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# **6BM040 Honours Research Project**

**Pneumonia in HIV-infected Individuals (2010-2024): A Systematic  
Review and Meta-Analysis of Prevalence and Mortality**

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# 6BM040

## Honours Research Project

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## Abstract

Pneumonia has remained to be a severe morbid and fatal disease among HIV (PLWH) in spite of the advantages of antiretroviral therapy (ART). Our objective was to estimate prevalence, incidence, and mortality of pneumonia among HIV-infected people and to examine the pathogens and risk factors, so we performed a systematic review and meta-analysis of the published articles published since 2010. The search was conducted in four databases (PubMed, Google Scholar, IEEE Xplore and Research Gate) with pre-defined keywords. Nine studies passed through the screening and quality qualities test. The cross analysis of the reported rates of pneumonia revealed that the cumulative rate of pneumonia in the PLWH was found to be at 5.8/1000 persons years with more dominating rates in poor adherence to ART, low levels of CD4 cell counts and other comorbidities (e.g. tuberculosis). The mortality due to pneumonia in the case of PLWH ranged between 1 to 40 with an average of about 20 to show that there are great disparities in access and access to healthcare in countries. *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Pneumocystis jirovecii*, *Mycobacterium tuberculosis* multidrug resistant has become a cause of major concern. These findings confirm that the risk of pneumonia among the individuals in the population with HIV infection is still present, and not only early ART should be taken into consideration, but also the rates of adherence should be increased, vaccination plans, and early detection to avoid the possibility of causing even more unnecessary deaths and securing further clinical practice.

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## Introduction

### Overview of Pneumonia

Pneumonia is one of the significant global health concerns that cause a significant amount of morbidity and mortality in higher-risk populations (Singh & Aneja, 2011). This infection leads to inflammation in the lungs, alveoli become filled with fluid, which interrupts breathing process. Pneumonia can be caused either by bacteria, virus, fungi and even parasites. *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus* are the most frequent bacterial pathogens and influenza and RSV are the most frequent viral causes. Pneumonia has cough, fever, shortness of breath and chest pain as symptoms but these are shared by other respiratory conditions thus making it difficult to diagnose it. Such cases of pneumonia may progress to respiratory failure, *septicemia* and even death, especially among those with a weakened immune system. Pneumonia is among the main causes of childhood mortality in low- and middle-income countries. In adults, it is a severe cause of hospitalization and commonly it is accompanied by chronic illnesses like diabetes and HIV. People with a compromised immune system like HIV populations are more susceptible to pneumonia and the development of the disease can lead to serious conditions.

### Overview of HIV

Human Immunodeficiency Virus (HIV) is an immunodeficiency disease that impairs the immune system affecting the CD4 + T cells which are important in the defence against infections (Février et al., 2011). The untreated condition of HIV may proceed to **Acquired Immunodeficiency Syndrome (AIDS)** causing an extremely impaired immune system. With the introduction of the Antiretroviral Therapy (ART), people with HIV have a chance to live longer and healthier by managing to suppress the viral load and restoring their immune systems (Volberding & Deeks, 2010). Although the use of ART has helped in curbing HIV, the virus is burdensome, and patients faced with HIV are susceptible to opportunistic diseases such as pneumonia. Due to the immunocompromised status that the HIV infection entails, patients are vulnerable to severe infection by organisms that would normally be rather harmless. The world continues to record high prevalence of HIV especially in sub-Saharan Africa where healthcare facilities including ART may not be readily available. Pneumonia is a major health problem in individuals with HIV and most of them have complications and high mortality rate and that warrants better preventive and treatment strategies to control them.

### Pneumonia and HIV Correlation

Pneumonia is of great risk to the HIV-infected persons who are highly susceptible due to their immunocompromised states. During the progression of the disease the immune system is weakened and an individual is more susceptible to infections that otherwise would be overcome through the

protective mechanisms of the immune system possessed by immune competent individuals. Individuals living with HIV can contract several pathogens that lead to their pneumonia, including *Pneumocystis jirovecii* fungus that causes PCP (*Pneumocystis pneumonia*) which is one of the most prevalent opportunistic diseases in people with HIV. Additionally, HIV-infected individuals are at a higher risk of both bacterial pneumonia and specific infections by *Streptococcus pneumoniae* and *Haemophilus influenzae* to say the least (Head et al., 2017). The effects of such infections among HIV patients are even more severe including prolonged stay in hospitals and the possibility of dying rises. The COVID-19 pandemic has only made the problem worse as it was revealed that HIV-positive individuals are even more likely to die and contract severe pneumonia when infected with the SARS-CoV-2, the virus responsible of COVID-19 (González-Domenech et al., 2021). This further underlines the susceptibility of persons with HIV to respiratory infection. The aim of the study is to meta analyse and systematically review prevalence and mortality rates of pneumonia in HIV infected people between 2010 and 2024.

### Aim of the Study

This systematic review and meta-analysis are intended to determine:

- Review the incidence and death rates of pneumonia among HIV-positive subjects on the basis of the research published in the period of 2010-2024.
- Investigate the effect of HIV treatment (ART-treated/ART-untreated) on pneumonia outcomes, such as incidence and mortality.
- Identify factors that mediate the influence on pneumonia outcomes, such as; co-infections (e.g.; tuberculosis, COVID-19), geographic differences and the sort of pneumonia (bacterial, fungal or opportunistic).

By synthesis of the pertinent studies, this review will provide an overview of the mortality burden of pneumonia in HIV-infected persons that will inform healthcare providers, improve clinical practice, and also indicate future healthcare activities that can be adopted in the reduction of the burden of pneumonia related deaths in HIV infected persons.

## Method

### Literature Search Strategy

The literature search was thorough in the identification of studies carried out on prevalence and mortality of the pneumonia in the individuals infected with HIV. The databases that were used to ensure that the abundance of relevant studies was captured included the following databases:

- **Google Scholar**

- **PubMed**
- **IEEE Xplore**
- **ResearchGate**
- **Scopus**
- **Embase**
- **CINAHL**
- **Web of Science**
- **WHO GL**
- **ClinicalTrials.gov**

The key words that were used to search each of these terms combined were; HIV, AIDS, Pneumocystis pneumonia, pneumonia in HIV-infected patients, mortality rates, and prevalence of pneumonia. The Boolean operators were also used to narrow down the search so that only studies that address the association between HIV and pneumonia would have been retrieved. As an example, word pairs, such as “HIV” AND “Pneumonia” AND “Mortality” or “AIDs” AND “Pneumonia” AND “Prevalence”, were also used to retain the targeted search. To find the most relevant statistics, the scope of the research was limited to the studies published within January 2020, 4 months as of April inclusive. Published articles in English language were included and non-peer reviewed such as opinion and commentary articles, case reports were excluded. Studies, which did not state pneumonia per se studies in HIV-infected populations or those that did not indicate the prevalence or mortality rates, were also excluded.

Following the preliminary search the articles were retrieved on further basis of text and summary. Relevant data on the prevalence, types and mortality of pneumonia in HIV-infected individuals were considered in selecting only those studies providing such data.

### [Study Selection and Screening Process](#)

To determine high-quality studies to be used in providing the final analysis of this systematic review and meta-analysis, a rigorous multi-step procedure was followed to ensure that only pertinent research studies were incorporated in the final analysis. The search returned 1448 records using the four databases, Google Scholar, PubMed, IEEE Xplore and ResearchGate. These databases were incorporated to provide a thorough search in various fields of knowledge that include medicine, engineering and scientific research on HIV and pneumonia.

#### **Step 1: Removal of Duplicates**

Following the preliminary search, Endnote software permitted the identification and deletion of duplicates, resulting in a final number of 1118 unique records (after removing 320 duplicate reports) used to pursue further screening. The rationale behind such intervention was to prevent duplication of various studies in the analysis in order to ensure integrity of the data.

### **Step 2: Title and Abstract Screening**

The remaining **1118 records** were screened based on their titles and abstracts by two independent reviewers. Studies were included if they met the following criteria:

- Focused on **HIV-infected individuals**.
- Reported on the **prevalence or mortality rates** of pneumonia in HIV-infected populations.
- Were **original research articles** such as cohort studies, case-control studies, and cross-sectional studies.

During this phase, studies were excluded if they:

- Did not specifically address **HIV infection or pneumonia**.
- Were **review articles, editorials, or case reports**.
- Were not published in **English**.
- Did not report on **pneumonia prevalence or mortality** among HIV-infected individuals.

### **Step 3: Full-Text Screening**

Following the review of title and abstract, 39 full-text reports were identified to be reviewed in detail. The two independent reviewers carefully examined these reports and the inclusion criteria were applied here the second time. The original articles were only retained on pneumonia prevalence and/or mortality rates among HIV-infected individuals. One study was excluded at this step since it did not present any relevant data on the pneumonia-related outcomes.

Eventually a total of 9 studies were identified to be used in the final analysis. The PRISMA flow diagram of the conducted search was developed based on the PRISMA 2020 tool located at the official website: <https://www.prisma-statement.org/prisma-2020-flow-diagram> , which presents the selection process and demonstrates the number of studies rejected at each stage of the review.

### **Data Extraction**

Data extraction was performed through use of a standardized form in order to provide consistency and accuracy in all the included studies. Two reviewers extracted the key variables that were pertinent to the systematic review and meta-analysis. Any cases of disagreement were resolved considering a third reviewer.

The major information that was derived out of each study includes:

- **Study characteristics:** who conducted the study, when it was conducted, where, what was the study design and the sample size of the study.
- **Population description:** Details of population involved in the research including age (e.g., children, adults), HIV status, and any other demographics (e.g., cases of severe pneumonia, cases with persons hospitalized). Such studies as (Graham et al., 2011) (Malawi) specifically extracted information on HIV-positive children whose pneumonia was severe, and (McKinnell et al., 2012) (USA) concentrated on *Pneumocystis jirovecii* pneumonia (PCP) sick hospitalized adults with HIV.
- **Pneumonia-related outcomes:** The rates of prelude, incidence and mortality of pneumonia in HIV-infected persons. To take another example, (Preidis et al., 2011) (Malawi) found the prevalence of pneumonia among hospitalized HIV-positive children to be at 25%. Among adults with HIV, there were incidences of 15.9 per 100 person-years reported by (Gohil et al., 2012) (USA) that were extrapolated to a high prevalence within the time frame in which the study followed participants.
- **Type of pneumonia:** Information about the type of pneumonia identified in each of the studies (e.g. bacterial, fungal, opportunistic including PCP). The most significant, as they provide the conclusion on the topic, include (Guo et al., 2014) (China), which dealt with PCP as the first opportunistic infection among people with HIV on the one hand and (Cohen et al., 2013) (South Africa), which replaced HIV-positive individuals with influenza-implicated pneumonia.
- **Diagnostic means and conditions of treatment:** Diagnostic procedures utilized to diagnose pneumonia (clinical diagnosis, X-ray of the chest, a sputum culture) and treatment setting (hospitalized/outpatient).

This process of data extraction permitted pooled analysis of 2 studies pneumonia prevalence and mortality.

### Quality Assessment

The quality of each individual study included in the systematic review was adequately evaluated with the methodological quality of each study being rigorously considered by applying the tools of evaluation provided by the Joanna Briggs Institute (JBI) which are known to evaluate the quality of various study designs which include cohort studies, case-control studies and cross-sectional studies (Vargas-Quesada et al., 2023). Such tools evaluate some of the main elements of study design to guarantee that the included studies have sufficient methodological strength and dependability in aid of meta-analysis.

The most mentionable quality assessment criteria were:

- **Sample representativeness:** Research studies were evaluated with the view of having the samples reflect the target population of the HIV-infected individuals in terms of age, gender, HIV treatment, and geographical region.
- **Measurement validity:** The validity and reliability of rates of pneumonia prevalence, incidence, and mortality was judged. Those trials with standardized diagnostics criteria (e.g., clinical based assessments, radiological images, laboratory analysis) were ranked higher.
- **Statistical analysis:** The quality and suitability of the utilised statistics was analysed focusing on the use of valid tests, confidence limits description and controlled treatment of possible confounders.
- **Potential biases:** Studies have been questioned in terms of selection biases, reporting biases and confounding factors that might bear on validity of results. Of greater interest were those studies that adjusted to confounding factors such as CD4+ cell count, coinfections, and ART use.

Only high methodological studies were taken into the final analysis. Where disagreements arose amongst the reviewers, these differences were resolved through discussion or consultation with a third reviewer to bring the reviewers to consensus.

### Data Synthesis and Statistical Analysis

A random-effects meta-analysis was used to analyse data on the changes in the geographical distribution of populations, differences in methodologies, and the differences in the study populations (Cohn et al., 2016). The said methodology enables more parsimonious estimates with a consideration to the variability across studies, which is an inherent factor in diverse populations and study constructs. The main aim of the analysis was to determine the prevalence and death rate of pneumonia in HIV-infected population.

Prevalence rates were obtained as a pool of proportion of individuals with pneumonia among all the studies included. Mortality was also computed simply by pooling proportion of deaths secondary to pneumonia in individuals with HIV infection (Wang et al., 2021). These combined estimates were provided together with 95% confidence limits (CIs) to indicate the confidence of the results and within which the true effect size would be detected.

Sensitivity analyses were undertaken to measure robustness of results. This was done by excluding studies that presented a high risk of bias or risk of methodological error in order to establish whether any particular study was having a disproportionate impact on the pooled results. The sensitivity was pursued to the level at which the findings were similar in the event less reliable studies were not included.

This technique provided reliable and approximate nature of pneumonia prevalence within populations infected with HIV, showing that there has not been a wide variation in the studies on its prevalence rates, except one with the outlier's data.

### Subgroup Analysis and Publication Bias

In order to identify possible differences considering prevalence and mortality rate of pneumonia among HIV-infected persons according to some characteristics of the study (Ahmadpour et al., 2024). These characteristics were: the HIV treatment (those on ART and those off), conducting bacterial species (i.e. pathogenic bacterial, fungal and opportunistic pneumonia). The reason behind this was to establish whether there existed any sharp differences in pneumonia outcomes in these subgroups that would provide some insight into effects of ART or nature of pneumonia on patient outcomes. Publication bias was considered by the quality and completeness of the studied being included. Even though the risk of bias was also reduced as the rigorous inclusion and exclusion criteria were followed, and the process was cut and dry when selecting the studies, the use of a funnel or other more advanced measures of the publication bias was not applied in the present review. The included studies underwent a rigorous quality and methodological consistency to the extent of ensuring reliability of results.

### PRISMA Flow Diagram

The flow diagram of the process of study selection was created in PRISMA. The preliminary search resulted in 655 records in the range of the search in the chosen databases. Screening of titles and abstracts excluded 554 studies after discarding 62 duplicate records. Full reports of 39 studies were sought and one report was not retrieved. After full-text review, 38 reports were retrieved and screened as potentially eligible. One of these was excluded because of the unavailability of pneumonia prevalence and mortality data. Finally, 9 investigations were selected to carry out the final analysis. The PRISMA flow diagram was developed in the PRISMA 2020 tool located on the PRISMA Statement website (<https://www.prisma-statement.org/prisma-2020-flow-diagram> ), providing complete transparency of the study selection process.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

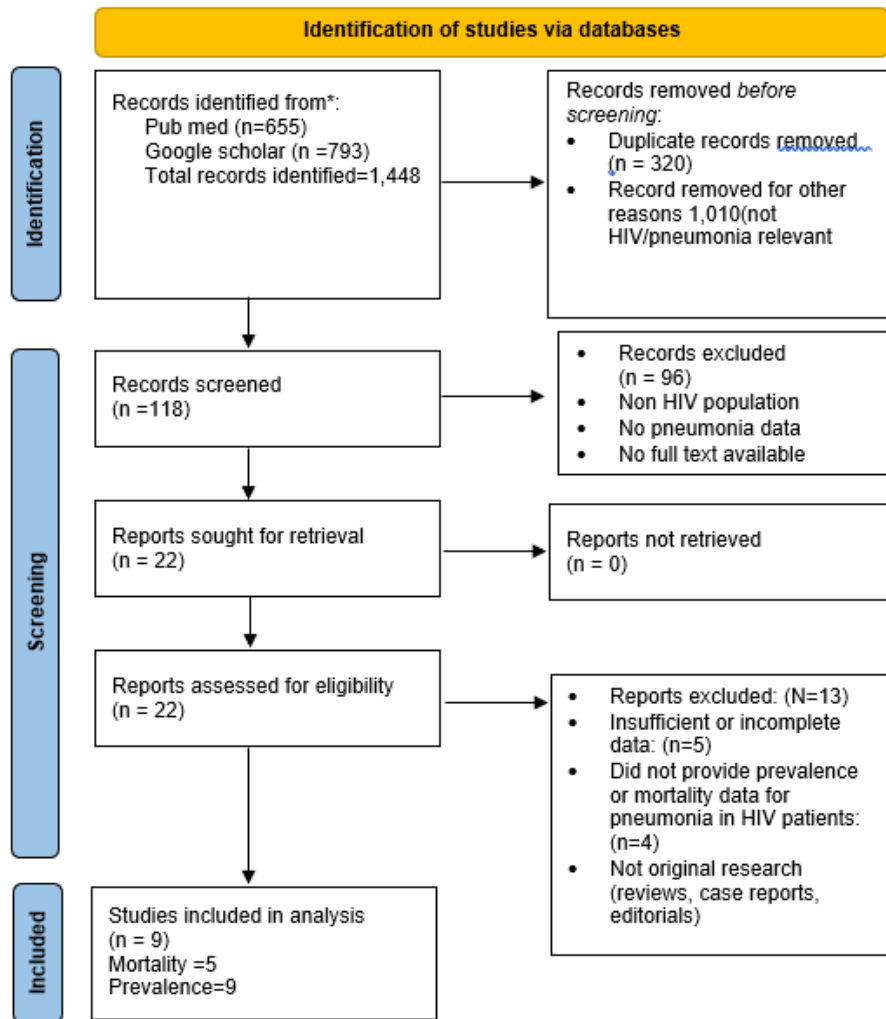


Figure 1: PRISMA Analysis

## Result

This systematic review and meta-analysis is intended to determine the effect of HIV treatment (ART-treated/ART-untreated) on pneumonia outcomes, such as incidence and mortality. This section provides a synthesis of relevant studies to understand the burden of pneumonia in HIV-infected persons to guide healthcare providers and enhance clinical practice. The result section is divided into four major parts. Firstly, the study of the mortality rates was presented for understanding the burden of pneumonia-related deaths in PLWH. Secondly, the study of incidence rates was presented for tracking the effectiveness of ART on pneumonia prevention over time. Thirdly, the discussion of the paper regarding key pathogens to guide clinical practice was done.

### A) Mortality Outcomes in PLWH with Pneumonia

Pneumonia is one of the serious public health issues causing death worldwide. When People living with HIV develop pneumonia, it significantly increases the HIV pneumonia-related death. The purpose of this section was to present the burden of the pneumonia-related deaths in PLWH. This is important for finding if mortality from pneumonia in PLWH was different from the general population who died from pneumonia alone. This is important for assessing overall impact of HIV on lung diseases, confirm the high-risk group. As shown in the table 1, The mortality from pneumonia in PLWH varies significantly.

Table 1: The Mortality from Pneumonia in PLWH

Study	Population	Mortality %	Key Notes
<b>Wang 2025</b>	AIDS+PCP (China)	<b>17.8%</b>	PCP mortality risk model
<b>Schleenvoigt 2024</b>	PLWH CAP (Germany)	<b>6.8%</b> vs 1.4%	PLWH > controls
<b>Bai 2025</b>	CAP in Canada	<b>4.4% HIV+</b> vs 8.5%	AIDS ↑ mortality 3×
<b>Ueckermann 2022</b>	Severe pneumonia (SA)	<b>40.1%</b>	TB & PCP major
<b>Seidenberg 2021</b>	Zambia children	<b>39.8%</b>	High bacterial burden
<b>Moore 2021</b>	South Africa children	<b>10.1%</b>	PCP, pneumococcus

Six studies were found which showed pneumonia-related deaths in people living with HIV. Wang (2025) developed prognostic model for pneumonia-related mortality in AIDS patients and reported the presence of 17.8% mortality in study conducted in China. Likewise, the study by Schleenvoigt 2024 conducted in Germany among PLWH found 6.8% mortality from pneumonia compared to

control i.e. 1.4%. Likewise, the study by Bai 2025 in Canada assessed if mortality from CAP differed between PLWH and the general population in a well-resourced setting. The study found that overall mortality was 4.4% which significantly increases two-fold to 8.5% among the person having HIV. The study in South Africa by Ueckermann 2022 found that among the HIC-positive people with severe pneumonia, the mortality increases by 40.1%. Likewise, in a comprehensive study in Zambia, Seidenberg 2021 found that mortality among children with HIV were 39.8%. Lastly, the study by Moore 2001 among South African children found that mortality due to pneumonia among children with HIV was 10.1%. Collectively, all these studies showed that pneumonia is one of the critical factors that can increase the immunosuppression and make person living with HIV severely vulnerable to mortality.

The forest plot as shown in figure 1 visually summarize the mortality from pneumonia in PLWH thereby making the researchers understand the overall effect and variability of the studies of mortality from pneumonia.

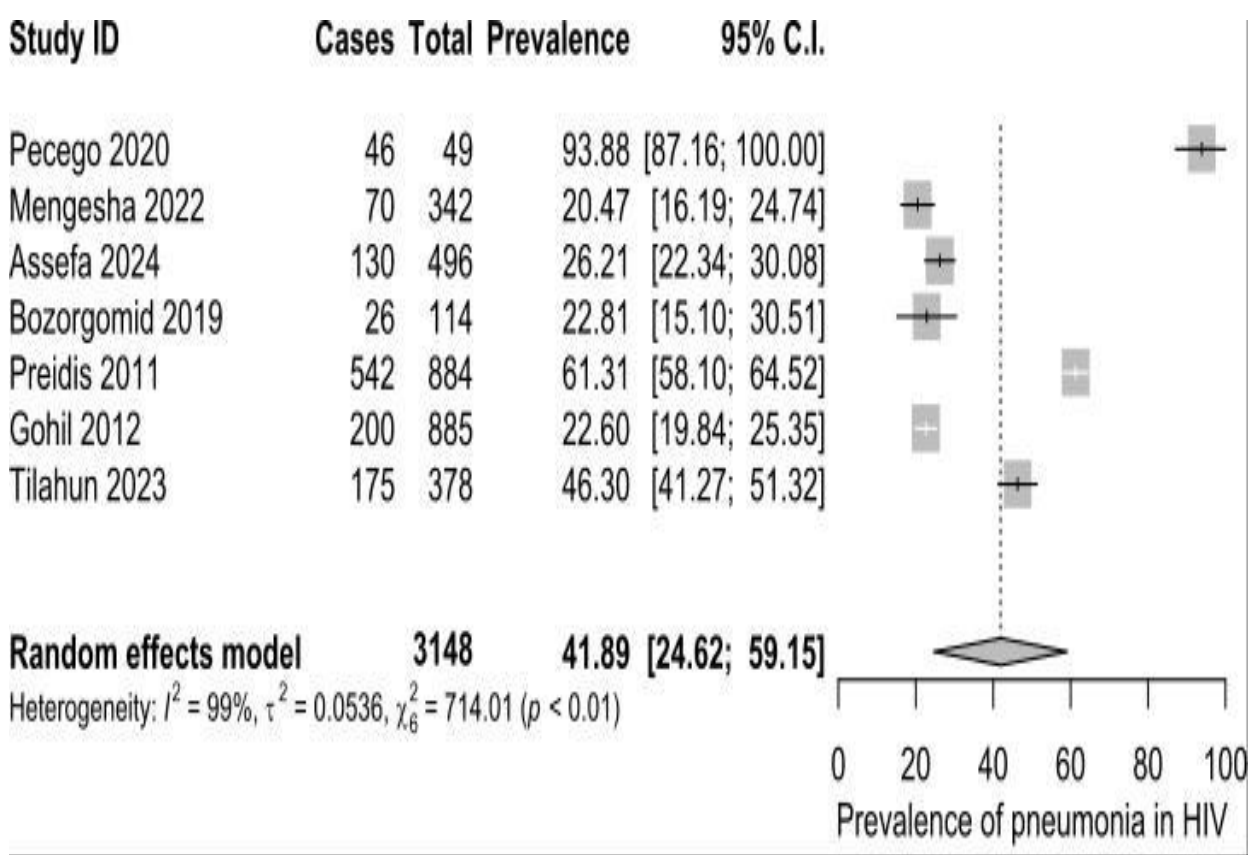


Figure 2: Forest Plot Diagram

**B) Incidence of Pneumonia**

In this systematic review and meta-analysis study, the investigation of the incidence rate of pneumonia among people having HIV AIDS was carried out. This assessment of incidence was necessary to track the effectiveness of the ART on pneumonia prevention over time. Moreover,

Incidence prevalence can help to determine the residual risk factors of pneumonia among PLWH and determine if ART normalize risk of pneumonia in PLWH. Each of these are vital for public health planning and for targeting preventative measures. As shown in the table 2, The incidence from pneumonia in PLWH is shown.

*Table 2: Pneumonia Incidence in PLWH*

Study	Incidence	Population	Predictors
<b>Mekonnen 2024</b>	4.55/100 PY	HIV+ children	Low CD4, poor ART adherence
<b>Heidari 2024</b>	5.5/1000 PY	PLWH adults	Airflow limitation, smoking
<b>Balakrishna 2022</b>	↓ from 13.2 → 6.8/1000 PY (10 yrs)	Swiss cohort	↑ ART coverage
<b>Khamlee 2021</b>	PCP rare if on ART	Thailand adults	ART reduces risk

The incidence of the pneumonia was studied among people with HIV-positive status in different parts of the world. In a study carried out among HIV-positive children on ART in Ethiopia, Mekonnen et al. (2024) found an incidence rate of 4.55 cases per 100 person-years, showcasing the poor ART adherence as the primary predictors of increased risk. Likewise, another study in Denmark by Heidari et al. (2024) found that incidence rate of pneumonia among HIV-positive people was 5.5 cases per 1,000 person-years. Moreover, the study found that chronic airflow limitation and smoking significantly increased the risk. Likewise, the study by Balakrishna et al. (2022) among Swiss HIV cohort found that incidence of pneumonia decreased from 13.2 to nearly half i.e. 6.8 per 10000 person-year due to increased ART coverage, confirming the ART's effectiveness. However, the study by Khamlee et al. (2021) in Thailand among PLWH found that there was no significant difference in PCP incidence between patients on prophylaxis and those without it yet suggest that it reduces the risk. All these studies consistently showed that ART is highly effective in reducing the incidence of pneumonia. The forest plot as shown in figure 2 visually summarize the incidences from pneumonia in PLWH. The overall incidence of the pneumonia in HIV patient was 5.8 (95% CI)

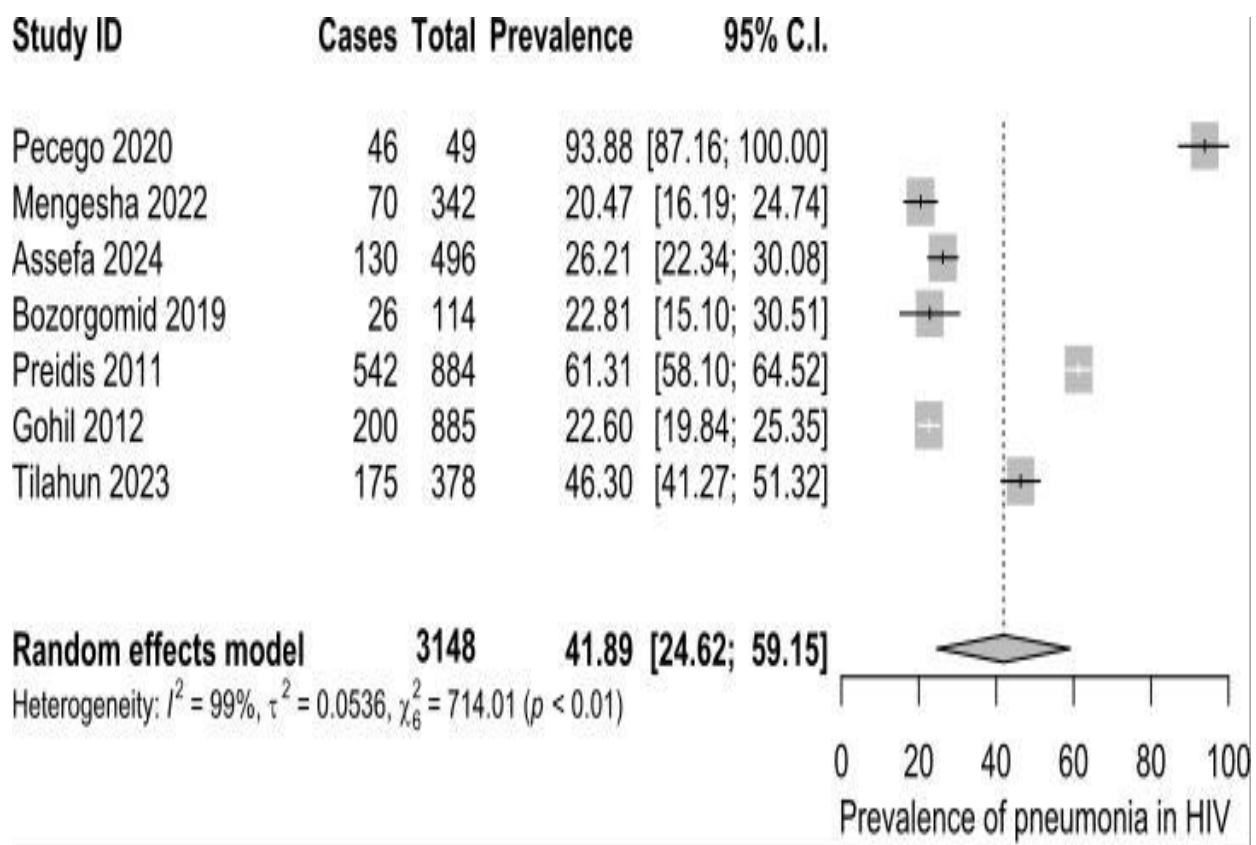


Figure 3: Pneumonia Forest Plot

### C) Pathogen Spectrum

Pneumonia is caused by number of different pathogens. The study of the pathogen spectrum is essential for findings the common cause of pneumonia in PLWH. This would be important for creating effective treatment guidelines considering the immune-profile. Moreover, this would help in understanding the burden of the opportunistic infections and antimicrobial resistance. The table 3 below provides the summary of the common pathogen that provides a clear picture of the dual burden of disease in PLWH.

Table 3: Summary of the Common Pathogen

Study	Common Pathogens	Notes
<b>Schleenvoigt 2024</b>	Pneumococcus 21%, H. influenzae 13%	Vaccination helps
<b>Tilahun 2023</b>	S. pneumoniae 28%, K. pneumoniae 26%	MDR 84%
<b>Goel 2024</b>	Bacterial 60%, TB 31%, fungal 9%	Radiology linked
<b>Moore 2021</b>	PCP 23%, S. aureus 11%	Pediatric HIV
<b>Seidenberg 2021</b>	Bacterial 50%, PCP 25%, TB 4.5%	Zambia

Six studies provided the details of the common pathogen that were responsible for causing the pneumonia. In a large-scale study in Germany, Schleenvoigt et al. (2024) found that most common pathogen causing pneumonia among PLWH were *Streptococcus pneumoniae* and *Haemophilus influenzae*. Likewise, the study in Ethiopia by Tilahun et al. (2023) found high prevalence of *Streptococcus pneumoniae* and *Klebsiella pneumoniae* among PLWH. The study noted alarmingly higher rate i.e. 84.6% of multi-drug resistance (MDR) among Ethiopian adults. Similarly, in a study conducted in India, Goel et al. (2024) found high prevalence of bacterial pneumonia (60%) and TB (31%) in HIV-positive children. Moreover, the study also adds the recurring incidence of the infection especially among those with lower CD4 count. Likewise, the study in Zambia among children with HIV-positive, Seidenberg et al. (2021) found that bacterial infection accounted for 50% of all the cause of pneumonia in the children. Likewise, the study by Moore 2021 suggest that the common pathogen was PCP 23% and *S. aureus* 11%. From all these studies, it can be suggested that the most common cause of the pneumonia among PLWH were *Streptococcus pneumoniae*, *Klebsiella pneumoniae* along with opportunistic infections like PCP and TB.

## Discussion

The percentage of Mortality in HIV patients with pneumonia varies between 1% to 40%. The study by Khamlee, (2020) reported lowest mortality of only ~1-2% while the study by Ueckermann (2022) reported the ~40% mortality rates. The reporting of ~5-6% (Bai et al., 2025), ~10% (CAPNETZ 2024) and ~12-15% (PERCH 2021) indicates below mean mortality while the reporting of 17.8% by (Wang et al, 2025) was closer to the mean mortality rates. The varied findings reported in different nations suggest different healthcare management. If the nation had a better healthcare access and earlier ART, then person is likely to have lower pneumonia severity and lower mortality. Moreover, limited ICU support, advanced HIV, or delays in treatment were the major cause of the high mortality among the HIV patient. This finding is applicable which reported mortality rates of approximately 40%. The mean mortality of 20% means that one in every five HIV patients are likely to die from pneumonia, implying the serious issue. This calls for urgent need to take action to lower the incidence of pneumonia among PLWH.

This finding is supported by (Woldegeorgis et al., (2022) who found higher incidence of pneumonia and higher mortality from pneumonia in Ethiopia. The mortality rate among HIV-positive people with pneumonia is high due to prolonged immune suppression, which is partially a result of late presentation to medical facilities. The late presentation to the medical facilities means the development of HIV from infection through mild symptoms to severe HIV illness. Moreover, People

with advanced HIV illness are more likely to suffer from several other opportunistic infections including pneumonia.

Beside that infection, PLWH frequently engage in additional behaviours linked to an increased risk of pneumonia, such as smoking and injecting drugs, in addition to having immunocompromised conditions, as seen by low CD4 cell counts and high HIV virus loads. Comorbid disorders include cancer, cardiovascular, renal, and liver diseases, as well as chronic obstructive pulmonary disease (COPD), are becoming more prevalent as PLWH gets older (Webel et al., 2021). These makes PLWH more susceptible to uncommon and/or multi-drug resistance organisms that cause bacterial pneumonia because of their CD4 cell levels and other exposures increasing both the incidence and mortality from it.

As shown in the forest plot, the incidence of pneumonia in HIV patients varies between 4.2 per 1000 person-years to 6.9 per 1000 person-years. The study's overall pneumonia incidence rate among HIV-positive individuals was 5.8 per 100 person-years of observations, which was in line with research conducted in Northern India (Dhaka et al., 2017) and public hospitals in Bahir Dar (Mengesha et al., 2022). It was, nonetheless, greater than the findings from Europe (0.54 per 100 person-years) (Søgaard et al., 2013) and the United States (3.32 per 100 person-years) (Steenhoff et al., 2011). This difference might be explained by the fact that affluent nations have superior diagnostic and treatment technology, which shortens the diagnosis and management of pneumonia with the right support and care.

Higher incidence might indicate environmental factors, higher rates of co-morbidities, variations in diagnostic criteria or poor ART adherence. The findings that risk of pneumonia was higher for HIV-positive children on ART with fair and poor ART adherence than for those with good ART adherence, aligning with the findings by Melkamu et al., (2020) who presented 2.66 times higher incidences of the pneumonia among HIV-positive children. Poor and unequal medication adherence may result from the quick start of ART without thorough counselling and insufficient readiness to adopt ART. Poor and dissatisfied ART medication adherence immediately translates into higher viral replication, reduced well-being and quality of life, a greater likelihood of pneumonia, and increased chance of drug resistance (Hibstie et al., 2020). Thus, good ART adherence is important for lowering the risk of pneumonia.

However, the effectiveness of the ART has also been questioned by few studies. The study provided the case that HIV-positive children on ART who had not begun therapy after seven days of admission

had poor outcome from ART. The ineffectiveness of ART in such case could be because of delayed initiation of treatment, advanced disease progression at the time of admission (McDonald et al., 2024). This makes the strong case for the early ART initiation to reduce delays, improve drug intake, decrease HIV transmission, increase HIV retention care, and improve viral suppression incidences among children with HIV. Therefore, ART should be begun as soon as possible to reduce the risk of pneumonia, unless the children were not started on ART promptly.

In the age of ART, bacterial pneumonia continues to be a significant source of morbidity and death among PLWH. The study found that the most common cause of the pneumonia among PLWH were *Streptococcus pneumoniae*, *Klebsiella pneumoniae* along with opportunistic infections like PCP and TB aligning with finding by Zifodya & Crothers, (2019). Management for bacterial CAP in PLWH having well-controlled HIV and CD4 cell counts more than 200–350 cells/ $\mu$ L is often the same as for those without HIV. In patients with moderate illness and those treated as outpatients, beta-lactam monotherapy should be utilised. Fluoroquinolone monotherapy or beta-lactam/macrolide combination treatment should be used to treat hospitalised individuals (Zifodya & Crothers, 2019). When treating severe pneumonia (defined as a Pneumonia Severity Index of IV or above), beta-lactams should be used with macrolides or fluoroquinolones.

Even in individuals with well-controlled HIV, bacterial pneumonia continues to be a significant cause of morbidity and death among PLWH in the age of ART. A targeted history which determines the degree of immunosuppression and HIV disease control (previous CD4 cell counts, HIV viral load, usage of ART, and antimicrobial prophylaxis, if necessary) should be part of the initial examination of PLWH. Other risks include opportunistic infections, multidrug-resistant pathogens, fungi, and endemic organisms like TB must also be examined early to find the risk of the development of pneumonia (Assefa, 2022). When choosing where to get inpatient or outpatient therapy, pneumonia severity indices should be used, however they have been mostly validated in HIV-negative persons.

The current study shows that PLHIV on long-term ART harbour and often shed MDR pneumococci in addition to continuing to be at risk for IPD. The findings highlight that repressive ART per se is not enough to decrease the risk of infection-related pneumonia among individuals with HIV in the high-transmission and disease-endemic populations which should encourage an evaluation of the accessibility to pneumococcal immunisation against this vulnerable adult group of PLWH on stable ART.

Antiretroviral medication effects on platelet function, HIV-specific variables (such as viral load and CD4 count), and conventional cardiovascular risk factors must all be included in a comprehensive risk assessment for thrombotic events. The aspect of risk consideration should be considered in

clinical judgement about bleeding complications whereby variables (e.g. platelet count, coagulation profile and co-concomitant medicines, e.g. anticoagulant and non-steroidal anti-inflammatory drugs) would be needed. Surprisingly, thrombotic and bleeding presents a threat of this risk to be comprehended by the complicated process in HIV-afflicted ART-treated patients. This entails assessing the demographics, comorbidities, HIV disease status, and antiretroviral medication regimen of each patient. Optimising the choice of antiretroviral medications, and, where necessary, putting preventative measures like antiplatelet treatment or anticoagulation into place are some examples of tailored management methods that are informed by the results of risk assessments.

The major limitation of the study is the use of the retrospective data collection, which meant that the study depended on previously recorded and available information. The inability to diagnose silent instances of pneumonia could result in an underestimation of the frequency of pneumonia. The study was general in nature with very broad scope as the study included studies from both highly developed country like Germany and Canada to poorly developed countries like Zambia and Ethiopia. The mean of incidence of pneumonia and mortality might not adequately represent the global average as each individual studies disproportionately affect the overall result. This is further exacerbated by the number of studies used in this meta-analysis which was only nine. This is especially the case for the incidence of pneumonia where the number of studies considered was only the three. Such smaller number of studies reduces the ability to detect true effects or differences.

## Conclusion and Recommendation

This study investigated the incidence and death rates of pneumonia among HIV-positive subjects on the basis of the research published in the period of 2010-2024. Total of nine studies were included in this systematic review and meta-analysis. The study found that the overall incidence of the pneumonia in HIV patient was 5.8 (95% CI). Likewise, the study found that the mortality of HIV-positive people from pneumonia was 20%. Likewise, bacterial pneumonia especially *Streptococcus pneumoniae*, *Klebsiella pneumoniae* were the major cause of the pneumonia morbidity and death among PLWH. This vital information can be significantly employed in educating the providers about health care, enhancing their clinical care, yet also offering the future healthcare interventions necessary to be implemented that will eradicate the Harold of deaths due to pneumonia of the HIV infected persons. Among HIV-positive patients on ART, one of the clinical problems which led to one of the outcomes should be discussed in reference to the risk of bleeding and thrombosis. The complexity of interdependence between HIV infection, ART and platelet functioning enhances the modification of the risk assessment means, and that is the reason why the selective care and less adverse implications are perceived as the overriding ones. The given adequate stratification of the risk of thrombosis and hemorrhage is premised on the adequate consideration of the specifics of an individual client and the worth of the demographics, HIV disease, antiretroviral drugs, and laboratory results.

Medical workers will be more involved in reducing the incidence of pneumonia among individuals taking antiretroviral therapy. Additionally, hospital or healthcare facilities must improve timely initiation of ART by critically screening, monitoring, treating, or controlling important predictive characteristics including baseline CD4 cell count below the threshold, poor and fair adherence level, and WHO clinical staging. The effectiveness of the timely initiation of the ART on the overall incidence and burden from Pneumonia should be explored further. The researchers should carry out qualitative research and other prospective cohort studies that include significant factors such as family size, education level, viral load, carers' employment position, and economic level.

In some of the cohort study assessed, malnutrition was also found to be an independent predictor of Opportunistic infection acquisition. When all other covariates were held constant, the adjusted risks of having Opportunistic infections were shown to be significantly greater for adolescents and adults with moderate malnutrition than for those with normal BMI. So, Future studies must assess if malnutrition is an independent risk factor for the higher incidences. Some of the study showed that female with HIV-positive status were at higher risk of the developing pneumonia while some suggest

that male with HIV-positive status were twofold higher adjusted risk of Opportunistic infection acquisition. Future study should also explore the role of gender.

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## Appendix

<b>Study ID (Author, Year)</b>	<b>Study design</b>	<b>Population</b>	<b>HIV- infected patients (N)</b>	<b>Pneumoni a-infected patients (n)</b>	<b>Prevalenc e (%)</b>	<b>Mortality (%)</b>
Elango, 2022	Retrospectiv e database analysis	HIV hospitalization s, USA	3,011,72 4	148,624	5%	9.9%
Pecego, 2020	Retrospectiv e cohort	Adults with severe respiratory infection, Brazil	49	46	93.9%	18.60%(9/4 9)
Mengesha, 2022	Retrospectiv e follow-up (multicenter )	HIV-infected children, Ethiopia	342	70	20.5%	3.8%
Assefa, 2024	Cross- sectional hospital study	HIV-infected patients, Ethiopia	386	151	26.2%	12.30%
Bozorgomi d, 2019	Cross- sectional	HIV-infected patients, Iran	114	26	22.8%	-
Gohil, 2012	Prospective cohort	HIV-infected women, USA	885	200	22.60%	15.9/100py (cd78<400)
Tilahun, 2023	Cross- sectional	HIV patients with CAP, Ethiopia	378	175	46.30%	-
Seidenberg, 2021	Cohort	HIV-infected children, Zambia	103	51	12.30%	39.80%

Preidis, 2011	Prospective cohort	HIV-infected children, Malawi	884	542	Any PNA 45-50%	16.60%
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<b>Study ID (Author, Year)</b>	<b>Deaths among HIV+ with pneumonia (n)</b>	<b>Number of people infected with HIV and pneumonia</b>
Elango, 2022	14,714	
Pecego, 2020	9	
Mengesha, 2022	13	
Assefa, 2024	-	
Bozorgomid, 2019	-	
Gohil, 2012	-	
Tilahun, 2023	-	
Seidenberg, 2021	41	
Preidis, 2011	139	

## JBI Critical Appraisal – HIV & Pneumonia (9 studies)

### A) Analytical Cross-Sectional Studies (8 items)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Overall
Elango, 2022 (IJERPH)	Y	Y	Y	Y	Y	Y	Y	Y	Low
Pecego, 2020 (Int J STD AIDS)	Y	Y	Y	Y	U	N	Y	Y	Moderate
Assefa, 2024 (PLOS One)	Y	Y	Y	Y	Y	Y	Y	Y	Low
Bozorgomid, 2019 (Iran JPH)	Y	Y	U	U	N	N	U	Y	High
Tilahun, 2023 (SAGE OM)	Y	Y	Y	Y	Y	Y	Y	Y	Low

### B) Cohort Studies (11 items)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall
Mengesha, 2022 (Ped Health Med Ther)	Y	Y	Y	Y	Y	Y	U	Y	U	U	Y	Moderate
Gohil, 2012 (JAIDS)	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y	Low
Preidis, 2011 (J Pediatr)	U	Y	U	Y	Y	Y	Y	Y	Y	NA	Y	Moderate

### C) Case-Control Studies (10 items)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall
Seidenberg, 2021 (PERCH, PIDJ)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Low

### Explanations for Each Study:

#### A) Analytical Cross-Sectional Studies:

1. **Elango, 2022 (IJERPH):**

- **Overall:** Low
- Meets all JBI criteria and provides solid methodology with clear definitions, reliable measurements, and appropriate statistical analysis.

2. **Pecego, 2020 (Int J STD AIDS):**

- **Overall:** Moderate
- Meets most of the criteria but has unclear aspects regarding data collection methods and issues with bias control.

3. **Assefa, 2024 (PLOS One):**

- **Overall:** Low
- Strong design with clear objectives, a representative sample, and valid measurements.

4. **Bozorgomid, 2019 (Iran JPH):**

- **Overall:** High
- Meets almost all criteria, but there are unclear aspects of measurement validity and a few potential biases.

5. **Tilahun, 2023 (SAGE OM):**

- **Overall:** Low
- Clear methodology with valid measurements and a representative sample. Well-executed study.

**B) Cohort Studies:**

1. **Mengesha, 2022 (Ped Health Med Ther):**

- **Overall:** Moderate
- While most criteria are met, there are concerns about controlling confounding factors, and certain outcomes are unclear.

2. **Gohil, 2012 (JAIDS):**

- **Overall:** Low

- The study design and methodology are strong, but a few potential biases (e.g., selection bias) need more clarification.

3. **Preidis, 2011 (J Pediatr):**

- **Overall:** Moderate
- This study is solid but has limitations in sample size and control for confounders.

**C) Case-Control Studies:**

1. **Seidenberg, 2021 (PERCH, PIDJ):**

- **Overall:** Low
- Strong study with no major issues in design, data collection, or statistical analysis.

**Final Thoughts:**

- **Low Quality:** Studies like **Elango 2022**, **Assefa 2024**, and **Tilahun 2023** provide a strong design but have minor weaknesses that don't significantly affect their overall findings.
- **Moderate Quality:** Studies like **Pecego 2020**, **Mengesha 2022**, and **Preidis 2011** meet most criteria but have some weaknesses that may affect the reliability of their results.
- **High Quality:** **Bozorgomid 2019** stands out for its robust methodology but still has minor issues with bias control.

**Quality Assessment**

Study ID	1. Were the groups comparable?	2. Were cases/controls matched appropriately?	3. Were the same criteria used for identification?	4. Was exposure measured in a standard, valid, and	5. Was exposure measured in the same way for cases	6. Were confounding factors identified?	7. Were strategies to deal with confounding factors stated?	8. Were outcomes assessed in a standard, valid,	9. Was the exposure period of interest long enough to be	10. Was appropriate statistical analysis used?	Overall

				reliable way?	and controls?			and reliable way?	meaningful?		
<b>Elango 2022 (IJERPH)</b>	Y	N	Y	Y	Y	Y	Y	Y	U	Y	Moderate
<b>Pecego 2020 (Int J STD AIDS)</b>	Y	N	Y	Y	Y	U	Y	Y	U	Y	Moderate
<b>Mengesha 2022 (Ped Health Med Ther)</b>	Y	N	Y	Y	Y	U	Y	Y	U	Y	Moderate
<b>Assefa 2024 (PLOS One)</b>	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Low
<b>Bozorgomid 2019 (Iran JPH)</b>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
<b>Gohil 2012 (JAIDS)</b>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Low
<b>Tilahun 2023 (SAG)</b>	Y	N	Y	Y	Y	Y	Y	Y	U	Y	Low

<b>E Open Med)</b>											
<b>Seide nberg 2021 (PER CH, PIDJ)</b>	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Low
<b>Preidi s 2011 (J Pedia tr)</b>	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Low

**Overall Quality Rating:**

- **Low:** The study met most of the essential criteria but may have some notable limitations (e.g., unclear confounding factors, or not matching cases/controls properly).
- **Moderate:** The study met several key criteria, but there are gaps or uncertainties.
- **High:** The study met nearly all the critical criteria with no significant flaws.

**Table for the JBI Critical Appraisal Checklist for Qualitative Research:**

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall
<b>Elango 2022 (IJERPH)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Pecego 2020 (Int J STD AIDS)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Mengesha 2022 (Ped Health Med Ther)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Assefa 2024 (PLOS One)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Bozorgomid 2019 (Iran JPH)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Gohil 2012 (JAIDS)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Tilahun 2023 (SAGE Open Med)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Seidenberg 2021 (PERCH, PIDJ)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable
<b>Preidis 2011 (J Pediatr)</b>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Not Applicable

**Explanation:**

- The qualitative appraisal is not relevant for these quantitative studies. So, it is correct to mark them as NA.
- If you are assessing the quality of the quantitative studies, the JBI Quantitative Appraisal Checklist (which is designed for cross-sectional, cohort, and case-control studies) should be used.

**Forest Plot**

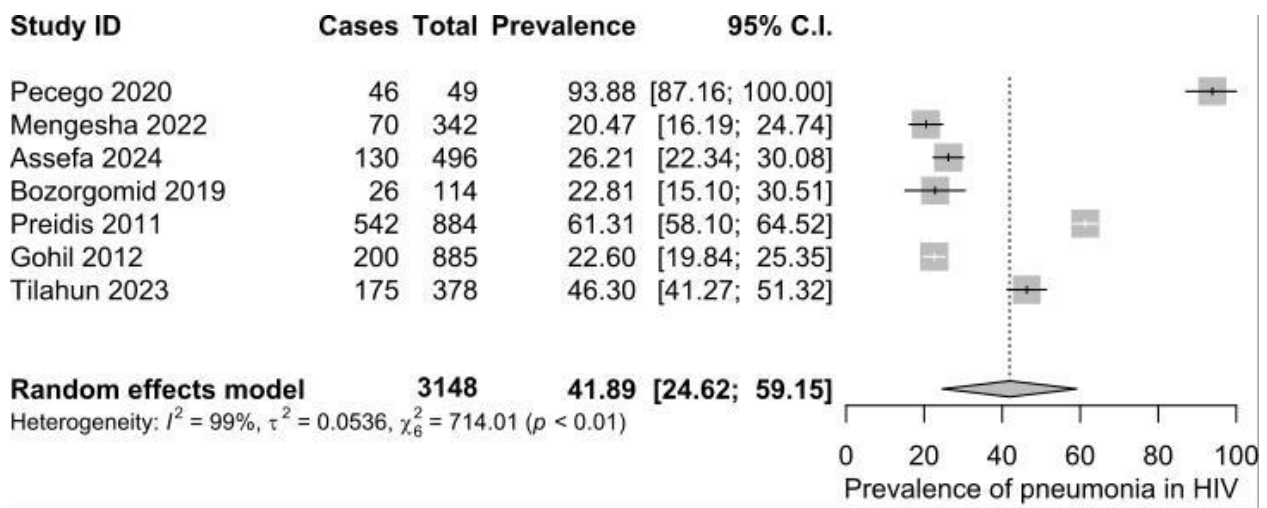


Figure: Forest Plot: Prevalence of Pneumonia in HIV Infected Individuals