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**Ethiopian Public Health Institute (EPHI),**

**Addis Ababa, Ethiopia**

**Research proposal on**

**Influenza Disease Burden Estimation in Ethiopia**

**Project no.\_\_\_\_\_\_\_\_\_\_\_** (To be given by SPHMMC-IRB)

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| **Influenza Burden of Disease Estimation in Ethiopia** | | | | | |
| Person(s) undertaking the project in order of contribution | | | | | |
| Name | Qualification (Area of study & Degree) | Institution/Company | Country | Role | Responsibility |
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| Contact address of the PI: Tel. Address:  Email: | | | | | |
| Study Period: | Date of commencement: | | Date of completion: | | |
| The institution at which the study is to be conducted and the address | | | | | |

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# Summary

# 1. Introduction

## 1.1 Background

Influenza is a viral infection that poses a significant public health challenge globally, with varying impacts across regions, including Africa and sub-Saharan Africa[[1]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5). Beyond its health effects, influenza disrupts economies, strains social systems, and influences political decision-making[[2]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-4827-0). The disease is characterized by seasonal outbreaks and pandemic potential, leading to substantial morbidity, mortality, and wider societal consequences[[3]](https://ms.academicjournals.org/manuscript/manuscripts1712914099AJHST11.04.240029OriginalSubmission.doc.doc.pdf). Understanding its burden is crucial for developing effective public health strategies and mitigating its multidimensional impacts[[4]](https://www.who.int/teams/global-influenza-programme).

Often, the majority of the population thinks of the flu as just a seasonal nuisance—a few days of fever, cough, and fatigue before life goes back to normal[[5]](https://www.who.int/news-room/spotlight/influenza-are-we-ready). However, influenza is far more than that; it is a harsh virus that takes lives, overwhelms health systems, and leaves lasting scars on economies and communities[[6]](https://www.greenfacts.org/en/global-public-health-threats/l-2/5-influenza-pandemic.htm). In places like sub-Saharan Africa and Ethiopia, where healthcare resources are stretched thin, the flu is not just a personal health issue; it is a crisis that affects everyone, from parents missing work to care for sick children to governments scrambling to contain outbreaks with limited tools[[7]](https://www.nber.org/digest/may20/social-and-economic-impacts-1918-influenza-epidemic).

Globally, influenza affects approximately 1 billion people annually, causing 3–5 million hospitalized severe illnesses and 290,000–650,000 respiratory deaths[[8]](https://www.stlouisfed.org/~/media/files/pdfs/community-development/research-reports/pandemic_flu_report.pdf). The economic toll includes lost productivity, billions in wages and GDP, healthcare costs, and strain on healthcare systems[[9]](https://www.icpsr.umich.edu/web/ICPSR/studies/22680). Socially, outbreaks overwhelm hospitals, disrupt education, and increase inequalities, with vulnerable groups like children, the elderly, and the immunocompromised facing higher risks. Politically, influenza shapes global health policies, as seen with WHO’s emphasis on vaccination and surveillance. Pandemics, like H1N1 (2009), trigger international cooperation but also expose disparities in resource allocation.

In Africa, influenza’s burden is worsened by weak healthcare infrastructure[[4]](https://www.who.int/teams/global-influenza-programme), competing diseases (e.g., HIV/AIDS, TB), and climate-linked transmission peaks (e.g., rainy seasons)[[1]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5). Economically, outbreaks reduce workforce productivity, disproportionately affecting informal sectors[[7]](https://www.nber.org/digest/may20/social-and-economic-impacts-1918-influenza-epidemic). Socially, limited healthcare access exacerbates mortality, while misinformation hampers prevention efforts. Politically, fragmented surveillance and vaccine inequity highlight Africa’s marginalization in global health governance [[13]](https://www.nber.org/digest/may20/social-and-economic-impacts-1918-influenza-epidemic). Despite these challenges, regional networks like Africa CDC are advancing preparedness [[14]](https://www.nber.org/digest/may20/social-and-economic-impacts-1918-influenza-epidemic).

Sub-Saharan Africa’s influenza response is uneven (11). Countries like South Africa and Kenya have surveillance systems, but others lack infrastructure, obscuring the true burden. Economically, frequent outbreaks drain scarce health resources, diverting funds from other priorities[[9]](https://www.icpsr.umich.edu/web/ICPSR/studies/22680). Socially, high disease prevalence erodes trust in health systems, particularly in rural areas. Politically, the 2009 H1N1 pandemic exposed gaps in preparedness [[10]](https://www.icpsr.umich.edu/web/ICPSR/studies/22680), spurring calls for localized vaccine production and equity in pandemic responses.

## 1.2. Influenza Surveillance and Burden in Ethiopia

Influenza surveillance in Ethiopia has made significant strides [[16]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5) since the establishment of the sentinel surveillance system in 2008[[15]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5). Starting in Addis Ababa, the system has expanded to cover diverse geographical regions across the country. Currently, influenza-like illness (ILI) and severe acute respiratory infection (SARI) surveillance are implemented in 12 of Ethiopia's subnational levels, encompassing 21 ILI/SARI surveillance sites[[17]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-4827-0). Supporting this effort are four sub-national respiratory virus testing laboratories, 12 regional health bureaus, and the National Influenza Center (NIC), which work in concert to monitor and respond to influenza activity across the nation[[15]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5).

Despite these advancements, Ethiopia faces a severe influenza burden due to its limited healthcare capacity and a high prevalence of comorbid diseases[[18]](https://ms.academicjournals.org/manuscript/manuscripts1712914099AJHST11.04.240029OriginalSubmission.doc.doc.pdf). Outbreaks place immense strain on the country’s underfunded healthcare system, disproportionately affecting rural populations. Social factors, such as communal living practices, may aggravate disease transmission[[22]](https://ms.academicjournals.org/manuscript/manuscripts1712914099AJHST11.04.240029OriginalSubmission.doc.doc.pdf), while vaccine hesitancy presents an ongoing challenge. Politically, Ethiopia's reliance on donor-funded surveillance programs highlights the pressing need for sustainable investment in influenza prevention and control[[15]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5). However, recent improvements in public health infrastructure provide a foundation for progress. Prioritizing influenza in Ethiopia’s national health agenda will be essential to mitigating the disease’s impact and building long-term resilience[[18]](https://ms.academicjournals.org/manuscript/manuscripts1712914099AJHST11.04.240029OriginalSubmission.doc.doc.pdf).

## 1.3. Rationale of the study

Respiratory infections remain a critical public health problem in Ethiopia, disproportionately affecting children under five years old. Despite influenza causing a significant public health problem in the country, evidence gaps persist for influenza-specific burden, particularly regarding age-stratified hospitalization rates, community-level disease transmission, and severity stratification needed for vaccine policy formulation. Influenza-specific contributions of respiratory infections remain unquantified, where age-stratified hospitalization rates for influenza-associated respiratory infections are lacking at national and sub-national levels. Due to the scarcity of evidence, current vaccination programs face implementation barriers due to insufficient burden data. Estimating the burden of influenza disease is important for designing evidence-based potential intervention mechanisms to prevent the emergence of seasonal influenza outbreaks.

## 1.4. Significance of the Study

In Ethiopia, comprehending the burden of influenza is essential for formulating evidence-based policies, allocating resources efficiently, and devising effective prevention and control strategies[17]. Informed decision-making is the cornerstone of successful public health interventions. By thoroughly studying the burden of influenza, health officials can collect vital data that helps in prioritizing control measures. Unfortunately, the absence of comprehensive national data poses a significant challenge to the development of targeted strategies. Nevertheless, small-scale studies have revealed that influenza is responsible for a substantial proportion of acute respiratory infections[[15]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-4827-0).

1. **Understanding the Severity of Influenza**: It is essential for evaluating its impact on various population groups, particularly vulnerable populations such as children, the elderly, and those with underlying health conditions. Studies indicate that children under five account for a large proportion of influenza-associated hospitalizations, and mortality rates are higher in low-resource settings[[15]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-018-3365-5). Recognizing these patterns can help policymakers develop targeted interventions.
2. **Public Health Planning & Policy Formulation**: By studying the burden of influenza, health officials can gather critical data that enables them to prioritize influenza control measures. Data from global estimates suggest that influenza leads to 3 to 5 million cases of severe illness annually, with 290,000 to 650,000 deaths worldwide[[19]](https://ms.academicjournals.org/manuscript/manuscripts1712914099AJHST11.04.240029OriginalSubmission.doc.doc.pdf). In Ethiopia, the lack of comprehensive national data hinders the development of targeted strategies. However, small-scale studies have indicated that influenza accounts for a significant percentage of acute respiratory infections[[15, 17]](https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-4827-0).
3. **Improved Disease Surveillance & Diagnosis**: Influenza is often misdiagnosed as malaria or pneumonia in Ethiopia, leading to under reporting. Limited laboratory capacity means many influenza-like illnesses go undetected. Strengthening surveillance efforts can improve diagnostic accuracy. Countries with robust surveillance systems can detect and contain outbreaks more effectively[17].
4. **Vaccination & Prevention Strategies**: Ethiopia currently lacks seasonal influenza vaccines. Studying the burden of influenza provides essential evidence to advocate for introducing these vaccines, ensuring better protection for the population [20]. Countries with annual vaccination programs have significantly reduced influenza-related hospitalizations and deaths. Monitoring circulating viruses helps in selecting appropriate strains for vaccines[21]. Global data indicate that mismatched vaccines can reduce effectiveness by 50%, highlighting the importance of continuous monitoring[22].
5. **Global Health Alignment & Reporting**: Studying the burden of influenza supports Ethiopia’s adherence to WHO Global influenza surveillance requirements[23]. Compliance ensures that the country remains aligned with international health standards and practices. Ethiopia’s data on influenza contributes valuable information to global burden estimates and vaccine recommendations. This participation enhances the global understanding of influenza dynamics. Strengthening cooperation for outbreak response across borders is essential in a globally interconnected world. A thorough understanding of the influenza burden facilitates better collaboration with neighboring countries in managing outbreaks [24].
6. **Pandemic Preparedness & Response**: Creating a foundation for detecting unusual influenza activity is vital for early warning systems. This baseline data enables health authorities to identify potential pandemics promptly [25]. Improving the capacity of health systems to respond to respiratory disease outbreaks is crucial for effective pandemic management[26]. Preparedness ensures that health systems are equipped to handle increased patient loads during outbreaks [27].

## 1.5. Research questions

1. What are the age-stratified mean annual rates of hospitalized influenza-associated Severe Acute Respiratory Infection (SARI) at national and sub-national levels in Ethiopia?
2. What are the age-stratified mean annual rates of non-hospitalized influenza-associated SARI at national and sub-national levels in Ethiopia?
3. What are the annual rates of influenza-associated illness for different clinical severities (mild, moderate, severe) at national and sub-national levels in Ethiopia?
4. What are the seasonal variations in influenza-associated SARI rates across different regions of Ethiopia?
5. How many influenza cases could be averted by implementing an influenza vaccination program in Ethiopia?

## 1..6. Study objectives

**1.6.1.  General objective**

The main objective of this study is to estimate the influenza disease burden at national and sub-national levels.

**1.6.2. Specific objectives**

* To estimate age-stratified mean annual rates of hospitalized influenza-associated SARI at national and sub-national levels in Ethiopia
* To generate model-based estimates for rates of non-hospitalized influenza-associated SARI
* To estimate and project annual rates of influenza-associated illness for different clinical severity (mild, moderate, severe) at national and sub-national levels.
* To estimate influenza burden averted using a hypothetical vaccine model.

# **2. Literature Review**

This literature review provides a comprehensive overview of the burden of influenza, focusing on low- and middle-income countries (LMICs) and Ethiopia. It explores the global impact of influenza, risk factors for severe outcomes, estimation models, and the impact of vaccination programs. Understanding the burden of influenza is crucial for developing effective public health strategies and policies. This review will inform the development of a national proposal for estimating the influenza burden in Ethiopia [28].

**2.1. Global Burden of Influenza:** Several recent studies highlight the significant impact of influenza globally. For instance, the 2017-2018 influenza season in the United States was marked by high severity, with 49 million flu illnesses, 960,000 hospitalizations, and 79,000 deaths [29]. This season underscored the importance of annual vaccination, which prevented an estimated 7 million illnesses, 109,000 hospitalizations, and 8,000 deaths [29].

A systematic literature review from 2012 to 2022 characterized the global burden of influenza in adults aged 18-64 years. It found that influenza infection in this age group can be disruptive, causing prolonged absence from the workplace, reduced productivity, and increased healthcare utilization. The review reported high levels of hospitalization and outpatient visits, particularly among adults with underlying comorbidities [30].

Globally, seasonal influenza infects as many as 1 billion people annually, making it one of the most common infectious respiratory viruses. The WHO Global Influenza Surveillance and Response System (GISRS) monitors circulating viruses and recommends which viruses to target in the flu vaccine for the upcoming season. This system plays a crucial role in preventing infection and reducing symptoms among high-risk groups [31].

In addition to seasonal influenza, pandemic influenza poses a significant threat. Historical data shows that past influenza pandemics, such as the 1918 Great Flu Pandemic, caused millions of deaths worldwide. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic highlighted the potential for influenza viruses to cause future pandemics [32].

A study published in 2023 emphasized the clinical burden of influenza on patients and healthcare systems. It reported that adults aged 18-64 years with underlying comorbidities were at higher risk of influenza-related hospitalizations, ICU admission, and mortality. The study also highlighted the need for greater investigation into indirect costs and prolonged absenteeism associated with influenza infection [30].

**2.2. Impact on Vulnerable Populations:** Influenza disproportionately affects vulnerable populations in LMICs, including children under five years, the elderly, pregnant women, and individuals with underlying health conditions. Studies in Kenya, Bangladesh, South Africa, Nigeria, and Uganda have highlighted the significant burden of influenza on public health, particularly among these groups [33-39].

For example, a study in Kenya from 2015 to 2020 found that the incidence of influenza-associated Severe Acute Respiratory Infection (SARI) was highest among children under five years, the elderly, and adults over 65 years [34]. Similarly, research in Bangladesh emphasized the significant burden of influenza among pregnant women, individuals with underlying health conditions, and young children, highlighting the need for targeted vaccination programs [36].

A study conducted in South Africa between 2016 and 2021 reported that influenza-associated SARI accounted for a considerable proportion of hospitalizations during the influenza season, with the highest rates observed in children under five years and individuals with underlying health conditions. These findings underscore the importance of continuous surveillance and vaccination efforts in LMICs to mitigate the impact of influenza [35].

Recent studies have continued to highlight the burden of influenza in LMICs. A 2022 study in Nigeria found that influenza-associated SARI remained a significant cause of hospitalization, particularly among children and the elderly [38]. Another study in Uganda in 2023 reported similar findings, with high rates of influenza-associated hospitalizations among young children and individuals with comorbidities [39].

A systematic review published in 2024 examined the burden of influenza among pregnant women in LMICs. The review found that pregnant women are at higher risk of severe influenza outcomes, including hospitalization and death, compared to non-pregnant women. The study emphasized the need for targeted vaccination programs to protect this vulnerable group [40].

**2.3. Risk Factors for Severe Influenza Outcomes:** High-risk groups for severe influenza outcomes include older adults, young children, pregnant women, individuals with chronic diseases, and those living in residential care settings. Risk factors for severe influenza outcomes can vary by region and socioeconomic status. For instance, individuals in urban areas may have better access to healthcare and diagnostic services compared to those in rural areas [41].

Recent studies have identified several risk factors associated with severe influenza outcomes. A multi-season cohort study from 2015 to 2020 found that adults with multiple high-risk conditions had significantly higher odds of severe outcomes, such as hospitalization and death [42]. Another study emphasized the importance of specific high-risk medical conditions, certain racial and ethnic backgrounds, pregnancy, and living in residential care settings as significant risk factors for severe influenza outcomes [43].

A study published in 2023 investigated the impact of socioeconomic status on influenza outcomes in LMICs. It found that individuals from lower socioeconomic backgrounds had higher rates of severe influenza outcomes, including hospitalization and death. The study highlighted the need for targeted interventions to address these disparities [44].

**2.4. Burden of Influenza in Ethiopia:** Historical data on the burden in Ethiopia shows that seasonal influenza A (H3N2), influenza A (H1N1)pdm2009, and influenza B viruses have been circulating in the country. The burden of influenza-associated SARI has been documented through various studies. A study conducted from 2009 to 2015 using sentinel surveillance data revealed that the positivity rate was highest among individuals aged 5-14 years, followed by those aged 15-44 years [15].

A comprehensive study conducted in Ethiopia from January 2021 to August 2022 aimed to estimate the proportion of confirmed influenza cases among patients presenting with SARI and influenza-like illness (ILI). Among the 6,193 patients included in the study, 11.1% tested positive for influenza. Higher influenza positivity was detected among ILI cases (26.4%) compared to SARI cases (3.8%). Peaks in influenza positivity occurred during February and December, indicating distinct seasonal patterns [18].

A study published in 2020 examined the burden and seasonality of medically attended influenza-like illness (ILI) in Ethiopia from 2012 to 2017. It found that the incidence of ILI was highest in the age groups of 15-44 years and 5-14 years. The seasonality of influenza in Ethiopia showed two peak seasons: October-December and April-June. These findings highlight the need for improved surveillance and vaccination strategies to reduce the burden of influenza in Ethiopia [17].

A study published in 2024 investigated the epidemiology of circulating influenza viruses in Ethiopia during the COVID-19 pandemic. It found that the pandemic had a significant impact on influenza surveillance and the circulation of influenza viruses. The study emphasized the need for strengthening influenza surveillance systems to better understand the burden of influenza in the context of concurrent pandemics [18].

**2.5. Estimation Models for Influenza Burden:** Various estimation models are used to estimate the burden of influenza, including mechanistic models, time-series models, and data integration models. These models are applied in different settings to predict influenza epidemics, inform public health responses, and support evidence-based policy decisions. Recent advancements in estimation models have improved the accuracy and precision of influenza burden estimates. For example, a 2024 study developed a mechanistic model that integrates historical data into influenza forecasting, showing increased accuracy for short-term forecasts and peak timing. This model uses historical surveillance data to predict future influenza activity, allowing for better preparedness and response planning [45].

Another study explored the use of state-of-the-art approaches from epidemiology and evidence synthesis to estimate the disease burden of seasonal influenza. The study developed time-series models for attributing counts of adverse respiratory health outcomes to influenza and data integration models for combining information across multiple sites. These models provide robust estimates of influenza-associated morbidity and mortality, supporting evidence-based policy decisions and resource allocation [46].

A study published in 2025 used the incidence-based disability-adjusted life years (DALYs) approach to measure the disease burden of seasonal influenza in Germany from 2015 to 2020. The study found that the highest burden estimates were observable for infants, children under the age of five, and the elderly. The main contributors to the disease burden were sequelae, primarily pneumonia, encephalitis, and myocarditis. This approach offers valuable insights into the impact of influenza on population health and highlights the importance of vaccination programs for vulnerable populations [47].

In the United States, a new calculation method was developed to estimate hospitalizations for influenza by state, age, and month using hospital-based surveillance data. This method aims to improve flu burden estimation and provide more accurate data for public health planning and resource allocation [48]. The European Centre for Disease Prevention and Control (ECDC) introduced the Burden of Communicable Diseases in Europe (BCoDE) project, which quantifies the disease burden of infectious diseases, including influenza, in disability-adjusted life years (DALYs) [49]. The BCoDE toolkit calculates country-specific DALYs and provides valuable data for evaluating the impact of influenza and other communicable diseases [50].

In Ethiopia, estimation models have been used to assess the burden of influenza-associated severe acute respiratory infection (SARI). A study conducted from 2009 to 2015 using sentinel surveillance data revealed that the positivity rate was highest among individuals aged 5-14 years, followed by those aged 15-44 years [15]. Another study conducted from January 2021 to August 2022 aimed to estimate the proportion of confirmed influenza cases among patients presenting with SARI and influenza-like illness (ILI). These studies highlight the importance of using estimation models to understand the burden of influenza and inform public health strategies in Ethiopia [18].

Overall, these estimation models play a crucial role in understanding the burden of influenza, guiding public health interventions, and informing policy decisions. By improving the accuracy and precision of burden estimates, these models help allocate resources effectively and develop targeted strategies to mitigate the impact of influenza.

**2.6. Mean Annual Rates of Hospitalized and Non-Hospitalized Influenza-Associated SARI** The mean annual rates of hospitalized and non-hospitalized influenza-associated Severe Acute Respiratory Infection (SARI) vary across different regions and age groups. In Ethiopia, the incidence of influenza-associated SARI was found to be higher in urban areas compared to rural areas, likely due to better access to healthcare facilities and diagnostic services in urban settings. Age-stratified data indicated that children under five years and adults over 65 years were at higher risk of hospitalization due to influenza [15].

A study conducted from 2012 to 2017 in Ethiopia found that the incidence rate of influenza-like illness (ILI) was higher in the age groups of 15-44 years and 5-14 years, with mean annual rates of 254.6 per 100,000 population and 49.5 per 100,000 population, respectively. The seasonality of influenza showed two peak seasons: October-December and April-June [17].

In Kenya, the mean annual rate of hospitalized influenza-associated SARI among all ages was 21 per 100,000 persons, while rates of non-hospitalized influenza-associated SARI were approximately four times higher at 82 per 100,000 persons. A systematic review of literature on influenza-associated disease burden in Kenya highlighted that hospitalizations with influenza in children under five years were 2-3 times higher than reported in the United States. The review emphasized the substantial burden in children under five years of age and the potential value of an influenza vaccination program targeting this age group [33].

In Egypt, the mean annual rate of hospitalized influenza-associated SARI was highest among individuals aged over 65 years and children under five years (51). A study conducted at a sentinel site in Egypt from 2013 to 2015 found that 21.04% of SARI patients tested positive for influenza, with 48.7% of cases involving influenza A viruses and 25% involving influenza B. The predominant age group was under five years of age, accounting for 443 cases. Another study in Egypt during the 2022-2023 winter season detected a resurgence of influenza and respiratory syncytial virus (RSV), with influenza causing a higher rate of infection than RSV [52].

These studies highlight the importance of understanding the mean annual rates of hospitalized and non-hospitalized influenza-associated SARI across different regions and age groups. Such data is crucial for developing targeted vaccination programs and improving surveillance systems to mitigate the impact of influenza [53].

**2.7. Hypothetical Vaccine Models in LMICs (2022-2025):** Influenza vaccination remains the most effective measure to prevent influenza and reduce its burden. Studies have shown that influenza vaccination can significantly reduce the incidence of influenza-related illnesses, hospitalizations, and deaths. In low- and middle-income countries (LMICs), including Ethiopia, the introduction of influenza vaccination programs has been associated with a decrease in the burden of influenza-associated SARI. However, challenges such as vaccine availability, coverage, and public awareness need to be addressed to maximize the benefits of vaccination programs [54].

Hypothetical models have been used to estimate the impact of vaccination programs in LMICs. These models suggest substantial public health benefits through vaccination, particularly in reducing the burden of influenza-associated SARI (55).

A comprehensive study conducted in 2023 highlighted the unique challenges and needs associated with influenza immunization programs in LMICs. The research emphasized the necessity for better estimates of vaccine impact on public health outcomes, the development of more affordable vaccines, and the enhancement of immunization delivery infrastructures. These findings underscore the importance of tailored strategies to improve vaccine uptake and effectiveness in these regions [56].

The Centers for Disease Control and Prevention (CDC) provided valuable insights into the potential impact of influenza vaccination during the 2023-2024 flu season. The CDC estimated that flu vaccination prevented approximately 9.8 million flu-related illnesses, 4.8 million medical visits, 120,000 hospitalizations, and 7,900 deaths. Although this data pertains to the United States, similar modeling approaches can be adapted to LMICs to estimate the burden averted by influenza vaccines. This highlights the potential for significant public health benefits through vaccination programs [57].

A pivotal study utilized mathematical models to estimate the impact of influenza vaccines on healthcare burden in LMICs. The model incorporated vaccine-derived protection against both infection and severe disease, suggesting substantial indirect protection, particularly from young adults to other age groups. This modeling approach provides a robust framework for understanding the broader implications of vaccination programs and supports the development of targeted immunization strategies [58]. A study conducted in Chile, Guyana, and Paraguay estimated vaccine-averted influenza illnesses among young children and older adults. The research applied a static compartmental model to estimate differences in influenza-associated respiratory disease events in the presence and absence of vaccination programs [59].

Another study modeled the public health impact of cell-based influenza vaccines compared to egg-based vaccines among people aged 0-64 years in the United States, demonstrating that cell-based vaccines could prevent additional symptomatic illnesses, outpatient visits, hospitalizations, ICU admissions, and deaths [60].

Additionally, a clinical trial study by CDC showed that cell-based vaccines provide greater protection against flu-related hospitalizations among Medicare beneficiaries aged 65 years and older during the 2017–2018 influenza season. However, similar benefits were not observed in subsequent seasons (2018–2019 and 2019–2020) [61].

# 3. Materials and Methods

## 3.1. Study Setting

Ethiopia is situated in the northeastern region of Africa, specifically in the Horn of Africa. It borders Eritrea to the north, Djibouti and Somalia to the east, Kenya to the south, Sudan to the west, and South Sudan to the southwest. Ethiopia is administratively divided into twelve regions (Afar, Amhara, Benishangul Gumuz, Gambella, Harari, Oromia, Sidama, Central Ethiopia, Somali, South West Ethiopia, and Tigray) and two city administrations (Addis Ababa and Dire Dawa city administrations). Ethiopia is the second most populous country in Africa, with a total population of around 109.5 million in 2024, with a near gender balance of 54,874,000 (50.1%) males and 54,625,000(49.9%) females. The country was predominantly rural, with 83,612,000(76.4%) residents living in rural areas, compared to 25,887,000 in urban centers (about 23.6%) (62).

Ethiopia’s health system is organized into a three-tiered structure that includes primary, secondary, and tertiary levels of healthcare. By the end of the 2024 Ethiopian Fiscal Year, Ethiopia's public health system included 15,357 health posts, 3,903 health centers, and 404 hospitals. These hospitals were categorized as 270 primary, 106 general, and 28 comprehensive specialized facilities. Over 328,951 health professionals were working within this public sector to provide healthcare services (63).

SARI sentinel surveillance was being implemented in Ethiopia in 17 selected hospitals located in the following regions and city administrations: Somali Region (Gode Hospital), Tigray Region (Mekele Hospital), Addis Ababa City Administration (Yekatit 12 Hospital Medical College, Zewditu Memorial Hospital, and St. Peter Specialized Hospital), Gambela Region (Gambela General Hospital), Afar Region (Dubti General Hospital), Oromia Region (Shenan Gibe Hospital and Adama Hospital Medical College), Amhara Region (Lalibela Hospital and Felege Hiwot Comprehensive Specialized Hospital), Benishangul-Gumuz Region (Asosa General Hospital), Sidama Region (Adare General Hospital), Southern Nations, Nationalities, and Peoples' Region (Arba Minch General Hospital), Dire Dawa City Administration (Dil Chora Hospital), Central Ethiopia Region (Butajira General Hospital), and Southwest Ethiopia Peoples' Region (Jinka General Hospital).Considering data completeness and geographical location of the Hospitals Felege Hiwot Hospital, Dilechora hospital, Adama hospital, Shenan Gibe hospital, and Adare Hospital were selected from Amhara, Dire dawa city administration, Oromia region and Sidama regions respectively for the base line assessment of this study.

## 3.2. Study design and period

To assess the influenza disease burden in Ethiopia, a retrospective facility-based cross-sectional study will be conducted using Severe Acute Respiratory Illness (SARI) sentinel surveillance data from 2023 to 2024. The study period was selected based on data completeness and to minimize potential confounding effects from the COVID-19 pandemic. Data collection is planned from May to September 2025

## 3.3 Data and data collection methods

**3.3.1 Data elements and source of Data**

Data will be collected in each of the selected sites for baseline assessment. This will be extracted through chart reviews from selected sentinel site health facilities (HFs). Meanwhile, information on community-level risk factors and health-seeking behavior will be gathered through a literature review. The key data elements are summarized in Table 1.

Table 1: Summary of data element sources

|  |  |  |
| --- | --- | --- |
| Data elements | Source | Strata |
| Number of total SARI/Respiratory admissions at sentinel sites | HMIS/Log book/Hospital Records | Age group |
| Number of  total respiratory admissions  in the catchment area of the sentinel site | HMIS/Log book/Hospital Records | Age group |
| Number of total influenza tested cases | Influenza sentinel surveillance | Age group |
| Number of total influenza positive cases | Influenza sentinel surveillance | Age group |
| Type of influenza virus (A/H1N1/H3N2, B) for positive cases | Influenza sentinel surveillance | Age group |
| Mid-year population estimates of the sentinel site catchment area | National census projections | Age group |
| Mid-year population estimates by region | National census projections | Age group |
| Prevalence of risk factors for respiratory infection by region: child malnutrition, low birth weight, non-exclusive breastfeeding, crowding, household air pollution exposure, and underlying medical conditions | Demographic Health Surveys  Published literature, Woreda profile | No |
| Proportion of healthcare seeking for respiratory illness by region | Demographic Health Surveys  Published literature, Woreda profile | Yes |

**3.3.3. Data Collection Tools and Procedures**

A standardized data extraction tool is designed specifically for this study to ensure consistency and completeness in the data collection (Annex 1). The tool is well structured to facilitate systematic extraction of relevant data from sentinel site health facility records. This tool is developed based on WHO guidelines for estimating seasonal influenza disease burden  [WHO, 2015], existing national influenza surveillance protocols, and inputs from key stakeholders and subject matter experts. The tool will be converted to Open Data Kit (ODK) format for efficient and accurate data entry. The ODK-based system will allow real-time data collection, validation, and transmission to a central database.

Data will be collected from selected sentinel surveillance sites where influenza-related admissions and cases are systematically recorded. Data collectors will be trained on data extraction protocols to ensure uniformity. During the data collection, trained data collectors will extract relevant data from health facility records using the prepared tool. Data on influenza positivity will be also collected (Annex 2). Information on community risk factors and health-seeking behavior will be collected through a literature review of relevant studies and reports (Annex 3). This literature may include the EDHS report, the Wereda profile report, published study findings, and so on.

## 3.4 Data management and quality assurance

Data collectors will follow apredefined protocol to ensure uniformity across sentinel sites. Training will be given for both data collectors and supervisors on data extraction and ODK usage. The central data management team will review and verify data on an ongoing basis. Periodic random checks and re-extraction of a sample dataset will be performed to cross-check the accuracy of extracted data.

A robust data management system will be implemented to ensure efficient handling, storage, and security of the collected data. To ensure data validation, the dataset will undergo automatic validation checks in the ODK system to monitor missing values, inconsistencies, and outliers. Incomplete or erroneous records will be flagged and resolved in coordination with data collectors, supervisors, and central data management teams. Regular feedback sessions with data collectors, supervisors, and the central data management team will be held to address inconsistencies.

## 3.5 Proposed Estimation Technique

**3.5.1 Base sentinel site respiratory rate estimation**

We will estimate the rate of respiratory hospitalization at selected SARI sentinel sites/base sites/ using the WHO manual for estimating the burden of seasonal influenza [WHO, 2015]. The number of respiratory admissions at selected sentinel sites will be collected from HMIS, logbook, and hospital records. The respiratory hospitalization rate at the sentinel site will be calculated for the catchment population.

*RespHospRatess* = \*100 000

Data on respiratory hospitalization in the catchment population will be extracted from HMIS, considering respiratory infection admissions both in the public and private health facilities in the catchment. We will identify the catchment population for the selected SARI sentinel site.

*Catchment population* = \* Catchment population size

Note: the SARI cases in the SS who came from outside of the SS catchment will be excluded through chart review.

The non-hospitalized respiratory rate will be estimated using the proportions of the health care-seeking behavior for respiratory infection.

Subsequently, the total respiratory rates in the sentinel site’s catchment area will be the sum of the two rates (that is, RespRatess **=** RespHospRate**ss +** NonHospRespRatess.This respiratory rate of the sentinel site reflects the rate of the region where the sentinel site exists.

**3.5.2 Extrapolation to different regions**

In this study, due to limitations in resources and complete data access, we will use an extrapolation approach to get an estimation for other regions in the country as recommended by WHO (WHO, 2015). That is, region-specific influenza burden will be estimated using the WHO method [WHO, 2015] such that the data collected at the base site regions will be extrapolated to other regions not included in the baseline assessment.  In this context, extrapolation refers to calculating the region-specific estimate by applying a risk factor adjustment factor, as outlined in the formula below. The adjustment factors will include respiratory infection risk factors and region-specific health-seeking behavior.

= \* \*

Where;

= (1+ - ) x ( – 1)

=

= Adjustment factor for region Y for risk factors of respiratory infection

= Adjustment factor for region Y healthcare-seeking behavior

= region other than base pooled region

= Selected risk factors

= Prevalence of risk factor *i* in region

= Prevalence of risk factor *i* in base pooled region

= Relative risk of respiratory infection due to risk factor *i*

*=* Proportion of health-seeking behavior for region Y

*=* Proportion of health-seeking behavior for the base pooled region

For the estimation of the pooled parameter (RespRate/number, risk factors, and health-seeking behavior), all the selected sentinel sites' data will be pooled together.

Note that the following assumptions are considered when extrapolating:

* The health-seeking behavior across the different age groups is assumed to be the same
* The respiratory rate of the sentinel site reflects the rate for the base region
* The relative risk and incidence rate for crowding, household air pollution exposure, and underlying medical condition are assumed to be the same across all age groups.
* The risk factors, child malnutrition, low birth weight, and non-exclusive breastfeeding,  will be used for only under five age groups
* The influenza positive proportion among cases that meet the SARI case definition is the same among all respiratory cases

**3.5.3. Estimate of Influenza-associated respiratory infection**

The influenza-associated respiratory rate will be estimated by multiplying the respiratory rate by the influenza positivity proportion. Similarly, the influenza subtype-specific rate will be calculated by multiplying the influenza-associated respiratory rate by the proportion of each influenza subtype.

Where;

= Influenza-associated respiratory rate in region Y (including base regions)

= Respiratory rate in region Y (including base region)

= Influenza proportion positive among respiratory cases

To get the number of influenza-associated respiratory cases, we will multiply the influenza-associated respiratory rate by the respective population size.

**3.5.4. Mean annual rates of influenza-associated illness based on clinical severity**

Quantifying the burden of influenza across the disease severity spectrum is important to understand and communicate the full impact of seasonal influenza on health systems and societies. To estimate the number and rates of influenza-associated illness based on clinical severity (mild/moderate, severe/critical, and deaths) at a national level, we will use influenza pyramid tool developed by WHO and the John Hopkins Center for Health Security (“Seasonal Influenza Disease Burden Estimator, <https://www.flutool.org>). This tool will generate the number and rates of influenza-associated illness on hospitalized, critical, mild/moderate, and death cases/rates across the age groups. In this case, the tool uses international conversion factors to estimate local influenza burden across the clinical severity.

A diagram of a pyramid

AI-generated content may be incorrect.

**3.5.5. Vaccine averted influenza-associated illnesses**

The annual number of influenza-associated illnesses that could be averted due to vaccination will be estimated using a hypothetical vaccine model recommended by WHO (REF).

## 3.6. Operational definitions

Hospitalized SARI case: A SARI case who was admitted to the hospital

Non-hospitalized SARI case:  A SARI case not visited/attended health facilities

Moderate/mild SARI: A SARI case with a mild illness that does not need hospitalization

Severe SARI: A SARI case that requires hospitalization

Death: Mortality due to SARI

SARI:  An acute respiratory infection with a history of fever or measured fever of ≥38 °C and cough, onset within the last 10 days, and requiring hospitalization.

Sentinel surveillance site: A hospital that is included as a SARI sentinel surveillance site.

Base site: A site selected to collect SARI data and extrapolate to other sites.

# 4. Benefits of the study

* Quantifying the Magnitude of moderate and death associated with influenza.
* Will help understand how influenza affects different age groups and at-risk populations.
* Help establish baseline levels and potential thresholds for severe influenza activity, which help for early warning.
* Providing Data for Policy and Investment Decisions: crucial for informing decisions about resource allocation and Vaccine introduction.
* Strengthening Surveillance Systems: provides valuable insights into the strengths and weaknesses of the existing SARI sentinel surveillance system in Ethiopia, a lead to improvements in data collection, reporting, and overall system effectiveness for ongoing monitoring of influenza and other respiratory illnesses.

# 5. Ethical Consideration.

Ethical clearance for this study will be obtained from the Ethiopian Public Health Institute’s Scientific and Ethical Review Board (SERO) prior to the commencement of the research. The study will adhere to both national and international ethical standards for research involving human data. Upon approval, the ethical clearance will be submitted to the designated health facilities to facilitate data collection. A written consent letter will be secured from all participating hospitals before initiating the actual data collection process. To ensure the protection of patient confidentiality, all collected data will be anonymized or de-identified.

Data abstraction information sheet (Anex…)

6. Strengths and limitations of the study

This study will estimate the burden of influenza in Ethiopia, which is the first which will generate important evidence to understand the extent of the problem, aiding in designing potential intervention mechanisms to prevent influenza outbreaks in the country. The limitations include……

# 7. Communication and dissemination plan.

The result of the study will be presented to Ethiopian Public Health Inistitute and Ministry of health. The finding will also be shared to regional health bureaus, public health institutes and relevant stakeholders. To reach the scientific community in the rest of the world the finding will be published on peer reviewed journal.

# Assumptions, risks, and mitigations

|  |  |  |
| --- | --- | --- |
| **Assumptions** | **Risks** | **Mitigation Strategies** |
| The surveillance system accurately reflects the incidence and severity of influenza. | Potential underestimation due to limitations in surveillance systems. | Scale up or down assessment using input from other sources like health-seeking behavior. |
| Access to healthcare and health-seeking behavior are consistent across the population. | Possible overestimation stemming from non-specific admission criteria and seasonal influences. | Check for concomitant outbreaks and adjust estimates accordingly. |
| No other significant outbreaks of diseases with overlapping symptoms occur simultaneously. | Bias in data collection, particularly concerning certain age groups. | Ensure accurate case identification and enrollment criteria. |
| Influenza activity and healthcare service utilization are primarily driven by local factors. | Statistical model uncertainty arising from the quality of historical data. | Use robust statistical techniques and validate models with historical data. |
| Historical data quality and appropriateness of chosen statistical techniques are reliable. | External factors such as the COVID-19 pandemic may impact influenza transmission dynamics. | Monitor external factors and adjust estimates to account for their influence on influenza transmission. |
| Specific at-risk groups or subpopulations are accurately reflected in the overall population estimates. | Certain at-risk groups or subpopulations may not be accurately reflected in the estimates. | Conduct targeted studies to better understand the impact on specific at-risk groups or subpopulations. |
| Budget and supplies | The study will be terminated due to shortage of budgets and supplies | * Prioritize the available resource with activities. * Mobilize additional grants from government or non-Government organization. * Collaborate with stakeholders. * Establish a budget monitoring system. |
| Data integrity | Bias in the representativeness | * Pretest whether the tool captures data consistently across different population groups. * Adjust the tool and sampling based on pretest finding. |
| Environmental Stability | May affect access to health care and significantly reduce case enrollment or withdrawal leading to incomplete data’s | * Cross-check collected data with data from alternate sources like, Registers, electronic health records, national health surveys or studies. |

# 8. Facilities available for the study

This study will be conducted by EPHI at the selected SARI sentinel surveillance sites (Adare General Hospital, Dil Chora Hospital, Adama Hospital Medical College, Shenen Gibe General Hospital, and Felege Hiwet Comprehensive Specialized Hospital), and the health facilities within the catchment areas of the respective sentinel sites.

# 9. Authorship right

Authorship and intellectual property rights of this study are for the Ethiopian Public Health Institute. The list of authors will be based on their substantial intellectual contribution in the entire process, starting from conception up to any preparation for dissemination/publication. The PI is responsible for ensuring everyone performs his/her duty in the execution of the project. The data that will be obtained from this project will be stored at the Ethiopian Pubic Health National Data Management Database and in both hardcopy and electronic form.

# 10. Declaration of conflict of interest

We declared that there is no individual and/or institutional conflict of interest in the technical aspect and administrative approaches of the proposed study protocol and for its implementation.

# 11. Assurance of the principal investigator

I, the undersigned, agree to accept responsibilities for:

* The scientific, ethical, and technical conduct of the research project,
* Requesting amendment for ANY change on the protocol that might need to happen during execution of the project, and obtain written approval for the request from EPHI-IRB,
* Submitting a progress report every year and a technical report within two months after completion of the project,
* Reporting any adverse event that might happen to the study participants, data collectors, supervisors, and coordinators during the investigation,
* Submitting scientific publications that emanate from the project within two months of publication, and
* Reporting any unprecedented protocol violation within seven days of the event if the project is approved as a result of this application.
* Submitting raw cleaned data to the EPHI Data Management Center after writing the final report

Name:

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date: \_\_\_\_\_\_\_\_\_/\_\_\_\_\_\_/\_\_\_\_\_\_

# 12. Commitment for signature of co-investigators

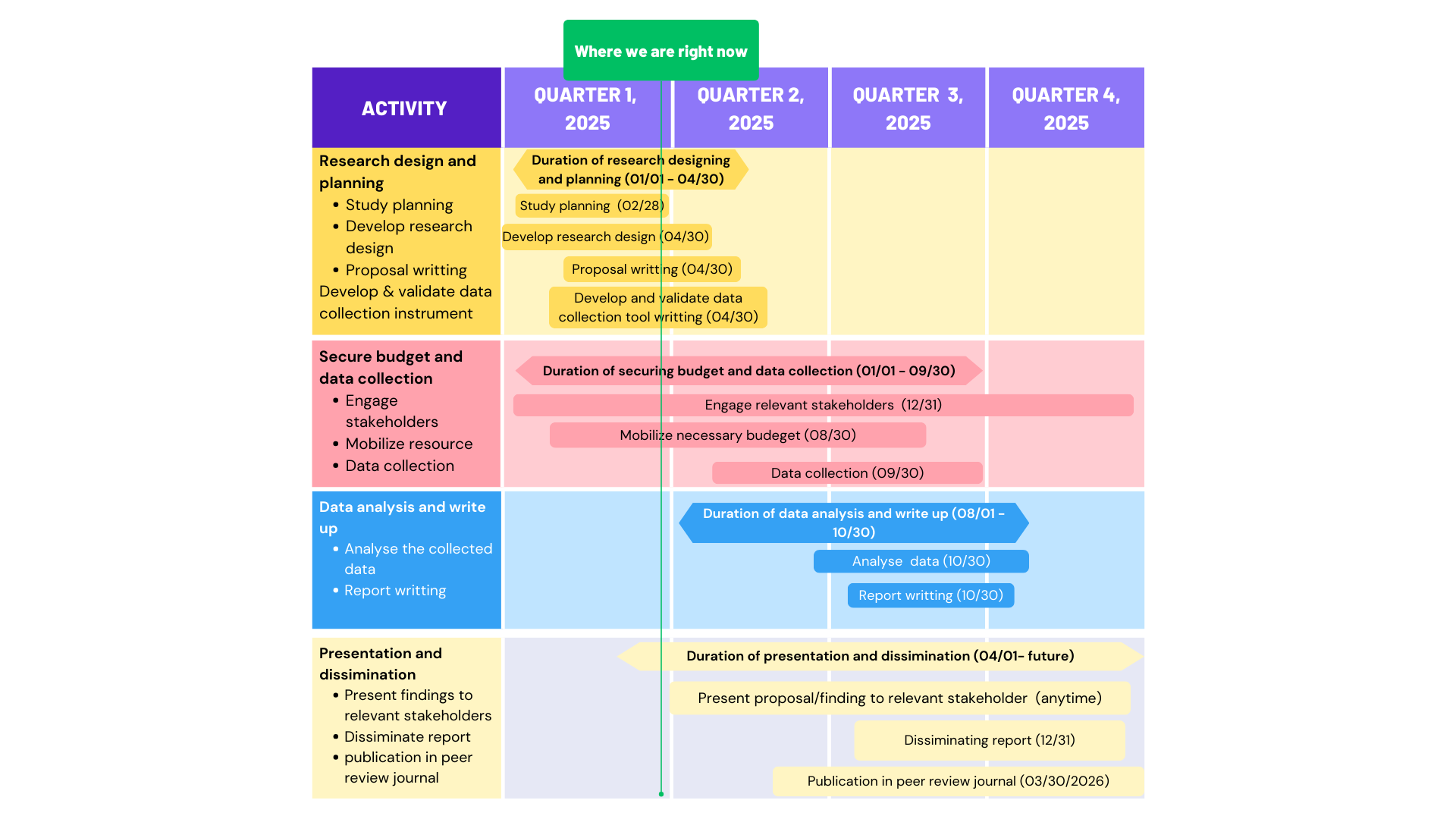
**Name Specific Roles and Responsibilities Signature**

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# 13. Comment and the occurrence of the responsible head for the principal investigator

Name Signature Date

# 14. Work plan/Time frame



# 15. Budget and Justification

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| S/N | Major Activity | Specific Activities | Unit Cost($) | Number of Participants/ Round | Number of days | Total Cost | Remark |
| 1 | Proposal write-up and data collection tool preparation workshop | proposal and data collection tool preparation, conduct a workshop, and prepare a report. | 50 | 20 | 7 | $7,000 | First draft completed, finalization, and proofreading |
| 2 | Discussion with Stakeholders(WHO, CDC,MOH, etc) | Invite stakeholders, presentation, discussion, and a way forward | 30 | 30 | 1 | $900 |  |
| 3 | Data Collection | Training for data collectors and supervisors | 50 | 30 | 7 | $10,500 |  |
| Deployment of data collectors and supervisors | 8 | 30 | 60 | $14,400 |  |
| 4 | Data analysis and report write-up | Data cleaning, analysis, and report write-up | 50 | 30 | 20 | $30,000 |  |
| 5 | Result Dissemination Workshop |  | 50 | 65 | 10 | $32,500 |  |
| 7 | Transport Cost (Both land and air, fuel) | For proposal write-up, data collectors and supervisors, data analysis and report preparation, for dissemination workshop, fuel |  |  |  | $22,320 |  |
|  | Tablet | For data collectors, 3 for each of the selected sentinel sites | 250 | 15 | - | $3,750 |  |
| 8 | Miscellaneous (10%) |  |  |  |  | $9,700 |  |
|  | **Total (USD)** |  |  |  |  | **$131,070** |  |

**Justification for Funding Request**

To successfully complete the project, all data elements outlined in the data element section must be collected and rigorously verified to ensure accuracy and reliability. Achieving high data quality requires the engagement of qualified data collectors, continuous monitoring, and strong supervision. Additionally, active coordination with national and regional authorities, sentinel sites, and non-sentinel health facilities within the catchment area will be essential.

A well-structured proposal, a standardized data collection tool, and properly trained data collectors are critical to maintaining data integrity. Data triangulation from multiple sources, thorough data cleaning, and close follow-up during the collection process will further enhance the quality of findings. Furthermore, to effectively disseminate results, we will organize a workshop focused on technical report writing, manuscript preparation for publication, and knowledge-sharing initiatives. These activities will ensure that the project’s outcomes contribute meaningfully to the broader scientific and public health communities. The requested budget of **$131,070** is essential to cover these critical activities and ensure the successful completion of the project.

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# **Annexes**

**Annex 1: Respiratory Admission by age group data collection form Selected Sentinel sites**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Name of Sentinel sites\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Year \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_** | | | | | | | |
| **Epi-weeks** | **Patient age group (in years)** | | | | | | **Total** | **Remark** |
| **<2** | **2-4** | **5 - 14** | **15 - 49** | **50 – 64** | **65+** |
| 1 |  |  |  |  |  |  |  |  |
| 2 |  |  |  |  |  |  |  |  |
| 3 |  |  |  |  |  |  |  |  |
| 4 |  |  |  |  |  |  |  |  |
| 5 |  |  |  |  |  |  |  |  |
| 6 |  |  |  |  |  |  |  |  |
| 7 |  |  |  |  |  |  |  |  |
| 8 |  |  |  |  |  |  |  |  |
| 9 |  |  |  |  |  |  |  |  |
| 10 |  |  |  |  |  |  |  |  |
| 11 |  |  |  |  |  |  |  |  |
| 12 |  |  |  |  |  |  |  |  |
| 13 |  |  |  |  |  |  |  |  |
| 14 |  |  |  |  |  |  |  |  |
| 15 |  |  |  |  |  |  |  |  |
| 16 |  |  |  |  |  |  |  |  |
| 17 |  |  |  |  |  |  |  |  |
| 18 |  |  |  |  |  |  |  |  |
| 19 |  |  |  |  |  |  |  |  |
| 20 |  |  |  |  |  |  |  |  |
| 21 |  |  |  |  |  |  |  |  |
| 22 |  |  |  |  |  |  |  |  |
| 23 |  |  |  |  |  |  |  |  |
| 24 |  |  |  |  |  |  |  |  |
| 25 |  |  |  |  |  |  |  |  |
| 26 |  |  |  |  |  |  |  |  |
| 27 |  |  |  |  |  |  |  |  |
| 28 |  |  |  |  |  |  |  |  |
| 29 |  |  |  |  |  |  |  |  |
| 30 |  |  |  |  |  |  |  |  |
| 31 |  |  |  |  |  |  |  |  |
| 32 |  |  |  |  |  |  |  |  |
| 33 |  |  |  |  |  |  |  |  |
| 34 |  |  |  |  |  |  |  |  |
| 35 |  |  |  |  |  |  |  |  |
| 36 |  |  |  |  |  |  |  |  |
| 37 |  |  |  |  |  |  |  |  |
| 38 |  |  |  |  |  |  |  |  |
| 39 |  |  |  |  |  |  |  |  |
| 40 |  |  |  |  |  |  |  |  |
| 41 |  |  |  |  |  |  |  |  |
| 42 |  |  |  |  |  |  |  |  |
| 43 |  |  |  |  |  |  |  |  |
| 44 |  |  |  |  |  |  |  |  |
| 45 |  |  |  |  |  |  |  |  |
| 46 |  |  |  |  |  |  |  |  |
| 47 |  |  |  |  |  |  |  |  |
| 48 |  |  |  |  |  |  |  |  |
| 49 |  |  |  |  |  |  |  |  |
| 50 |  |  |  |  |  |  |  |  |
| 51 |  |  |  |  |  |  |  |  |
| 52 |  |  |  |  |  |  |  |  |
|  | **Remark**   * Use tally to facilitate counting * Do not include patients who came from out of the catchment area. * Consider the following list of disease under the category of respiratory disease * Aaa * Bbbbb * Fvfv fvfv | | | | | | | |

**Annex 2: Total SARI samples tested and laboratory result, January 01, 2023 –December 31, 2024**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Age group  (years) | Total number of SARI samples Tested | Number of influenza positive cases | | | |
| AH1 | AH3 | B | Total |
| 0 - 4 |  |  |  |  |  |
| 5 - 14 |  |  |  |  |  |
| 15 - 49 |  |  |  |  |  |
| 50 - 64 |  |  |  |  |  |
| 65+ |  |  |  |  |  |
| Total |  |  |  |  |  |

**Annex 3: Data collection/Extraction form for risk factors and Health Seeking behavior for respiratory infection**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Crowding** | | | | **Indoor Air Pollution** | | | | **Malnutrition** | | | **Non-Exclusive Breastfeeding** | | | **Low Birth Weight** | | | **Healthcare Seeking for Respiratory Infection** | |
| Region | n | Prev | RR | n | | Prev | RR | n | | Prev | RR | n | Prev | RR | n | Prev | RR | n | Prev |
| Addis Ababa |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Afar |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Amhara |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Oromia |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| B/Gumuz |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| C/Ethiopia |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Dire Dawa |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Gambella |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| S/Ethiopia |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Sidama |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Somali |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Harari |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Tigray |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| S/W/Ethiopia |  |  |  |  | |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| n= Number of study participants; Prev: Prevalence rate; RR= Relative Risk | | | | | | | | | | | | | | | | | | | | |

Annex 4: Data abstraction information sheet