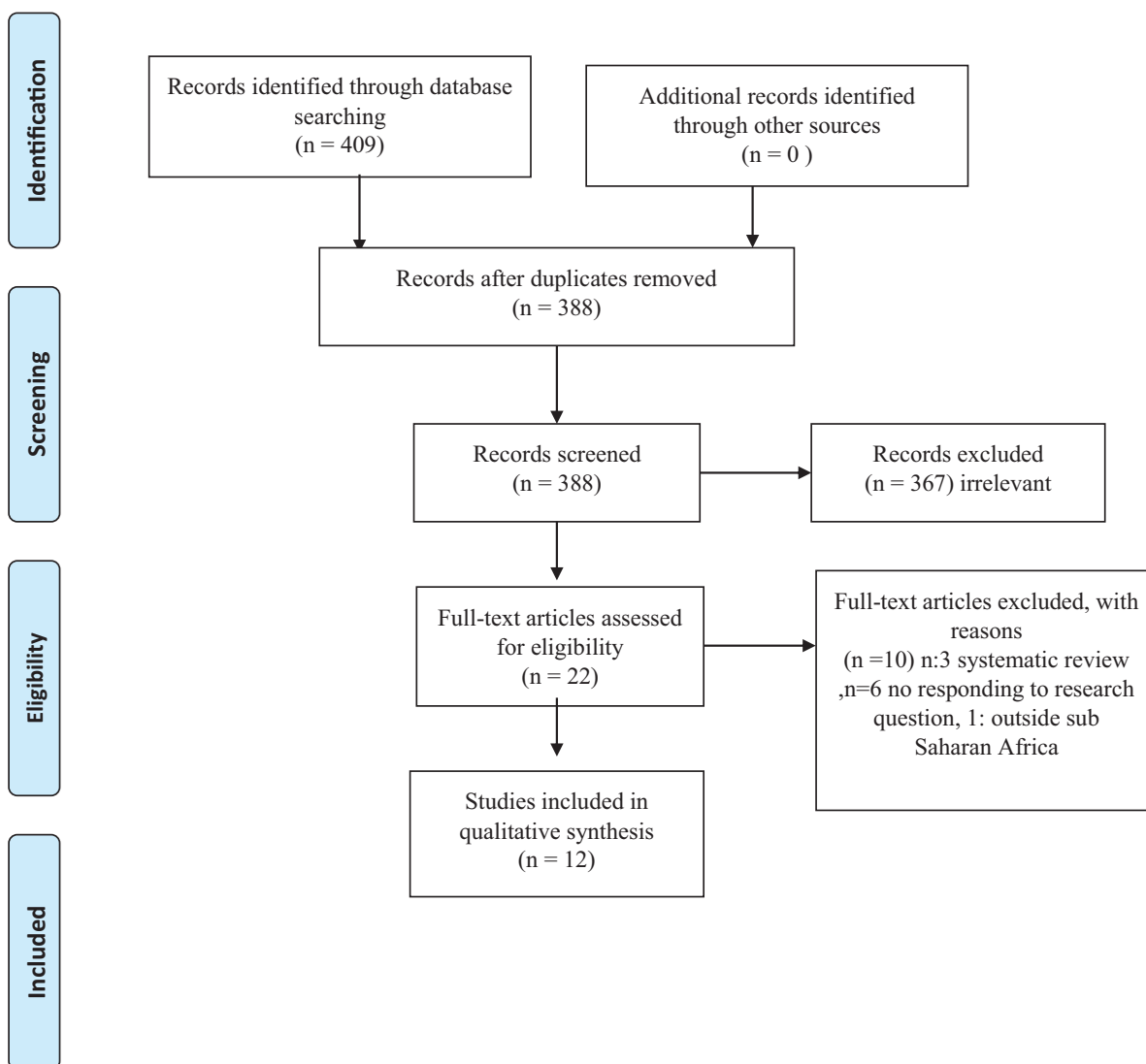
**Figure 1.** PRISMA flow diagram. From: Moher et al.[17] A total of 409 articles were retained, after applying the exclusion criteria the number of studies was reduced to 12 articles.

study designs of the included studies, we noticed 7 retrospective chart/cohort studies,[18–20,23,26,28,29] 3 prospective studies,[21,22,25] 2 cross-sectional study.[24,27] All included studies were aimed at assessing either cause of death or the most frequent diagnoses among PLHIV during the antiretroviral therapy era. In all included studies the commonest cause of hospitalization was tuberculosis[18–24,26,27,29] except in 1[28] and the most common cause of death was tuberculosis in all the included studies[18–24,26–29] except in 2.[29,30] We summarized the characteristics of all included studies in Table 1, and from this list, we extracted data related to the causes of hospitalization and death in the modern ART era in Sub-Saharan Africa. Most of the articles reported on death than hospitalization, and tuberculosis was the most disease reported (Table 1).

A total of 398 studies were excluded as they did not meet the inclusion criteria, of those 10 underwent a full manuscript review and were found to have no valuable data for the following reasons: 3 systematic reviews,[31–33] 1 article outside of Sub-Saharan Africa,[34] 6 articles not responding to the research question.[35–40]

Figure 2 reports the prevalence (%) of articles that described the causes of death and of hospitalization. Six articles reported both causes of death and hospitalization, 5 articles reported causes of death and 1 reported causes of hospitalization. Tuberculosis was the most reported disease by many of the articles. Fifty-eight percent and 92% of analyzed studies investigated TB to be most reported disease that conduct to hospitalization and death respectively, followed by cryptococcal

**Table 1**

**Characteristics of the included studies.**

| Authors and date of publication, geographic location, conducted date | Sample size | % female | Average Age, yr | Intervention | Aim of the study | Study design | Outcomes Causes of hospitalization (N, %) | Outcomes Causes of death (N, %) |
|---|---|---|---|---|---|---|---|---|
| Agaba et al, 2011, Nigeria Conducted date: January–December 2007 | 354 | 69.2 | 35±9 | Use of ART | Determine clinical characteristic and predictor of mortality in hospitalized HIV infected Nigerians | Retrospective chart review | TB (119, 33.6%), CCM (31, 8.8%), septicemia (13, 16.4%), AT (41, 11.6%), CD (23, 6.5%), OM (17, 4.8%), other infections (15, 4.2%), ADC (4, 1.1%), NHRI (32, 9%), NSD (14, 4%) | TB (37, 30.1%), CCM (16, 13.0%), Septicemia (21, 17.1%), AT (4, 3.3%), CD (10, 8.1%), OM (12, 9.8%), other infection (8, 6.5%), ADC (3, 2.4%), NHRI (7, 5.7%), NSD (5, 4%) |
| Namutebi et al, 2013, Uganda Conducted date: January–March 2011 | 201 | 50 | 34 | On ART | Determine causes and outcomes of hospitalization in adults on ART. | Prospective cohort study | TB (37, 18%), CCM (22, 11%), Zidovudine—with anemia (19, 10%), sepsis (10, 5%) and Kaposi's sarcoma (10, 5%). | 42 patients (21%) died: TB (10, 24%), CCM (8, 19%), Sepsis (5, 12%), UNS (9, 21%), other illnesses (10, 24%). |
| Saavedra et al, 2017, Ghana Conducted date: January 2012–October 2013 | 547 | 53.8 | 41.5 | Most of the patients were not on ART. | Investigate most frequent admitting diagnosis and causes of death | Retrospective study (medical records) | Anemia (76, 34.2%), Toxoplasmosis: (65, 29.3%), pneumonia: (65, 25.7%), TB (45, 20.3%), HIV wasting syndrome: (44, 19.8%), GE (28, 12.6%) | TB (77, 34.7%), Anemia (67, 30.2%), cerebral toxoplasmosis (61, 27.5%), pneumonia (51, 23.0%), GE (23, 10.4%). |
| Solomon et al, 2018, Ethiopia Conducted date: May 1–August 30 2017 | 744 | 40.5 | 24 | Receiving ART | Elucidate the spectrum, magnitude and determining factors of the major opportunistic infections | A cross-sectional study | Pulmonary tuberculosis (118, 18%), SCAP (107, 16.3%), and oral candidiasis (103, 15.6%). | Bacterial meningitis (16, 28.6%), PTB (13, 23.8%), SCAP (13, 23.8%). |
| Okome et al, 2014, Gabon Conducted date: January 1, 2002–September 30, 2010 | 687 | 57 | 34 | Administration of ART | Establish an epidemiologic profile of opportunistic diseases | A retrospective study | TB (114, 24.89%), herpes zoster (HZ) (73, 15.94%), CT (65, 14.19%), OC (65, 14.19%), and severe pneumonia (SP) (43, 9.39%), CM (2, 0.44%) and pneumocystosis (1, 0.21%), KS (9, 1.96%) | |
| Ogoina et al, 2012, Nigeria Conducted date: January 2006–December 2009 | 207 | 47.3 | 36 | Administrating ART | Examine morbidity and mortality patterns of hospitalized patients | A retrospective cohort analysis of routinely collected medical records | TB (16, 29.1%), sepsis (6, 7.3%), chronic diarrhea (6, 7.3%), KS (1, 1.8%), viral meningoencephalitis (1, 1.8%), CCM (1, 1.8%), herpes zoster (1, 1.8%), AT (10, 18.1%), renal failure (2, 3.6%), hypertensive heart failure (2, 3.6%) | TB (7, 36.9%), sepsis (4, 21.1%), KS (1, 5.3%), VME (1, 5.3%) CCM (1, 5.3%), RF (1, 5.3%) SP (1, 5.3%), acute bacterial meningitis (1, 5.3%). |
| Gyuse et al, 2010, Nigeria Conducted date: January 2005–December 2007 | 350 | 61 | 35.4 | Introduction of ART | Determine the causes of death among to plan strategies in improving mortality | Retrospective study | | TB (24.0%), followed by sepsis and septicemia (13.0%), meningitis, encephalitis and anemia (11.0%), respiratory diseases (5%), hepatitis (2%), gastrointestinal disease (3%), and RF (3%). |
| Macpherson et al, 2009, South Africa Conducted date: October 2005–September 2007 | 1131 | 67 | 37 | Initiated on ART | Determine relative contribution of death to cohort exit and causes and predictors of mortality | Retrospective cohort study | | TB (47, 44.3%) and diarrhoeal diseases (26, 24.5%), meningitis (5, 4.7%), hepatic failure (3, 2.83%), opportunistic malignancies (KS, prostate, cervix, bladder, endometrium) (7, 6.59%), pneumonia (2, 1.89%), septicemia (4, 3.77%), HIV encephalopathy (1, 0.94%), diabetic ketoacidosis (1, 0.94%), renal failure (1, 0.94%) |

**Table 1**

(continued).

| Authors and date of publication, geographic location, conducted date | Sample size | % female | Average Age, yr | Intervention | Aim of the study | Study design | Outcomes Causes of hospitalization (N, %) | Outcomes Causes of death (N, %) |
|---|---|---|---|---|---|---|---|---|
| Kouanda et al, 2012, Burkina faso Conducted date: January 2003–December 2008 | 5608 | 70 | 35 | Receiving ART | Investigate causes of death and the factors associated with mortality in a cohort of patients on ART | Retrospective cohort study | AIDS (64%) and non-AIDS related (36%). | Wasting (113, 26.9%), TB (67, 16%), esophageal /pulmonary candidiasis (22, 5.2%), chronic diarrhea (17, 4.1%), Cryptococcosis (16, 3.8%), Toxoplasmosis (16, 3.8%), encephalopathy /dementia (7, 1.7%), pneumocystosis (7, 1.7%), OM (5, 1.2%), Leishmaniasis (5, 1.2%), BP (4, 1.0%), cytomegalovirus disease (1, 0.2%), anemia (22, 5.2%), septicemia (13, 3.1%), respiratory disease (16, 3.8%), AT (16, 3.8%), metabolic disease (13, 3.1%), myocardiopathy (14, 3.3%), BM (4, 1.0%), high blood pressure (4, 1.0%), depression (3, 0.7%), septic abortion (2, 0.5%). |
| Meintjes et al, 2015, South Africa Conducted date: June 2012–October 2013 | 585 | 57.8 | 35.3 | ART | Describe hospital level disease burden and factors contributing to morbidity and mortality | Cross-sectional study with prospective follow-up | TB (238, 40.7%), Bacterial infection (100, 17.1%), AIDS other than TB (64, 10.9%). Major organ dysfunction (59, 10.1%), other diagnosis (35, 6.0%), Venous thromboembolis (1, 5.3%), Drug related (24, 4.1%), non-communicable diseases (22, 3.8%), psychiatric (9, 1.5%), none diagnosed (3, 0.5%). | TB (37.2%) and other AIDS- (24.4%). |
| Moore et al, 2011, Uganda Conducted date: May 2003–December 2006 | 1132 | 73 | 38 | ART | Describe mortality over time and to determine clinical conditions associated with death | Prospective study | | Most common condition TB (21% of deaths), Candida disease (15%), cryptococcal disease (12%), Pneumocystis jiroveci pneumonia (8%) and KS (6%) |
| Mzileni et al, 2008, South Africa Conducted date: July 2004–December 2006 | 3073 | 67.4 | | ART | Describe mortality trends and causes of deaths | Prospective observational study | | TB (42, 20.5%), CD (25, 12.2%), CCM (18, 8.8%), bacterial pneumonia/pneumocystis pneumonia (12, 5.8%), KS and lymphoma (17, 8.3%), hepatitis (6, 2.9%). |

% = percentage, ADC = AIDS-demented complex, AT = ARV toxicity, CCM = cryptococcal meningitis, CD = chronic diarrhea, GE = gastroenteritis, KS = kaposi sarcoma, N = number, NHRI = non-HIV related illness, NSD = no specified diagnosis, OM = opportunistic malignancies, RF = renal failure, SCAP = severe community-acquired pneumonia, TB = tuberculosis, UNS = undiagnosed neurological syndromes.
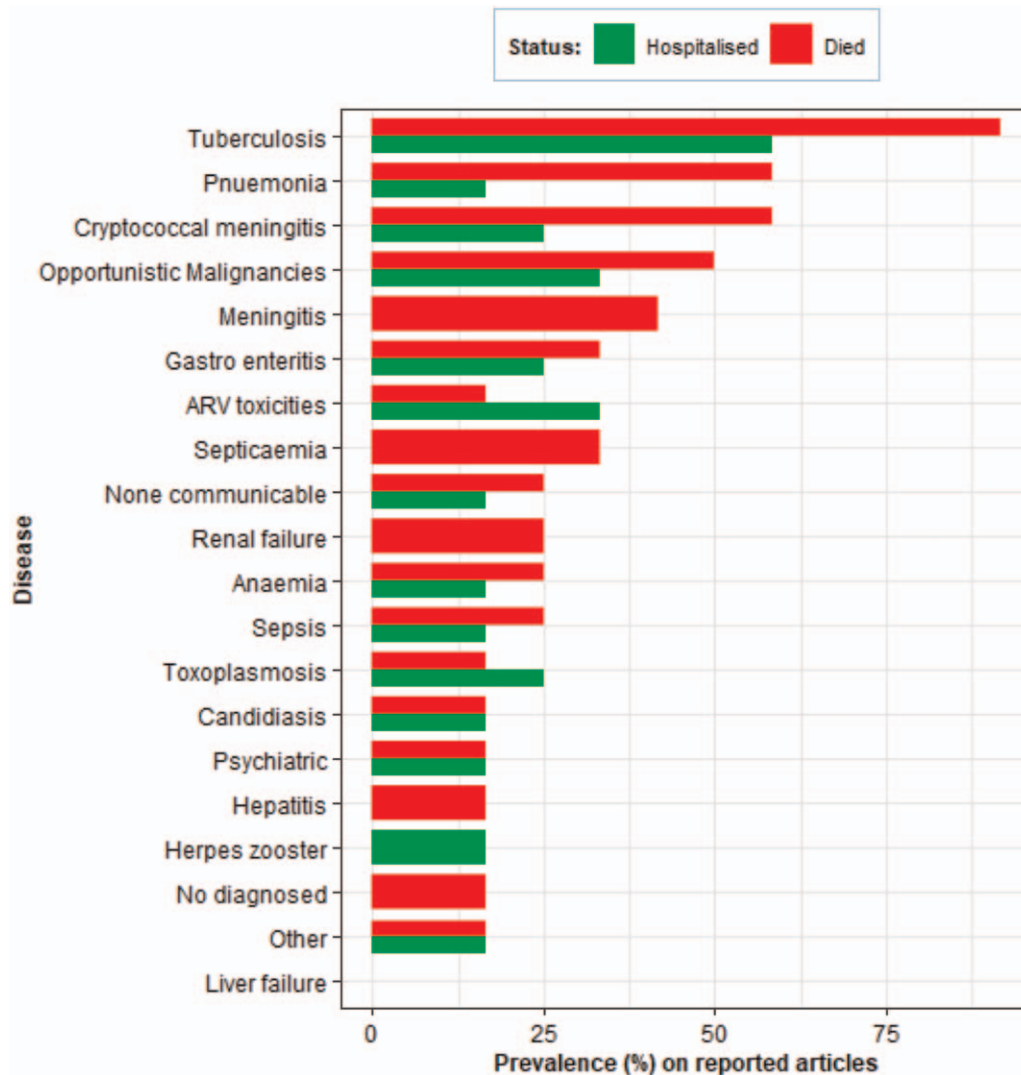
**Figure 2.** Prevalence of articles. The prevalence (%) of articles that described the causes of death in red and of hospitalization in green. Six articles reported both causes of death and hospitalization, 5 articles reported causes of death and one reported causes of hospitalization.

meningitis. The least reported disease was Candidiasis with 17% of hospitalizations and 17% of deaths.

Table 2 reports tuberculosis, anemia, and toxoplasmosis were the leading reason of hospitalization 40.7%, 34.2%, and 29.3%, respectively. Pneumocystosis is the least cause of hospitalizations accounting for 0.2%.

In Table 3, tuberculosis, anemia, and meningitis were the leading cause of death at 44.3%, 30.2%, and 28.6%, respectively. The least cause of death was pneumocystosis with 1.4%.

## 4. Discussion

The objective of this study was to identify the causes of hospitalization and causes of death among PLHIV in the ART era in Sub-Saharan Africa. The causes reported were opportunistic infections, opportunistic malignancies, and non-AIDS related. Among opportunistic infections, in most of the included studies, tuberculosis was the commonest leading cause of hospitalization

and death among people living with HIV. It accounted for between 18% and 40.7% of hospitalization (Table 2) and 16% and 44.3% (Table 3) of death. The prevalence of death reported due to tuberculosis was higher than what had been reported in Thailand.[41] This may be a consequence of many countries in Sub-Saharan Africa not having well developed medical analysis laboratory, therefore late diagnosis of tuberculosis could imply the increased rate of mortality. Non-expanding access and late initiation of antiretroviral therapy and anti-tuberculosis treatment in some countries in Sub-Saharan Africa could also increase the burden of the disease.[42] Studies conducted in Rio de Janeiro, Brazil estimated 80% of reduction of tuberculosis incidence for PLHIV associated with the use of antiretroviral therapy.[43]

Many patients in Sub-Saharan Africa arrived at the hospital at an advanced stage of disease with cluster of differentiation 4 (CD4) $\leq 200$ cells/mm$^3$. Many patients do not have information on disease because of lack of counseling and testing services in the region.[44]

If patients start ART at the higher baseline CD4 count, there is a potential to decrease morbidity and mortality.[45] Among the

**Table 2**

**Prevalence of the cause of hospitalization.**

**Diagnosis**

| | Number of studies | Min | Q1 | Q2 | Q3 | Max |
|---|---|---|---|---|---|---|
| Tuberculosis | 7 | 18 | 19.1 | 24.9 | 31.4 | 40.7 |
| Anemia | 2 | 10 | 16.1 | 22.1 | 28.2 | 34.2 |
| Toxoplasmosis | 3 | 1.8 | 8 | 14.2 | 21.7 | 29.3 |
| Pneumonia | 2 | 16.3 | 18.7 | 21 | 23.3 | 25.7 |
| Cachexia | 1 | 19.8 | 19.8 | 19.8 | 19.8 | 19.8 |
| ARV_toxicities | 4 | 4.1 | 8.5 | 10.8 | 13.2 | 18.1 |
| Septicemia | 1 | 16.4 | 16.4 | 16.4 | 16.4 | 16.4 |
| Herpes | 2 | 1.8 | 5.3 | 8.9 | 12.4 | 15.9 |
| Candidiasis | 2 | 14.2 | 14.5 | 14.9 | 15.2 | 15.6 |
| Gastroenteritis | 3 | 6.5 | 8.7 | 10.9 | 11.8 | 12.6 |
| Cryptoccocal meningitis | 3 | 1.8 | 5.3 | 8.8 | 9.9 | 11 |
| Others | 2 | 4.2 | 5.9 | 7.6 | 9.2 | 10.9 |
| Non communicable disease | 2 | 3.6 | 5 | 6.3 | 7.7 | 9.1 |
| Sepsis | 2 | 5 | 5.6 | 6.2 | 6.7 | 7.3 |
| Malignancies | 4 | 1.8 | 1.9 | 3.4 | 4.8 | 5 |
| No_diagnosed | 1 | 4 | 4 | 4 | 4 | 4 |
| Renal failure | 1 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 |
| Meningitis | 1 | 1.8 | 1.8 | 1.8 | 1.8 | 1.8 |
| Psychiatric | 2 | 1.1 | 1.2 | 1.3 | 1.4 | 1.5 |
| Pneumocystosis | 1 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |

Q2 = median.

included studies, one reported from Ghana did not find tuberculosis as the first cause of hospitalization in Sub-Saharan Africa, it reported anemia as the first cause of hospitalization.[28] The included studies reported that anemia accounted for 34.2% of hospitalization (Table 2) and 30.2% of death (Table 3). Similarly, in America, another study among African women living with HIV found almost the same result.[46] Anemia is a known independent risk factor for death among patients living with HIV. It has been reported that 59% of patients who suffer from anemia are likely to die even if other opportunistic infections associated with it are treated appropriately.[47] Anemia is known to be multifactorial, several factors such as poor nutrition, malaria, hookworm infection, and other infections have been reported among its causes.[48] Other studies showed a relation between the prevalence of anemia and HIV.[49,50] This may be a result of late initiation of ART. A study in South Africa showed that early initiation of ART resolved 66% of anemia in HIV positive patients after just 1 year of treatment.[51] Two of the

**Table 3**

**Prevalence of the cause of death.**

**Diagnosis**

| | Number of studies | Min | Q1 | Q2 | Q3 | Max |
|---|---|---|---|---|---|---|
| Tuberculosis | 8 | 16 | 22.4 | 24 | 35.8 | 44.3 |
| Anemia | 2 | 5.2 | 8.1 | 11 | 20.6 | 30.2 |
| Meningitis | 4 | 1 | 4.7 | 5.3 | 11 | 28.6 |
| Toxoplasmosis | 2 | 1.7 | 8.2 | 14.6 | 21.1 | 27.5 |
| Gastroenteritis | 4 | 4.1 | 7.1 | 9.2 | 13.9 | 24.5 |
| Others | 1 | 6.5 | 11 | 15.4 | 19.9 | 24.4 |
| no_diagnosed | 2 | 4 | 9 | 14 | 19 | 24 |
| Pneumonia | 6 | 1 | 3.6 | 5.8 | 8.7 | 23 |
| Sepsis | 2 | 13 | 17 | 21 | 21.1 | 21.1 |
| Septicemia | 3 | 3.1 | 3.6 | 8.4 | 14 | 17.1 |
| Candidiasis | 2 | 5.2 | 7.7 | 10.1 | 12.6 | 15 |
| Cryptoccocal meningitis | 6 | 0.4 | 3.5 | 8.8 | 12 | 13 |
| Malignancies | 5 | 1.2 | 5.5 | 6.3 | 7.9 | 9.8 |
| Non communicable disease | 3 | 1.4 | 2.1 | 2.8 | 5.1 | 7.4 |
| Renal failure | 2 | 0.9 | 2 | 3 | 4.2 | 5.3 |
| ARV_toxicities | 2 | 3.3 | 3.4 | 3.5 | 3.7 | 3.8 |
| Hepatitis | 1 | 2 | 2.2 | 2.5 | 2.7 | 2.9 |
| Liver failure | 1 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 |
| Psychiatric | 2 | 0.7 | 1.1 | 1.5 | 2 | 2.4 |
| Pneumocystosis | 1 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 |

Q2 = median.

included studies in Burkina Faso,[29] and in Ethiopia,[27] did not find tuberculosis as the most cause of death, they found wasting syndrome and bacterial meningitis, respectively. Similarly, out of the included studies, other studies did not find tuberculosis as the first leading cause of hospitalization and of death, in Europe, precisely in French Guyana, they reported that among AIDS-related deaths the most frequent diseases were histoplasmosis and toxoplasmosis.[52]

In Taiwan, Asia, it was reported that the first HIV-associated opportunistic infections were esophageal candidiasis.[53] Opportunistic malignancies accounted between 1.8% and 5% of hospitalization (Table 2) and 1.2% and 9.8% of death in our included studies (Table 3). It was noticed that kaposi sarcoma was the most reported[18,21,22,25] as cause of hospitalization and death among PLHIV. Lack of detecting early neoplasm through screening may imply the increase of the disease in Sub-Saharan Africa because many medical laboratories in Sub-Saharan Africa do not have devices and laboratories required to support the screening.[54] Many people initiate ART when kaposi sarcoma is already at advanced stages.[55] Similarly, in India, kaposi sarcoma had been reported as the most opportunistic malignancy between 2% and 5%.[30]

Among non-AIDS related, in some of our included studies, ARV toxicities were shown to cause morbidity and mortality.[18,19,21] The prevalence was almost the same in the 3 studies. To reduce morbidity and mortality, counseling about the adverse effects of antiretroviral drugs and aggressive monitoring of patients must be conducted before and after initiation to the antiretroviral therapy.[56] Other non-AIDS related conditions such as non-communicable disease, psychiatric, had been reported on in some of our included studies.[18,22,24,29] A better knowledge of the commonest comorbidities is very important to improve health promotion, prevention, and care among HIV patients. Poverty, limited access to ART, malnutrition, and interruption of supply at the program level had been found to be among the factors which limit the control of HIV and the effectiveness of ART in African countries.[18]

In conclusion, tuberculosis was the most common cause of hospitalization and death in Sub-Saharan Africa according to the included studies, this was followed by other infectious diseases, opportunistic malignancies, and other non-AIDS related causes. To reduce morbidity and mortality in the ART era, all the different causes of hospitalization and causes of death must be attended to.

## Acknowledgments

## Author contributions

Manimani Riziki Ghislain conceptualized the study and prepared the manuscript under the guidance and supervision of Nombulelo Magula. Manimani Riziki Ghislain and Gloire-Aime Aganze Mushebenge identified, selected, and screened the articles for eligibility, and the discrepancies were resolved by the intervention of Nombulelo Magula. The process of literature selection and reasons for exclusion and inclusion were all authors including contribution to the development and design of the study. Manimani Riziki Ghislain and Nombulelo Magula contributed to the methodology and reviewing of the manuscript. All authors contributed to the final version. All authors read and approved the final manuscript.

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