ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCE

SCHOOL OF PUBLIC HEALTH

TIME TO RECOVERY AND PREDICTORS AMONG COVID-19 PATIENTS UNDER HOME-BASED ISOLATION AND CARE SERVICES IN ADDIS ABABA, ETHIOPIA

BY

AYELE BIZUNEH GIZAW (DVM)

A THESIS SUBMITTED TO THE SCHOOL OF PUBLIC HEALTH OF THE COLLEGE OF HEALTH SCIENCES AT ADDIS ABABA UNIVERSITY IN THE PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF PUBLIC HEALTH WITH SPECIALTY IN EPIDEMIOLOGY AND BIOSTATISTICS

JUNE, 2024

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I undersigned agree to accept all responsibilities for the scientific and ethical conduct of this research project and declare that this thesis is my original work in partial fulfillment of the requirement for the Master of Public Health in Epidemiology and Biostatistics

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Approval of the primary advisor

This thesis work has been submitted with our approval as university advisor.

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APRROVAL BY EXAMINATION BOARD

This thesis by Ayele Bizuneh Gizaw is accepted in its present form by the board of examiners as satisfying thesis requirements for the review of degree of masters of public health in Epidemiology and Biostatistics

Professor Wakgari Deressa	______________	June 13, 2024
Internal examiner	Signature	Date
Aman Yesuf (Assistant Professor)	______________	June 13, 2024
External examiner	Signature	Date

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Acronyms and Abbreviations

AAU	Addis Ababa University
CoV	Corona virus
COVID-19	Corona Virus Disease 2019
CT	Cycle threshold
BMI	Body mass Index
ECDC	European center for disease prevention and control
EPHI	Ethiopian Public Health Institute
HBIC	Home Based Isolation and Care
HR	Hazard Ratio
AHR	Adjusted Hazard ratio
MERS-CoV	Middle East Respiratory Syndrome
ODK	Open Data Kit
RDT	Rapid Diagnostic Testing
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SARS	Sever acute respiratory Syndrome
SARS- CoV-2	severe acute respiratory syndrome coronavirus 2
SERO	Scientific and Ethical Review Office
WHO	World Health Organization

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Abstract

Background: The COVID-19 pandemic has significantly impacted health systems globally. Ethiopia has recorded over 7,574 COVID-19-related deaths and nearly 500,000 confirmed cases. While 81.3% of cases in Ethiopia have been handled via home-based isolation and Care (HBIC), there are still uncertainties about the health consequences for patients receiving this type of care.

Objectives: The objective of this study was to investigate the recovery experience of COVID-19 patients under home-based isolation and care services in Addis Ababa between January 17, 2023 and June 23, 2023. This includes time to recovery, recovery incidence rates, and associated factors.

Methods: This retrospective cohort study was conducted in Addis Ababa from January 20,2024 to June 23, 2024. The study population comprised 272 COVID-19 patients who received HBIC from January 17 to June 23, 2023. Secondary data from the Ethiopian Public Health Institute and Armauer Hansen Research Institute was analyzed using Kaplan-Meier survival estimates and Cox regression model.

Results: The analysis revealed an overall median recovery time of 7 days among COVID-19 patients within the HBIC. Specifically, vaccinated individuals had median recovery time of 7 days, while unvaccinated individuals had median recovery time of 8 days. The findings also indicated incidence density rates of 11.64, 13.19, and 10.34 recoveries per 100 person-days for the overall, vaccinated patients, and unvaccinated patients, respectively. Factors associated with time to recovery among COVID-19 patients under HBIC were: being vaccinated (AHR: 1.62, 95% CI: 1.18-2.23), Aged 30-39 (AHR: 2.13, 95% CI: 1.27-3.58), Absence of comorbidities (AHR: 1.87, 95% CI: 1.16-3.01), Prior infection (AHR: 2.11, 95% CI: 1.37-3.22), using public transport (AHR: 0.45, 95% CI: 0.32-0.65), smoking history (AHR: 0.44, 95% CI: 0.22-0.86), absence of mask use (AHR: 0.39, 95% CI: 0.28-0.55), lack of hand hygiene practice (AHR: 0.72, 95% CI: 0.53-0.99), and BMI ≤18.5 Kg/M^2 (AHR: 0.67, 95% CI: 0.48-0.95) or 25-29.9 Kg/M2 (AHR: 0.38, 95% CI: 0.15-0.96).

Conclusion: This study revealed the median time, rate and associated factors under home based isolation and care service. The relatively shorter median time among vaccinated groups indicate the viability of vaccination in recovery trajectories. The varying recovery rate with the different covariates and significant association of those covariates with time to recovery indicates the need for considering tailored interventions in those patients.

Keywords: COVID-19, Home-Based, Isolation, Care, Time to Recovery, Recovery Rate

1. Introduction

1.1 Background

Coronavirus disease 2019 (COVID-19) is a life-threatening infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). SARS-CoV-2 virus is rapidly transmissible pathogenic virus that emerged in late 2019 in Wuhan, China (2). The recent report from World Health Organization indicates the pandemic has caused a total of over 775 million cases and 7, 043, 660 million deaths globally. In the African region over nine million confirmed cases and 175, 505 deaths had been reported since the start of the pandemic (3). In Ethiopia over 500, 000 confirmed cases and 7,574 deaths have been registered (4), where 334,103 confirmed cases were registered and followed in Addis Ababa (5).

One of the strategies to contain the transmission of the virus and reduce surge on the hospitals is isolation and care of mild and moderate COVID-19 case at home. Ethiopia is also implementing home based isolation and care (HBIC) for COVID-19 patients including Addis Ababa (6). About 400,313 (81.3%) of the confirmed cases have been followed through HBIC services in the country (4). In Addis Ababa about 299, 362 or 89.6 % of COVID-19 Case managed under HBIC. Factors such as older age, sex, and underlying medical conditions, viral load, host-immune response, variant type and cross-reactive from other coronaviruses will affect clinical outcomes of COVID-19 patients under home isolation and care (2,7).

There are uncertainties about SARS-CoV-2 infection and resulting health outcomes that need new research and evidences (8). Development of knowledge on health outcomes of COVID-19 patients is important for decision making, preventive measures, treatment and policy issuance. Although research and development of vaccine and medicine have contributed to reduced length of recovery time, hospitalization, severity and mortality the virus continued to evolve and infect thousands of people (8).

Therefore, this study had critical role in resolving the uncertainties and generated substantial evidences on recovery time among mild COVID-19 patients isolated and cared at home. Therefore, the aim of this study was to investigate the recovery experience of COVID-19 patients under home-based isolation and care services in Addis Ababa between January 17, 2023, and June 23, 2023.

1.2 Statement of the problem

COVID-19 pandemic has posed many challenges to the health systems including disruptions of health care delivery and routine surveillance systems (9). Although World Health Organization COVID-19 emergency committee has decided to not further classify COVID-19 as international public health emergency, it still infect 17,937 people and causes large number of deaths worldwide, with an excess mortality of approximately 169 deaths per day (10).

The COVID-19 pandemic has underscored the importance of home-based isolation and care (HBIC) as a crucial strategy for managing the disease, particularly in resource-limited settings. While HBIC has proven effective in controlling outbreaks and reducing healthcare system strain, understanding the factors that influence recovery time for COVID-19 patients under HBIC remains a critical knowledge gap. Existing studies primarily focus on hospitalized patients, leaving a significant gap in knowledge about the recovery experiences of those isolated and cared at home (11). This lack of data hinders the development of effective guidelines and interventions to support home-based care and improve the quality of care for both patients and caregivers.

Obviously, there is a significant disparity in the quality of life and cost-effectiveness among home and facility based isolation for addressing mild and moderate patients (12). Studies have demonstrated its cost-effectiveness, with HBIC costing significantly less per person than facility-based care(13,14). Moreover, successful implementation of HBIC has been observed in various countries, such as India, where 93.3% of patients completed their isolation at home(14), and Uganda, where 96.0% of participants recovered at home(15).

Despite the cost-effectiveness and potential benefits of HBIC, there's a limited understanding of the specific factors that contribute to quicker or slower recovery times for COVID-19 patients under HBIC. These knowledge gaps make it difficult to optimize patient outcomes and public health response. Therefore, responding to the question at what median time and rate are patients recovering and what factors associate with time to recovery from COVID-19 diseases for patients under HBIC is crucial to optimize patient outcomes and understanding the effectiveness of the HBIC in management covid-19 patients focusing on recovery outcome.

This study sought to answer the question: What factors are associated with the time to recovery for COVID-19 patients undergoing home-based isolation and care in Addis Ababa, Ethiopia?

Therefore, this study aimed to reveal the recovery experience of COVID-19 patients undergoing home-based isolation and care (HBIC) services in Addis Ababa, Ethiopia, by identifying factors associated with their time to recovery.

1.3 Rationale of study

While global and regional recommendations for the isolation and des-isolation of COVID-19 patients exist, significant uncertainties remain particularly regarding optimal recovery time and factors influencing it. Although research has illuminated aspects of COVID-19 management in hospitalized settings, there is a critical gap in understanding the recovery experiences of patients managed under home-based isolation and care (HBIC) in resource-constrained settings like Ethiopia(8).

In Ethiopia, HBIC plays a vital role, with 81.3% of confirmed cases receiving care at home. However, a lack of data on recovery status, time to recovery, and the factors influencing these aspects presents a significant challenge for optimizing patient outcomes and public health response(4).

Furthermore, the absence of separate isolation recommendations tailored to the severity levels of COVID-19 patients (critical, severe, moderate, and mild) further highlights the need for evidence-based guidelines (8). The European Centre for Disease Prevention and Control (ECDC) underscores the importance of individualized isolation periods based on severity levels (16).

This study aims to address these critical knowledge gaps by investigating the recovery time of COVID-19 patients under HBIC in Addis Ababa, Ethiopia. The findings will provide valuable insights into factors influencing recovery time, contribute to the development of evidence-based guidelines, and ultimately enhance the effectiveness of HBIC strategies in Ethiopia.

1.4 Significance of the study

This study holds significant value for patients, caregivers, public health professionals, clinicians, health policymakers, and the scientific community in Ethiopia. Understanding recovery times for COVID-19 patients managed under home-based isolation and care (HBIC) is crucial in this context, where HBIC is the dominant care model.

The evidence generated from this study will empower patients by providing them with realistic expectations regarding their recovery journey, enabling active participation in their healing process. Caregivers will benefit from the study's insights into the signs and symptoms of COVID-19 recovery, equipping them to provide more effective and compassionate support to their patients at home.

For public health professionals, this study will provide evidence-based information to optimize resource allocation, inform decision-making on isolation, and discharge, and enhance the effectiveness of public health interventions. The findings will also inform the development of evidence-based guidelines for home isolation and management of COVID-19 patients in Ethiopia, contributing to more effective response to the pandemic and its impact in Addis Ababa, Ethiopia.

2. Literature review

2.1 Corona Viruses

Coronaviruses (CoVs) are a large group of viruses common in animals and human. They are zoonotic pathogens originating in animals and can possibly transmit to humans through various ways including direct contact. Coronavirus has four genera; those are alpha, beta, gamma, and delta. The genus beta categorized into four different lineages ranging A to D and evidences indicate that SARS-CoV-2 is belonging to the B lineage, which is similar group of another epidemic prone coronavirus, SARS-CoV (17,18).

2.2 Coronavirus disease 2019

Coronavirus disease 2019 is infectious disease and is caused by the SARS-CoV-2 virus. SARS-CoV-2 virus is noble coronavirus emerged in Wuhan city of China causing severe to mild respiratory distress (19,20). There are controversial suggestions and speculations that SARS-CoV-2 virus is constructed in the laboratory, released accidently. Including genomic features of CoVID-19, the available scientific evidences indicate SARS-CoV-2 is not constructed in the laboratory rather it is more suggestive of spillover from the natural zoonotic sources such as bats and Civets (18,21).

2.3 Magnitude of the problem

Globally, 775 251 779 confirmed cases and 7 043 660 deaths have been reported globally as of 12 April 2024. Of the global total cases the European region shares about 36% (279 243 990) while the American region takes the largest number of deaths, 3 015 459 (43%) from the global reported deaths. Western Pacific region takes the second largest shares of global reported case, 208 379 324 (27%) where the African region takes the lowest cases, 9, 577, 797 (1%) and deaths, 175, 505 (2%) from the global COVID-19 report(3).

In Ethiopia as of October 15 2023, about 501,103 confirmed COVID-19 cases and 7,574 deaths were recorded from the beginning of COVID-19 pandemic in the country (5). In Addis Ababa from the beginning of COVID-19 pandemic over 341,459 COVID-19 confirmed cases were registered (5).

2.4 Survival of patients with COVID-19

In Africa, Nigeria reported that the overall incidence rate of recovery has been found 4.70 (95% CI: 41.89-50.15) per 100 person-day observation. In the western Ethiopia, an overall 4.38 (95% CI: 3.84, 4.99) incidence rate of recovery per 100 person-day observation has been reported (22,23). Several articles on survival time of COVID-19 patients in different parts of Ethiopia reported a median time of recovery ranging from five and twenty six days (22,24–28).

The lowest median time of recovery (five days) has been reported from south Ethiopia with normal body temperature (AHR=0.52, 95% CI= 0.25–1.00), normal breathing rate (AHR=5.37, 95% CI=1.40–20.57) and severe disease status (AHR=0.33, 95% CI=0.16–0.6) a significant the main predictors of time to recovery (29). The higher time of recovery (twenty six) is reported from northern of Ethiopia, Tigray region with shortness of breath (AHR=2.08, 95% CI: 1.07–3.98) and body weakness (AHR=2.62, 95% CI: 1.20–5.72) as the main significant determinant of time to recovery form COVID-19 (24).

2.5 Risk factors and determinants

Risk factors for COVID-19 disease severity and recovery outcomes are crucial in survival modeling among COVID-19 patients. Variables such as age, residence, sex, contact history, are the frequently reported predictors of time to recovery from COVID-19 in the reviewed literatures under this section of interest(22,25–31). Additionally, clinical variables such as vaccination, disease severity, treatment setting, comorbidity, vaccination status and symptoms are main predictors of recovery time from COVID-19 disease(24).

2.5.1 Socio-demographic variables

The impacts of SARS-CoV-2 infection have not been equally distributed among the different socio-demographic disparities among the victims of COVID-19 disease. Many literatures found socio-demographic variables such as gender, age, occupation, family size, social event, marital status, educational level etc. have significant association with time to recovery from COVID-19 disease(22–25,27,28,30–32).

2.5.2 Vaccination status

Immunization against SARS-CoV-2 virus is found crucial in minimizing, hospitalization rate, infection severity and improving outcomes, more essentially in high-risk group patients. In many studies unvaccination status has been found predictor of longer hospital stay time, ICU admission, mechanical ventilation and death(33,34). The average time hospital stay is lower in vaccinated group patients when compared to unvaccinated group of COVID-19 patients(35). The natural prior infection with SARS-CoV-2 has also significant effects on the outcomes of re-infected COVID-19 patients, has lower risk of hospitalization. Moreover, Hybrid immunization has greater impacts on the outcomes of COVID-19 patients whenever it exist(36,37). In Ethiopia form the beginning of COVID 19 vaccination to 16 October 2023, a total of 44,657,591 people received full vaccination series, bringing coverage of 66% and 41% from the target and total population respectively (5).

2.5.3 Comorbidities

Presence of previous comorbidities and underlying conditions determines recovery time and recovery rate of COVID-19 patients (26). COVIDI-19 patients without comorbid illness have faster time to recovery than individuals having at least one underlying condition (22,25,29,31). The most common underlying condition or comorbidities which determine survival time and recovery rate includes chronic disease such as asthma, heart disease, hypertension, Diabetics, kidney disease, HIV, Cancer and Tuberculosis (22–31,38).

2.5.4 Body mass index (BMI)

Abnormal body mass index category had significantly impact on time to recovery from COVID-19 disease compared to normal BMI. COVID-19 symptoms resolution study from Ethiopia reported that abnormal BMI has strong association on time to resolve symptoms (85). Another study in China reported that BMI>24 kg/m^2 was an independent predictor of severe COVID-19 disease progression(39). A community-based study in United Kingdom showed increases odds of hospital admission among overweighted COVID-19 patients compared with normal (40). The significant association between abnormal BMI and hazard of recovery may be due to metabolic dysregulation, chronic inflammation, and impaired immune function in individuals with higher BMI leading to prolonged illness duration (41).

2.5.5 Smoking

Smoking has strong association with severe respiratory disease and is known risk factor for worsening COVID-19 outcomes (42). A study from southwest Ethiopia found a 29% increment in hazard of severe COVID-19 disease among smokers (43). Studies conducted in China had reported that smoking was predictor of unfavorable outcomes of COVID-19 patients(44,45). Smoking induce inflammation, increased mucus production, tissue damage, airway thickening, and emphysema, all of which can impair lung functions leading to worsen respiratory illness and respiratory failure (46).

2.5.6 Previous infection history

Previous infection with SARS-COV-2 virus put potential immune-mediated mechanisms at play for protecting consecutive SARS-COV-2 infection and attributed potentially milder illness and faster recovery (47). A population-based study in Japan reported protective effects of prior infection against Omicron reinfection(48). Another meta-regression systematic review found that prior infection was 82.5% effective in protecting against severe COVID-19 disease outcomes (49). A study in Australia found that prior infection with SARS-CoV-2 led to faster viral clearance during breakthrough infections (47).

2.5.7 Symptoms

The most common symptoms presentation for COVID-19 includes; Cough, Fatigue, Fever, Headache, chest pain, Myalgia, Loss of smell, Nasal obstruction, generalized seizures, Asthenia, Rhinorrhea, shortness of breath, arthralgia, myalgia, fatigue and Sore throat (50,51). The proportion of symptoms in hospitalized patients will differ from patient to patient and include fever (70%-90%), dry cough (60%-86%), shortness of breath (53%-80%), fatigue (38%), myalgias (15%-44%), nausea/vomiting or diarrhea (15%-39%), headache, weakness (25%) and rhinorrhea (7%) (52).

2.5.8 Severity of the disease

The clinically observed COVID-19 disease has three different severity levels, which include mild, moderate, and severe cases. Mild COVID-19 patients are those with symptomatic infection but without evidence of viral pneumonia or hypoxia. Moderate COVID-19 patients are those who exhibit indicators of viral pneumonia, such as fever, fast breathing, dyspnea, cough, and oxygen saturation greater than or equal to 90%. Severe COVID-19 cases are characterized by the presence of severe pneumonia and an oxygen saturation of less than or equal to 90% (53).

2.5.9 Viral variants

Viruses are constantly evolving and changing over time while spreading between susceptible hosts. When these changes are significantly different from the original virus, they are known as variants(54). Numerous variants of SARS-CoV-2 identified over the pandemic time and these variants show genetic differences with respect to the original Wuhan strain. Thus, the so-called variants of public health concern have appeared which includes alpha, beta, gamma, delta and omicron(54). Among the SARS-COV-2 Variants of Concern, Alpha, Beta, Delta and Omicron variants were detected in Ethiopia by the genomic sequencing(55). The variants of SARS-CoV-2 have different recovery impacts on COVID-19 patients. Study performed in Bahrain shows that patients infected with SARS-CoV-2 virus of the delta variant have found slower recovery time than alpha variant, and this is also true for unvaccinated and vaccinated patients (56).

2.5.10 Cycle Threshold Values and Viral load

Real-time RT-PCR is the gold standard confirmatory test available for coronavirus disease 2019. In RT-PCR, Cycle Threshold (CT) values are primarily utilized to predict SARS-CoV-2 infection and viral load. SARS-CoV-2 virus testing using RT-PCR is implemented by amplification of target nucleic acid occurs with number of cycles (rounds). Those numbers of amplification cycles are known as CT values. This method has important clinical role as the CT values can be associated with the viral load (57).

Threshold cycles have inversely correlated with Viral load, the higher number of CT values the smallest viral load will measured. The CT values are categorized in to three groups based on the amount cyclic amplification values of the given RT-PCR test. Group one contains CT values ranging from ≤25, group two contains CT value from 25-35 and the third group have CT values from ≥35. There are significant variations in viral load and recovery times among patients with and without pneumonia. Patients who had pneumonia (severe and moderate disease) had higher viral load and slower recovery times than those without pneumonia (58). However, there are studies that contradict severity of the disease is correlate with the RT-PCR Cycle Threshold (CT) values and viral load of SARS-CoV-2 virus (53,59).

2.5.11 Non-pharmaceutical interventions (NPIs)

Frequent hand washing after touching high-touch surfaces can significantly reduce viral load and inoculum size, potentially leading to faster viral clearance and improved recovery outcomes(60).

Studies have consistently demonstrated the effectiveness of hand hygiene in reducing the incidence and severity of COVID-19. Study in Australia found a 51% decrease in COVID-19 incidence and a reduction in mortality rate associated with strict adherence to thorough hand washing(61,62). Similarly, a study in Hong Kong reported a 42% reduction in the risk of SARS-CoV-2 infection through consistent hand washing and disinfection practices(63). Furthermore, a meta-analysis study also found a 28% daily reduction in infection risk associated with a tenfold increase in hand washing frequency(64).

Studies have consistently demonstrated that mask usage reduced risk of infection, lower viral load, and improved recovery outcomes. A study conducted in Tunisia reported an increased likelihood of recovery among individuals who used masks(65). Similarly, a study among orthopedic surgeons in Wuhan found that wearing any type of respirator mask consistently was associated with an 85% decrease in risk of new SARS-CoV-2 infection(66). Additionally, studies from India and other countries have shown that mandatory mask-wearing resulted in asymptomatic manifestation and earlier seroconversion among infected individuals, facilitating faster recovery104,105).

Public transportation, such as buses and shared conveyances, can pose an increased risk of COVID-19 transmission due to the potential for close contact and exposure to the virus. Studies have shown that individuals who travel on public transportation for extended periods or in close proximity to infected individuals have a higher risk of contracting COVID-19. For instance, a survey in Italy found that 40% of a public bus company's employees were positive with SARS-CoV-2, and 19.3% of tested bus surfaces were positive for the virus(67). On the other hand, a study in India reported secondary attack rate of 79.3% among individuals who had high-risk travel exposures at least 6 hours (68).

2.5.12 Isolation and de-isolation of patients

Isolation and care for COVID-19 patients should be given at health facilities. Home based isolation and care (HBIC) is an alternative to manage mild and asymptomatic patients when isolation at health facility is impossible. HBIC is strategy for isolation of mild, moderate and asymptomatic COVID-19 patients at home after screened and positive for SARS-CoV-2 virus, by insuring availability of infection prevention materials, caregivers, adequate space and with minimal remote support from health care workers (12,69).

Asymptomatic, mild and moderate symptomatic patients who are without known risks of comorbid and less than the age of 60 years eligible for HBIC (6,12). The availability of caregivers infection prevention infrastructure, adequate family and social support are the main challenges to implement this program (15). The new recommendation of World Health Organization for isolation of symptomatic COVID-19 patients is ten days and five days for asymptomatic patients (8). According to ECDC report there is separate isolation time for vaccinated, severe, moderate, mild and imunnocompromized patients (16).

2.5.13 Methodological issues

Most research on COVID-19 has been done on hospitalized patients with a pre-prepared and validated and published study protocols. Home based COVID-19 study protocols are not well available and retrievable from common searching engines. A recently published study protocol home based COVID-19 protocol from Netherlands recommends use of cohort study of non-hospitalized COVID-19 patients (11). There were minimal expected ethical challenges in conducting this research activities. The study imposes minimal risk to the study participants. In this study secondary data from Armauer Hansen Research Institute (AHRI).

2.5.14 Summary of the review

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus which has been caused global pandemic. It has imposed large challenges to human and the health system globally. Conducting study on non-hospitalized COVID-19 patients is crucial to public and health care system since most of previous studies are hospital based. The global, regional and national recommendations on isolation or des-isolation of COVID-19 patients are made with very low certain evidences. Survival of COVID-19 cases and associated factors are not still well known and need further research. The current uncertainties and knowledge gaps in this regard require new evidence and future research to determine optimal survival rate, duration of isolation and recovery time among COVID-19 patients.

2.5.15 Conceptual Framework

The below diagram is a conceptual framework for a research project on the time to recovery from COVID-19 disease among patients under home-based isolation and care in Addis Ababa, Ethiopia. First patients tested positive for COVID-19 at a health facility. After testing, these patients are then screened for level of severity, eligibility criteria, and comorbidities. If patients fulfilled the eligibility criteria, then patients were followed for a maximum of 14 days and provided home-based isolation and care (HBIC). The framework considers several clinical and related factors, Socio-demographic factors, non-pharmaceutical interventions (NPIs). The conceptual framework provides a comprehensive approach to understanding the complex factors that may influence the time to recovery from COVID-19 among patients under home-based isolation and care in the Addis Ababa context.

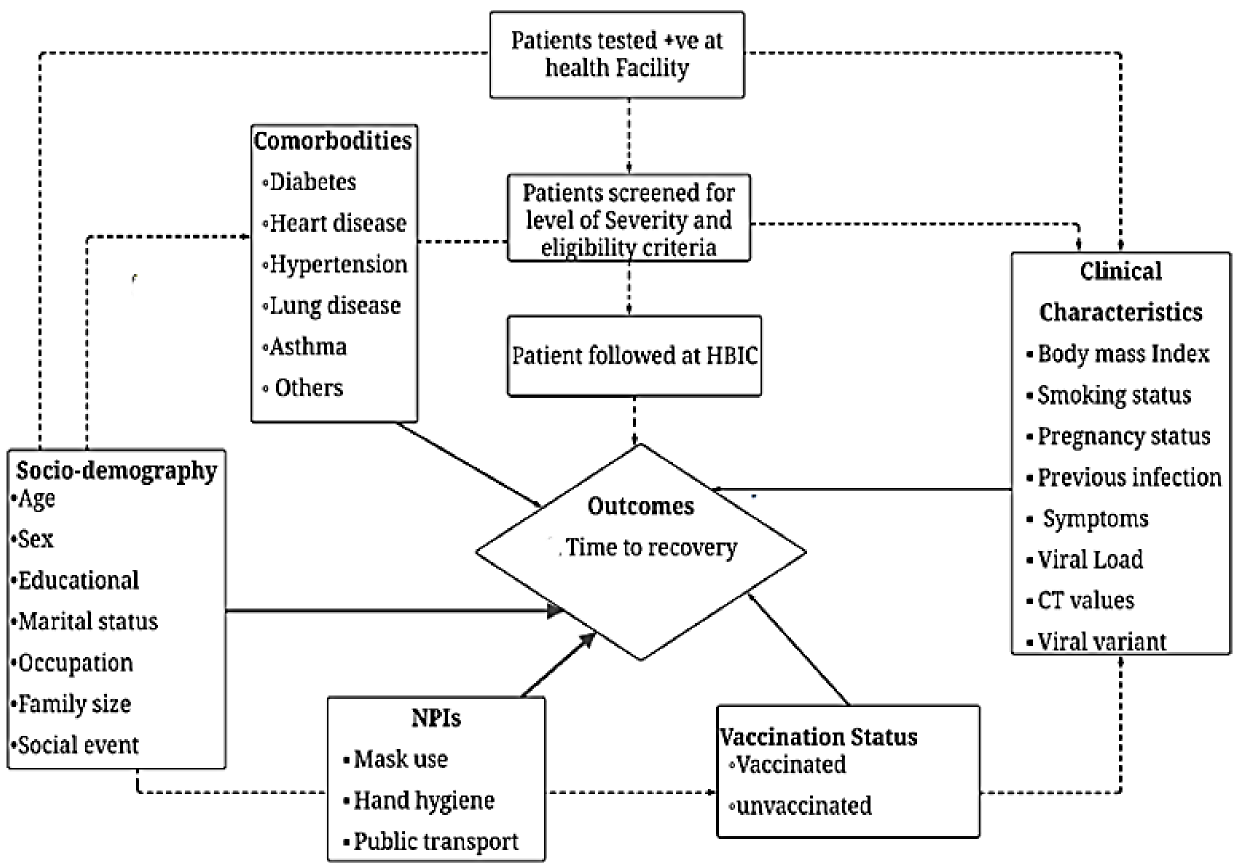

Figure 2.1 Conceptual framework for determinants of recovery time for COVID-19 patients in Addis Ababa, Ethiopia, 2023/2024 (13,15,70,71)

3. Objectives

3.1 General objectives

The primary objective of this study is to investigate the recovery experience of COVID-19 patients under home-based isolation and care services in Addis Ababa between January 17, 2023, and June 23, 2023. This involves assessing the time to recovery, recovery incidence rates, and associated factors.

3.2 Specific objectives

1. To determine the overall time to recovery for COVID-19 patients receiving home-based isolation and care services in Addis Ababa between January 17, 2023, and June 23, 2023, and to compare the recovery times between vaccinated and unvaccinated individuals.
2. To determine the recovery rates and compare the entire survival experience between levels of different recovery predictors of COVID-19 patients receiving home-based isolation and care services in Addis Ababa between January 17, 2023, and June 23, 2023.
3. To identify factors associated with the time to recovery of COVID-19 patients under home-based isolation and care in Addis Ababa between January 17, 2023, and June 23, 2023, using the Cox proportional hazards regression model.

4. Methodology

4.1 Study design and period

A secondary data analysis was conducted for mild COVID-19 patients from August 25, 2023 to June 03, 2024 in Addis Ababa Ethiopia by using data from Armauer Hansen Research Institute (AHRI) which was initially collected from January 17, 2023 to June 23, 2023 among patients isolated and cared at their home in Addis Ababa using a prospective.

4.2 Study setting

The study was conducted in non-facility-based settings, specifically in patients' homes, following initial triage at health facility. Patients received home-based isolation and care services for a 14-days follow-up period in Addis Ababa. Participants were recruited from twenty-four health facilities across nine sub-cities: Addis Ketema, Akaki Kality, Bole, Gulelle, Kirkos, Kolfe Keranio, Lideta, Arada, and Yeka. Lami kura and Lafto did not included in the data source study due to resource constraints.

Addis Ababa is the capital city of Ethiopia. It has 13 public hospitals and 102 health centers (72). It is multi-ethnic city with estimated total population 3.6 million (73). The city has a total area of 540 square kilometers and its altitude is ranging from 2,000 to 2,800 meters above sea level. It has 11 sub-cities, and 116 Woredas (74).

4.3 Populations

4.1.1 Source population

The source population consisted of individuals both vaccinated and unvaccinated over 18 years of age who presented to healthcare facilities between January 17, 2023, and June 23, 2023, with symptoms of acute respiratory illness and were suspected of having SARS-CoV-2 infection. The age above 18 years was selected due to vaccine priority categorization(75).

4.1.2 Sampling population

The sample population comprised both vaccinated and unvaccinated individuals over 18 years of age residing in Addis Ababa and presented to healthcare facilities with mild to moderate COVID-19 symptoms. They tested positive for SARS-CoV-2 virus using rapid diagnostic testing (RDT) during screening test between January 17, 2023, and June 23, 2023. These individuals were randomly selected from the larger sampling population of SARS-CoV-2 positive patients.

4.1.3 Study population

The study participants were patients in Addis Ababa who tested positive for SARS-CoV-2 using rapid diagnostic testing (RDT) during initial screening and were subsequently confirmed positive through Real-Time PCR (RT-PCR) between January 17 and June 23, 2023.

4.4 Inclusion and Exclusion criteria

Inclusion criteria

Patients were included in the study participants after screening the following criteria:

- Residency in Addis Ababa
- If the time period included in the study was from January 17, 2023 to June 23, 2023
- Patient should be above the age of 18 years
- Should be tested positive for SARS-Cov-2 virus using rapid diagnostic testing (RDT) at the time of screening and confirmed positive using RT-PCR
- For vaccinated groups should count 14 or more days after partially or completely vaccinated with recommended doses of Covid-19 vaccine on the date SARS-CoV-2 RNA or antigen detection

Exclusion criteria

Participants were excluded from the study with the following criteria:

- Patient who was below the age of 18 years
- Patient tested positive with RDT during screening and negative using Real time PCR (RT-PCR)
- Patients who discontinued consenting and providing information during follow up time
- Patients whose resident area was out of Addis Ababa
- Patients who missed the main variables or information needed for further analysis

4.5 Sample size determination

Objective 1: In this study the desired 80% power to detect an improvement of 32% shorter median recovery time in the vaccinated patients than unvaccinated was used(76). By taking a median recovery time of 11 days from the previous study among unvaccinated COVID-19 patients in Ethiopia (77), in our study we expect 7.5 days of median recovery time for the vaccinated group with an effect size of 3.5 day less recovery time, at a significance level of α = 0.05, 95% confidence level and hazard ratio for the desired effect size, ∅= 1.4676 and with a maximum of 14 days follow plan (6,12). Schoenfeld formula (78) for manual survival sample size calculation formula was used. Based on this number of events required for the log rank test, d was;

$$d = \frac{4\left(z_1 - \frac{\alpha}{2} + z_1 - \beta\right)^2}{[\log(\emptyset)]^2} = 213 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

$$n = \frac{2d}{2 - e^{-\tau\lambda 0} - e^{-\tau\lambda 1}} = 258 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

After determining the final sample size, we calculated the expected number of participants lost to follow-up using an assumed attrition probability of 3%.

$$n* = \frac{n}{1-l} = 266 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

- d is Number of events required for the log rank test
- z_1-α/2 is standard normal variate for level of significance
- z_1-β is standard normal variate for power
- (∅) is hazard ratio
- e is a mathematical constant (Euler's number) in the natural logarithm
- λ0 and λ1 are hazards for the minimum (7.5 days) and maximum (11 days) median time respectively
- τ is the total follow uptime for each participant of the study (14 days in this case)
- n is the total number of enrollees in the study before adjusting to lost to follow up
- l stands for lost to follow up (3%)
- n* is the total number of the final enrollees adjusted for lost to follow up

Objective 3: a double population formula for cox regression sample size calculation was implanted to calculate sample size for the cox regression for the significant variables in the previous study.

$$n = (Z\_\alpha/2 + Z\_\beta)^2 * (p1(1-p1) + p2(1-p2)) / (p1 - p2)^2$$

Where: n = the required sample size Z_α/2 = the standard normal deviation corresponding to the desired level of significance (5%), Z_β = the standard normal deviation corresponding to the desired power (e.g., 0.84 for 80% power) p1 = the expected proportion of the event (recovery) in the reference group, and p2 = the expected proportion of the event (recovery) in the comparison group.

Previous study	Variables	Proportion of event	Sample size
(79)	Sex	P1= 0.42, p2= 0.58	169
(80)	Vaccination	P=0.32, p2= 0.68	143
(81)	Comorbidity	P1= 0.69 p2= 0.31	140

4.6 Data Source

The data source for this study was from the Armauer Hansen Research Institute (AHRI). The data was previously collected using a prospective cohort study design, which is registered with the protocol number EPHI-IRB-415-2021. The data was collected with a 14-day follow-up time duration for each COVID-19 patient, to study vaccine effectiveness and vaccination breakthrough outcomes among COVID-19 cases in Addis Ababa from January 17, 2023, to June 23, 2023. The dataset contains a total of 327 patients, including exposed and control groups or vaccinated and unvaccinated patients. The dataset contains major variables and indicators, including socio-demographic characteristics (age, sex, educational status, occupation, and family size), clinical characteristics (body mass index, smoking status, pregnancy status, previous infection, viral load, CT values, and viral variant), comorbidity, and vaccination status.

A probability simple random sampling technique was used to identify study participants. During an initial triage at the health facility, healthcare professionals collected demographic, clinical, vaccination status, and rapid diagnostic test (RDT) information using structured questionnaires administered through ODK. Further tests using PCR to confirm viral presence and genomic sequencing to identify viral variants were performed on the patients' samples. In the meantime, daily follow-up of patients was conducted via phone calls by assigned healthcare professionals. At the end of the 14-day period, a final record was submitted to the national server found at the Ethiopian Public Health Institute, including details of symptom resolution (recovery status). This record included the date the patient was deemed recovered and the decision made by healthcare professionals (Annex I).

4.7 Data Retrieval Method

In this study, cohort for the nested case control study design in the previous study was used. This study aimed to determine the time to recovery, recovery rate, and associated factors among COVID-19 patients receiving home-based isolation and care (HBIC) services in Addis Ababa. A secondary data analysis approach was employed, utilizing existing data collected during a previous study. The study did not involve active data collection. The existing data was thoroughly examined for quality and consistency, ensuring its suitability for survival outcome analysis. Data was screened for appropriateness, and ensuring completeness of variables.

After data cleaning, 273 participants remained eligible for the study. Initial raw data included 327 participants, but 17 were PCR test negative, 3 were unconfirmed with PCR, 3 were under 18 years old, 19 resided outside Addis Ababa, and 12 had missing variables (e.g., vaccination status, date of first test). Then to ensure a 1:1 ratio of vaccinated and unvaccinated participants, the final dataset was adjusted to 272 participants (136 vaccinated and 136 unvaccinated) which was the final sample size used for analysis in this study.

4.8 Study variables

Dependent variables(outcomes)

- Recovery status
- Time to recovery

Independent variables/Exposures variables/

The following variables were considered as independent variables in this study;

Sociodemographic and related variables: Age, Gender, Occupation, Family Size, Social event, Marital status, Educational Level, Hand hygiene, Mask usage and public transport usage

Clinical and related variables: Body mass index (BMI), Smoking, Pregnancy status, Symptoms, Positive contact, Previous infection history, SARS COV-2 variant, cyclic threshold (CT), Viral load value on admission, comorbidity and vaccination status.

4.9 Operational definitions and measurements

COVID-19 patient: any patient with respiratory disease symptoms or without symptoms who will tested positive for COVID-19 antigen using rapid diagnostic test as screening procedure and real time R-PCR as a confirmatory laboratory test.

Asymptomatic patient: any patient who has been positive test for COVID-19 but does not has any symptoms related to COVID-19 disease.

Symptomatic patient: any patient who tested positive for COVID-19 and has any symptoms for covid-19.

Mild Disease: Mild COVID-19 was defined as having symptoms of COVID-19 such as fever, cough, sore throat, fatigue, headache, myalgia, nausea, vomiting, diarrhea and loss of taste and smell with no shortness of breath and normal oxygen saturation (SpO_2) in room air.

Moderate Disease: was defined as COVID-19 patients with lower respiratory symptom/s, who have infiltrates on chest X-ray. They are also able to maintain oxygenation on room air ($SpO_2 \leq 94\%$) but >90% with mild pneumonia.

Severe Disease: was defined as COVID-19 patients with $SpO_2 \leq 90\%$ in room air with >50% lung infiltrates on chest radiograph.

Deisolation: deisolation is when someone with COVID-19 or exposure is cleared by health authorities based on symptom resolution and time elapsed since exposure, indicating they're no longer infectious.

Recovery: Recovered from COVID-19 disease as reported by patient and confirmed by health professional based on the presence or absence of symptoms and other health complications. The patient should be free of any symptoms including fever.

Event: Achieving recovery from COVID-19 disease within the follow up time as defined for recovery.

Censoring: COVID-19 patients lost to follow-up, transferred to health facility, died, discharged against consent they were provided for the study and completed the follow-up period without achieving recovery.

Time to recovery: The time in days, between the dates first laboratory tested positive using RDT of COVID-19 infection to recovery from COVID-19 as self-reported by the patient and confirmed by the appropriate health professional during follow up period as defined in recovery (in days).

Median time of recovery: is the time when 50% of the patients recovered

Home based isolation and care: Isolation of patients with mild, moderate and without symptoms in their home after screened and positive for SARS-CoV-2 virus, by ensuring availability of infection prevention materials, caregivers, adequate space and assisted by health care workers remotely.

Non-pharmaceutical interventions (NPIs): refers in this study refers to regular use of face masks in risk area, hand hygiene practice when exposed to risk area and reduced use of public transport to minimize the risk of severe COVID-19 disease.

Lost: COVID-19 patients who left from the study with unknown status of the expected outcome

Smoking: defined as individuals who reported smoking tobacco products (such as cigarettes, cigars, or pipes) regardless of frequency or quantity at the time of the assessment, or who had quit smoking within the last 12 months prior to the study

Close contact with confirmed case: is defined as being within 1 meter of the patient(s) who has been confirmed to have SARS-CoV-2 virus infection at any time within the last 14 days.

Social Event attendance: Individuals who attended a social indoor event or gathering with more than 10 people in the 14 days prior to testing positive for SARS-CoV-2 virus were considered social event attendees. This includes activities such as attending church, parties, weddings, sporting events, or visiting a bar or restaurant.

Public Transport Usage: Individuals who used public transportation, such as buses, shared vans, or trains, as their means of transportation more than once within the 14 days prior to testing positive for SARS-CoV-2 virus were considered public transport users.

Mask Usage: Individuals who often or always wore a mask in indoor settings outside their home and moreover in high-risk area such as mass gathering place were considered mask users.

Hand Hygiene: Individuals who always practiced hand hygiene using alcohol-based hand rub or soap and water as recommended after exposure to potential SARS-CoV-2 virus contaminants were considered to have good hand hygiene.

Comorbidities: Underlying conditions such as diabetes mellitus, cardiovascular disease, hypertension, asthma, rheumatic disorders, lung disease, renal disease, and liver disease were considered as comorbidities in this study.

4.10 Data management

Data and information obtained was handled on confidential and secured manner starting from time of receiving waiver to result dissemination/or out of the project life time mentioned in this document. Computer was used to clean data for further analysis. After the data encoding and cleaning ended the data was checked for some quality and uncleaned issues, additional data clearance procedures was performed based on the objectives of the study, method of data analysis and software that will be used to analyze the data.

4.11 Data analysis

Time to recovery: The overall survival estimate was computed using the Kaplan-Meier survival estimate. The Kaplan-Meier method was used to estimate the median time to recovery from covid-19 illness during the follow up time using Kaplan-Meier curve method.

Comparison between groups: After constructing the Kaplan-Meier curve for categories of the variables, then conducted a log-rank test to scrutinize the disparity in recovery times between the categories by employing 95% confidence level. If the resulting p-value fell below the predetermined confidence threshold or p values of 0.05, it was taken as there was significant distinction in the time taken for event recovery between the categories.

Covariate identification: A Cox proportional hazard regression analysis was conducted to identify covariates associated with recovery time, ensuring the proportional hazard assumption was met through the Schoenfeld residuals test. Bivariable Cox regression was performed for each covariate which met the proportional hazard assumptions to select variables to be interred in to the multivariable Cox regression. Covariate selection was conducted using a significance threshold of $p \leq 0.25$. Following the identification of significant variables through bivariable Cox regression, multivariable regression was employed to ascertain factors associated with the duration of COVID-19 recovery.

Recovery rate: The cumulative recovery rate for each group was calculated as a percentage of with number of recoveries within the group to the total number of recoveries. A survival person-time method was used in recovery incidence rate calculation, where the total time at risk for each individual was calculated during the follow-up period. The recovery incidence density rate was then determined by dividing the total number of recovered individuals by the total person-days at risk.

Model Adequacy testing: The proportional hazard assumption of the regression model was evaluated using both statistical tests and graphical plots to assess the overall model fit. Schoenfeld residual proportional hazard (PH) test was implemented to test either the proportional hazards assumption is met or not for the overall model. Cox-Snell residual plot was used to visually inspect the goodness of fit of the overall Cox regression model. Furthermore, Harrell's C or concordance index (C-index) was implemented to test the predictive accuracy of the cox regression model which measures concordance between the predicted probabilities and the observed outcomes.

4.12 Data quality assurance

Before review and abstraction of data records, an assessment of data appropriateness and quality was conducted. This proactive step was aimed to identify and address any inconsistencies, inadequacies, or issues related to reliability, timeliness, and completeness in the data.

4.13 Ethical consideration

Prior to commencing this research, ethical clearance was obtained from the Ethical Review Committee at Addis Ababa University, School of Public Health. Written consent was waived by EPHI-AHRI in accordance with their institutional data sharing policy. Confidentiality and privacy of all information were rigorously maintained throughout the study. The study design prioritized the well-being of participants, ensuring no or minimal harm. Moreover, full adherence was given to any consent agreements established during the primary data collection process of the preceding study.

4.14 Dissemination of findings

The findings from this study will be communicated with Addis Ababa University, Ministry of Health (MoH) and Addis Ababa Health Bureaus through public thesis defense, poster presentation and technical report. Additionally, it will be published in peer-reviewed journal.

5. Results

5.1 Socio-demographic characteristics

In this study about 272 COVID-19 patients were included for final analysis. Female participants were slightly dominant in the study reaching 154(56.62%) where 89.6% of them recovered. The mean age of the participants was 36 (SD ±14.8) years and with the age group 30-39 years attained the highest percentages of recoveries. The majority of the study participants were office workers (136, 50%) followed by housewives. Participants with primary education had the highest number of participants (83, 30.5%), while those with non-formal education had the lowest participants (35, 12.9%). Smoking was less prevalent at 7.35% among the participants (**Table 5.1**).

Table 5.1 Sociodemographic and related characteristics of COVID-19 patients at HBIC, Addis Ababa, Ethiopia (January 17 - June 23, 2023)

Variable	Category	Recovery status		Total, n (%)
		Recovered, n (%)	Censored, n (%)	
Sex	Male	103(87.3)	15(12.7)	118(43.4)
	Female	138(89.6)	16(10.4)	154(56.6)
Age	18-29	95(86.4)	15(13.6)	110(40.4)
	30-39	66(95.7)	3(4.3)	69(25.4)
	40-49	36(87.8)	5(12.2)	41(15.1)
	>50	44(84.6)	8(15.4)	52(19.1)
	Marchant	6(85.7)	1(14.3)	7(2.6)
	Office Worker	121(89)	15(11.0)	136(50)
Occupation	self employed	33(89.2)	4(10.8)	37(13.6)
	student	18(90)	2(10.0)	20(7.3)
	Retired	12(92.3)	1(7.7)	13(4.8)
	Housewife	51(86.4)	8(13.6)	59(21.7)
Educational level	Non-formal	26(74.3)	9(25.7)	35(12.9)
	Primary	76(81.6)	7(8.4)	83(30.5)
	Secondary	66(89.2)	8(10.8)	74(27.2)
	Higher	73(91.3)	7(8.7)	80(29.4)
Social event attendance	Yes	157(89.2)	19(10.8)	176(64.7)
	No	84(87.5)	12(12.5)	96(35.7)
Using mask	Yes	119(93.7)	8(6.3)	127(46.7)
	No	122(84.1)	23(15.9)	145(53.3)
Smoking status	Yes	11(55)	9(45.0)	20(7.4)
	No	230(91.3)	22(8.7)	252(92.6)
Public transport usage	Yes	186(86.1)	30(13.9)	216(79.4)
	No	55(98.2)	1(1.8)	56(20.6)
Hand hygiene practice	Yes	68(93.2)	5(6.8)	73(26.8)
	No	173(86.9)	26(13.1)	199(73.2)
	0-2	41(82)	9(18)	50(18.4)
Family size	3-5	133(90.5)	14(9.5)	147(54)
	>6	67(89.3)	8(10.7)	75(27.6)

5.2 Clinical characteristics

About half of the participants (50%) had received at least a single dose of COVID-19 vaccine. Comorbidities were present in 15.1% of the participants. Prior infection was reported by 15.4% of the participants. Approximately 68.7% of the participants were categorized as having a normal BMI, while 24.4% were overweight and 6.9% were either underweight or obese. The majority of the patients (89%) had a viral load below 25 cycles, while 5.1% had a viral load between 25-35 cycles and 5.9% had a viral load above 35 cycles. The majority (94.1%) of the participants were infected with Omicron variants of the SARS-CoV-2 virus, while 5.9% had undetectable viral variants. The study found an overall cumulative recovery rate of 88.6% within the 14-day follow-up period. The recovery rate was higher among vaccinated patients (91.9%) compared to unvaccinated patients (85.3%). Participants with no comorbidities had a higher recovery rate (91.3%) compared to those with comorbidities (73.2%). Similarly, participants without a positive contact history had a higher recovery rate (90.5%) compared to those with a positive contact history (80.4%). Participants with a previous SARS-CoV-2 infection had a higher recovery rate (97.6%) compared to those without a previous infection (87.0%). There were no reported deaths or defaults in this study. The remaining participants (11.4%) were recorded as censored, which included those who survived past the follow-up time (5.15%), were lost to follow-up (4.41%), or were transferred to a health facility (1.84%).

Table 5.2 Clinical characteristics of COVID-19 patients under HBIC, Addis Ababa, Ethiopia (January 17 - June 23, 2023)

Variable	Category	Recovery status		Total
		Recovered, n (%)	Censored, n (%)	
Vaccination	Vaccinated	125(91.9)	11(8.1)	136(50)
	Unvaccinated	116(85.3)	20(14.7)	136(50)
Comorbidity	Yes	30(73.2)	11(26.8)	41(15.1)
	No	211(91.3)	20(8.7)	231(84.9)
Positive contact	Yes	41(80.4)	10(19.6)	51(18.8)
	No	200(90.5)	21(9.5)	221(81.2)
Previous infection	Yes	41(97.6)	1(2.4)	42(15.4)
	No	200(87.0)	30(13.0)	230(81.6)
BMI	Overweight	60(90.9)	6(9.1)	66(24.4)
	underweight	6(85.7)	1(14.3)	7(2.5)
	Obese	10(83.3)	2(16.7)	12(4.4)
	Normal	165(89.2)	22(10.8)	187(68.7)
Viral load	<25	214(88.4)	28(11.6)	242(89)
	25-35	13(92.9)	1(7.1)	14(5.1)
	35+	14(87.5)	2(12.5)	16(5.9)
Viral Variants	Omicron	227(88.7)	29(11.3)	256(94.1)
	Undetectable	14 (87.5)	2(12.5)	16(5.9)

All patients included in this study exhibited mild symptoms of COVID-19, characterized by low-grade fever, mild cough, and a general sense of fatigue. Headache was the most commonly reported symptom, while dyspnea was the least frequent.

Table 5.3 Descriptive Analysis of Symptomatic Characteristics of COVID-19 Patients under HBIC, Addis Ababa (January 17 - June 23, 2023).

Variables (symptoms)	**Category**	**Recovery status**		**Total**
		Recovered, n (%)	**Censored, n (%)**	
Cough	Yes	101(80.2)	25(19.8)	126(46.3)
	No	140(95.9)	6(4.1)	146(53.7)
Fatigue	Yes	98(83.8)	19(16.2)	117(43)
	No	143(92.3)	12(7.7)	155(57)
Headache	Yes	112(82.3)	21(17.8)	133(49)
	No	129(92.8)	10(7.2)	139(51)
Sore throat	Yes	102(87.2)	15(17.8)	117(43)
	No	139(86.7)	16(13.3)	155(57)
Dyspnoea	Yes	14(66.7)	7(33.3)	21(7.7)
	No	227(90.4)	24(9.6)	251(92.3)
Loss smell	Yes	36(80.0)	7(20.0)	43(15.8)
	No	205(89.5)	24(10.5)	229(84.2)
Loss taste	Yes	70(84.3)	13(15.7)	83(30.5)
	No	171(90.5)	18(9.5)	189(69.5)
Fever	Yes	118(90.8)	12(9.2)	130(47.8)
	No	123(86.6)	19(13.4)	142(52.2)
Coryza	Yes	9 (81.8)	2(18.2)	11(4)
	No	232(88.9)	29(11.1)	261(96)
Myalgia	Yes	17(77.3)	5(22.7)	22(8.1)
	No	224(89.6)	26(10.4)	250(91.9)

5.3 Recovery rates

The overall duration of follow-up time was 2070 person-days (PDs). The overall incidence density rate of recovery was 11.64 events per 100 person days (PDs) (95% CI: 10.20-13.20). Vaccinated patients had incidence density rate of 13.19 per 100 PDs (95% CI: 11.00-15.70). In comparison, unvaccinated patients had lower rate of 10.34 per 100 PDs (95% CI: 8.60-12.40). Patients with comorbidities had incidence density rate of 8.1 per 100 PDs (95% CI: 5.60-11.50), compared to those without comorbidities who had a higher rate of 12.41 per 100 PDs (95% CI: 10.80-14.20). Smokers had lower incidence density rate, 5.33 per 100 PDs (95% CI: 2.90-9.60) compared to non-smokers, 12.33 (95% CI:10.80-0.140) per 100 PDs. Patients with history of prior infection had incidence density rate of 18.98 (95% CI:13.50-25.00) per 100 PDs, while those without had rate of 10.78 (95% CI: 9.40-12.40) per 100 PDs. **Table 5.4** provides valuable insights into how different factors may influence the recovery rate per persons days.

Table 5.4 Incidence density of recovery among COVID-19 patients under HBIC, using significant on log-rank test and multivariable Cox regression, Addis Ababa, Ethiopia (Jan17 - June 23, 2023)

Variable	Category	Person time	Event	Incident rate per 100 PDs (95%CI)
Vaccination status	Yes	948	125	13.19(11.00-15.70)
	No	1122	116	10.34(8.60-12.40)
Comorbidity	Yes	371	30	8.10(5.60-11.50)
	No	1699	2011	12.41(10.80-14.20)
Public Transport	Yes	1698	186	10.95(9.40-12.60)
	No	372	55	14.78(11.30-19.20)
Smoking status	Yes	206	11	5.33(2.90-9.60)
	No	1864	230	12.33(10.80-14.00)
Previous infection	Yes	216	41	18.98(13.90-25.70)
	No	1854	200	10.78(9.30-12.30)
Using mask	Yes	801	119	14.85(0.124-17.70)
	No	1269	122	9.61(8.10-11.40)
Hand hygiene	Yes	489	68	13.90(10.90-17.60)
	No	1581	173	10.94(9.40-12.70)
Fatigue	Yes	996	98	9.83(8.00-11.90)
	No	1074	143	13.31(11.30-15.60)
Overall		**2070**	**241**	**11.64(10.20-13.20)**

Footnote: PDs stand for person days

5.4 The overall Kaplan Meir survival curve estimate

Kaplan-Meier survivor functions curve was used to measure the survival time. The overall median time of recovery was 7 days (IQR 6-9). Unvaccinated individuals had longer median recovery time compared to vaccinated individuals, 8 days (IQR 7-10) and 7 days (IQR 5-8) respectively.

The first events occurred on the second day of follow up time and the survival probability were 0.9890 (95% CI: 0.96-0.99) with standard error of 0.0063. Significant drop was observed on the day 7 and 61 events occurred with 0.4837 survival probability. The survival probability remained unchanged from day 13 to day 14, as no new events were observed during that time period. **Table 5.5** shows decreasing trend in the survival probability over time.

Table 5.5 Life table for COVID-19 patients receiving Home-Based Isolation and Care in Addis Ababa, Ethiopia (January 17 - June 23, 2023)

Time in days	Beg. total	Event	Censored	Probability of survival	Standard error	[95% conf. int.]	
0	272	0	0	1.00	0.00	---	---
1	272	0	0	1.00	0.00	---	---
2	272	3	0	0.9890	0.0063	0.96	0.9964
3	269	11	0	0.9485	0.0134	0.9146	0.9692
4	258	22	0	0.8676	0.0205	0.8213	0.9027
5	236	18	2	0.8015	0.0242	0.7489	0.8442
6	216	24	2	0.7124	0.0275	0.6545	0.7624
7	190	61	2	0.4837	0.0305	0.4227	0.5419
8	127	34	4	0.3542	0.0293	0.2971	0.4116
9	89	36	3	0.2109	0.0254	0.1635	0.2625
10	50	16	1	0.1434	0.0222	0.1033	0.1899
11	33	5	0	0.1217	0.0208	0.0846	0.1660
12	28	9	3	0.0826	0.0178	0.0522	0.1217
13	16	2	0	0.0723	0.0170	0.0437	0.1102
14	14	0	14	0.0723	0.0170	0.0437	0.1102

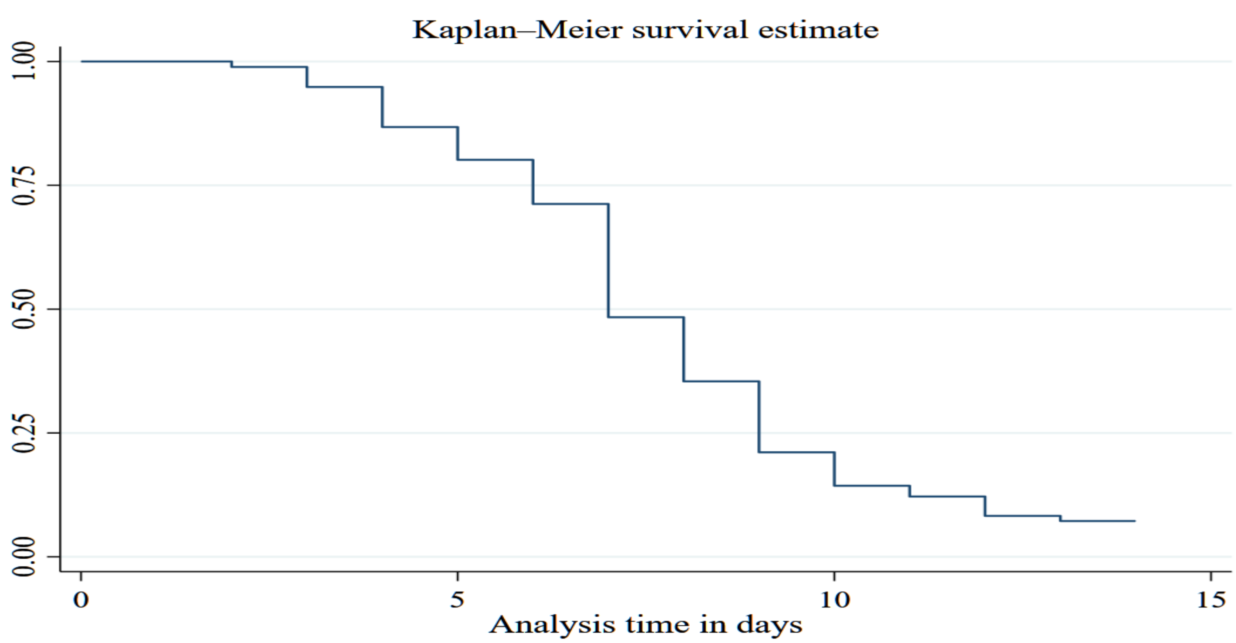

Figure 5.1 Overall Kaplan-Meier survival curve for COVID-19 patients followed at HBIC, Addis Ababa, Ethiopia (January-June 2023)

5.5 Kaplan-Meier survival graphs for selected predictors

Vaccination appears to provide some protective effect, as reflected in the lower survivor function for vaccinated individuals compared to unvaccinated individuals within respective median survival time. The unvaccinated group has longer survival time compared to the vaccinated group. In this study, patients with history of SARS-COV-2 virus infection have lower survival proportion with median survival time of five days compared to their counter parts**.** Patients who have smoking history exhibit a higher initial survivor function (up to time 6), but it decreases over time. Generally, Non-smokers have a higher survivor function, indicating better survival probabilities with seven days median survival time.

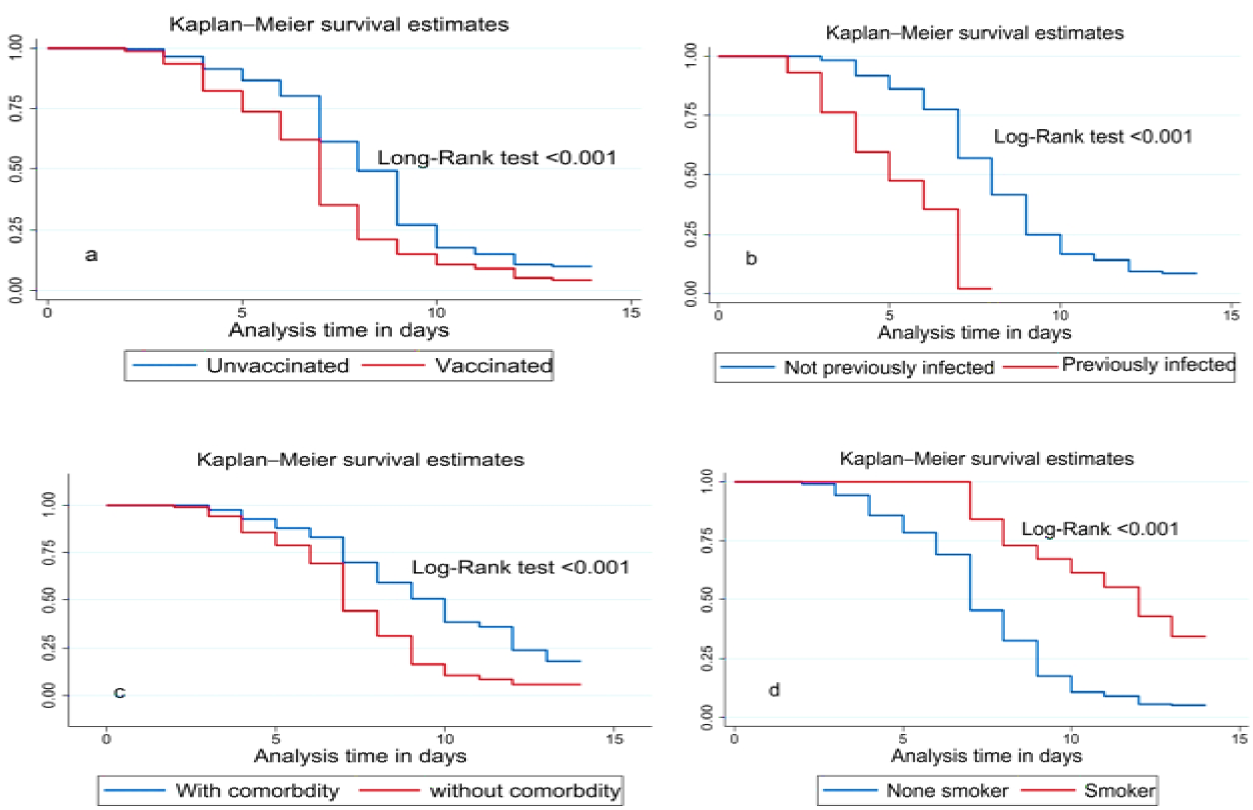

Figure 5.2 Kaplan-Meier survival curves for COVID-19 patients with and without vaccination followed at HBIC, Addis Ababa, Ethiopia (January-June 2023): **a**) by vaccination status, **b**) by prior infection status, **c)** by comorbidity status and **d**) by smoking status

The log-rank test was used to assesses whether differences in the survival function exist among specified groups and the levels of factor variable. Those variables such as vaccination status ($p<0.0001$), Comorbidity ($p<0.0001$), positive contact ($p<0.0018$), smoking status($p<0.0001$), previous infection (p<0.0001), using public transportation (p<0.0036) and hand hygiene (p<0.0005) have significant difference in their survival functions. **Table 5.6** showed the difference in survival function between groups of selected variables.

Table 5.6 Log-Rank test for survival function differences in COVID-19 patients by selected significant Covariates (Addis Ababa, Ethiopia, January 17 - June 23, 2023)

Variable	**Category**	**Observed effects**	**Expected effects**	**χ^2**	**Log-rank test (pr> χ^2)**
Vaccination status	Yes	125	98.38	16.3	0.0001
	No	116	142.62		
Age	18-29	95	88.29	6.78	0.0791
	30-39	66	56.14		
	40-49	36	43.83		
	>50	44	52.74		
Comorbidity	Yes	30	50.32		
	No	211	190.68	14.27	0.0002
Public Transport	Yes	186	200.73	8.49	0.0036
	No	55	40.27		
Smoking status	Yes	11	30.42	19.69	0.0001
	No	230	210.58		
Educational level	Non-formal	26	38.73		
	Primary	76	72.69	7.48	0.0580
	Secondary	66	65.65		
	Higher	73	63.93		
Prior infection	Yes	41	14.00		
	No	200	227.00	69.42	0.0001
Positive contact	Yes	41	58.99	9.74	0.0018
	No	200	182.01		
Using mask	Yes	119	69.66		
	No	122	171.34	69.15	0.0000
Fatigue	Yes	98	130.57		
	No	143	110.43	24.21	0.0001
Hand hygiene	Yes	68	48.90		
	No	173	192.10	12.27	0.0005
	Overweight	60	63.38	5.48	0.1400
BMI	underweight	6	8.51		
	Obese	10	15.94		
	Normal	165	153.16		

Footnote: Variables included in this table are those either significant for log rank test or later on multivariable cox regression or both.

5.6 Model Adequacy Testing

The proportional hazard assumption of the regression model was evaluated using statistical tests and graphical plots to assess the overall model fit. The study examined a null and alternative hypothesis with Schoenfeld residual proportional hazard (PH) test to assess PH assumptions as follows:

H0 (Null Hypothesis): The proportional hazards assumption is met, meaning that the hazard ratio is constant over time.

H1 (Alternative Hypothesis): The proportional hazards assumption is not met, meaning that the hazard ratio is not constant over time.

The test produced chi-squared (χ^2) statistic of 32.06 and a corresponding p-value of 0.5139. Since p-value was higher than 0.05 and the test failed to reject the null hypothesis. Based on this, the test result showed that the hazard ratio was likely to be constant over time which indicates proportional hazards assumption was not violated. Therefore, Cox regression model was fit for the dataset and the model was suitable for making inferences about the relationships between the covariates and recovery time.

Furthermore, the Cox-Snell residual plot was used to visually evaluate the goodness of fit of the Cox regression model. The plot revealed that the observed residuals closely adhered to the reference line associated with the expected residuals, aligning within a 45-degree angle. This indicates that the model fits the actual data well and effectively captures the underlying recovery patterns of the COVID-19 patients under study.

The predictive accuracy of the model was assessed using Harrell's C (C-index). The C-index analysis revealed a value of 0.8288, indicating that the model correctly predicts the hazard of the event occurring for 82.88% of the patient pairs. This high concordance index indicates the model has strong predictive power and effectively capturing the relationships between the covariates and the outcome variable (time to recovery).

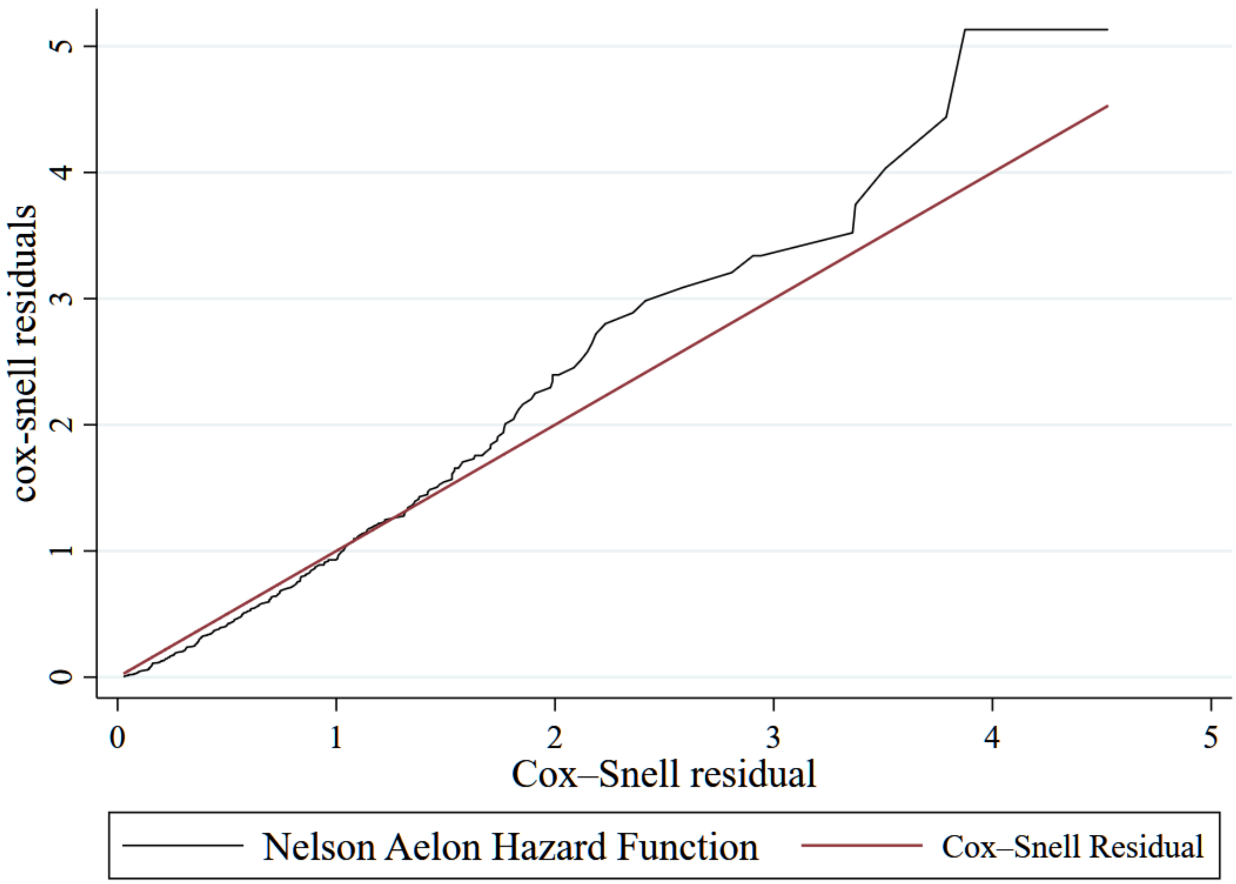

Figure 5.3 Cox-Snell residual plot assessing model fit for Home-Based COVID-19 Care data in Addis Ababa (January-June 2023).

Finally, graphical assessment was performed to check the proportional hazards (PH) assumption for covariates significantly associated with recovery time. This was done using the Cox-Snell residuals. The plot of –ln (-ln (Survival)) against the natural logarithm of the analysis time (–ln (Analysis Time)) was generated (Figure 5.7). The resulting graphs were roughly parallel, not crossing each other frequently, indicating that the PH assumption was not violated. This suggests that applying the multivariable Cox regression analysis was suitable for the current data being used

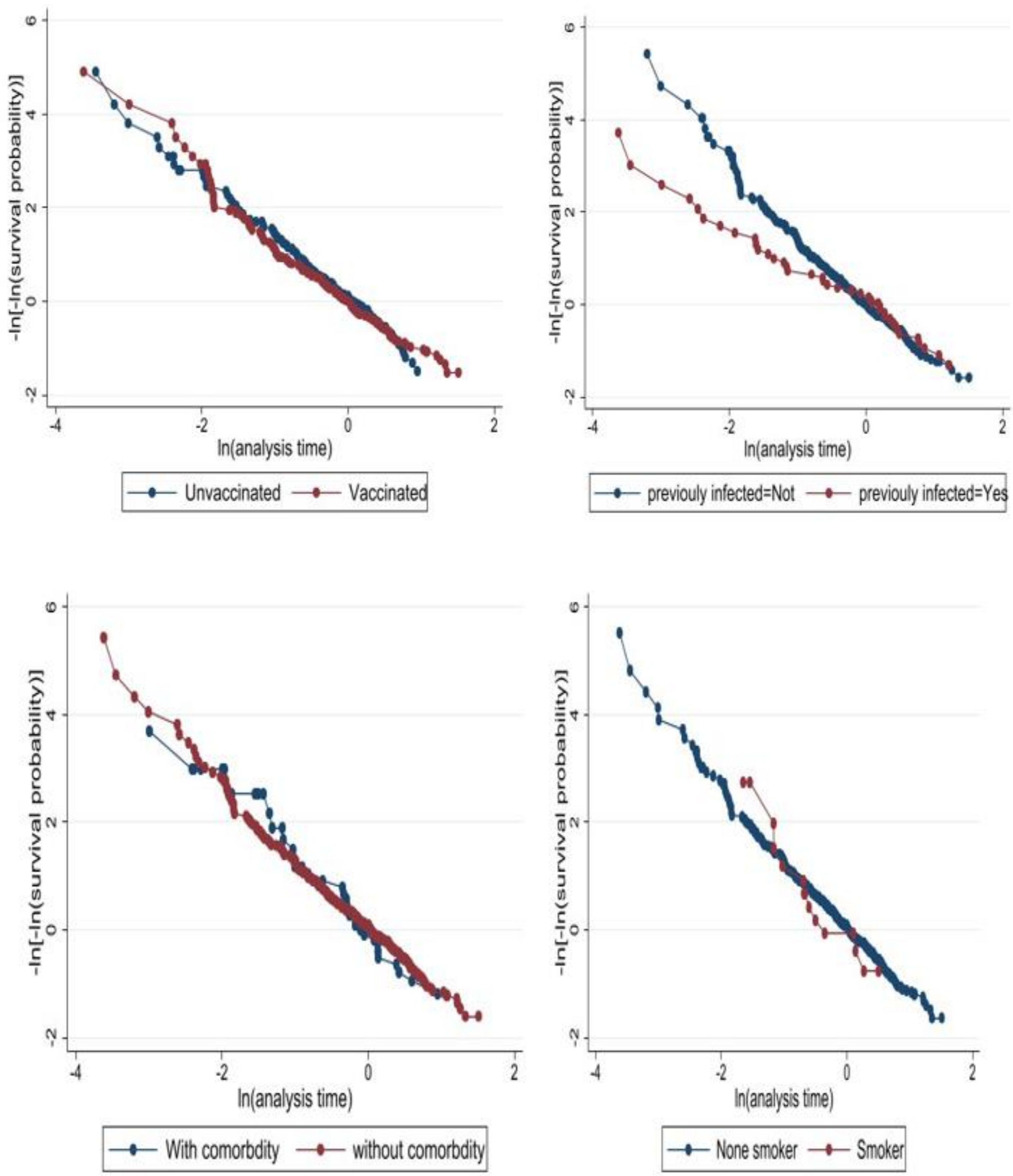

Figure 5.4 Graphical assessment of assumptions for statistically significant factors in Cox Regression Model.

5.7 Predictors of recovery time from COVID-19 disease among home isolated patients

To assess the impact of independent covariates on the outcome, we employed the Cox proportional hazards regression methods. Bivariable Cox regression was applied for examining the effect of individual predictors on the outcome variable and multivariable Cox regression was considered to observe the joint effects of those predictor variables on the outcome (time to recovery).

Bivariable Analysis

This study examined the association between one predictor variable (independent variable) and the survival outcome (time to recovery) using the bivariable cox regression to get insights into how individual predictors affect time to recovery independently. Based on this, variables such as Sex, age group, vaccination status, vaccine doses, comorbidity, hand hygiene, positive contact, public transport, smoking status, previous infection, using mask and symptoms such as, cough, fatigue, headache, sore throat, dyspnea, smell loss, taste loss, educational level, viral load, social event, occupation, and fever were associated to the time to recovery (outcome variable) of COVID-19 patients at $p \leq 0.25$ during the bivariate analysis. Variables such as family size, CT Value, and the presence of coryza and myalgia symptoms were not found to be statistically significant predictors of the outcome at a significance level of $p \leq 0.25$ at this stage.

Multivariable Analysis

Variables with a p-value of 0.25 or less during bivariable analysis and meeting the proportionality hazard assumption testing were inserted into the multivariable analysis. Variables such as vaccine doses and social event participation were excluded from the multivariable analysis due to failure to meet the proportionality hazard assumption and concerns regarding collinearity.

Vaccinated individuals had 62% higher hazard of recovery compared to unvaccinated individuals **(AHR: 1.62, 95% CI:1.181-2.231).** After adjusting for other variables, individuals aged 30-39 had a 2.13 times higher hazard of recovery compared to the reference group (>50) **(AHR: 2.13 95% CI:1.274-3.583)**. Individuals without comorbidities had an 87% higher hazard of recovery compared to those with one or more comorbidities **(AHR: 1.87 95% CI:1.165-3.014).** Using public transport was associated with a 55% lower hazard of recovery from COVID-19 illness compared to who did not use public transport **(AHR: 0.45 95% CI: 0.320-.655).** Smokers had a significantly lower hazard of recovery (44% lower) compared to non-smokers **(AHR: 0.44 95% CI: 0.223-0.869).** Individuals with a previous infection with one of the variants of SARS-COV-2 virus had a 2.11-time higher hazard of recovery compared to those without a previous infection **(AHR: 2.11 95% CI 1.374-3.226).** Absence of using mask was significantly associated with lower hazard of recovery (61% lower) compared to using mask **(AHR: 0.39 95% CI: 0.284-0.555).** absence of fatigue (**AHR 1.48 95% CI:1.08-2.04)** was significantly associated with time to recovery. Individuals who did not practice regular hand hygiene had a 28% lower hazard of recovery compared to those who did regular hand hygiene practice **(AHR: 0.72 95% CI: 0.532-0.991).** Overweight and Underweight individuals had a significantly lower hazard of recovery, 33% (**AHR: 0.67 95% CI: 0.483-0.952**) and 62% (**AHR: 0.38 95% CI: 0.154-0.969**) respectively lower compared to those with normal BMI. Other variables included in the multivariable analysis such as Sex, educational level, positive contact, viral load, occupation, cough, headache, sore throat, dyspnea, loss of smell, loss of taste, and fever showed no significant differences in hazard.

Table 5.7 Factors Associated with Time to Recovery in Home-Isolated COVID-19 Patients: Cox Regression Analysis (Addis Ababa, January 17 - June 23, 2023).

Variable	Category	Recovery status		CHR (95% CI)	AHR (95% CI)	P-value
		Recovered, n(%)	Censored, n(%)			
Vaccination	Yes	125(91.9)	11(8.1)	1.58(1.22-2.03)	1.62(1.18-2.23)	0.003*
	No	116(85.3)	20(14.7)	**1**	**1**	
Sex	Male	103(87.3)	15(12.7)	0.83(0.64-1.07)	0.89(0.64-1.24)	0.519
	Female	138(89.6)	16(10.4)	Ref	Ref	
Age	18-29	95(86.4)	15(13.6)	1.29 (0.90-1.85)	1.37(0.82-2.30)	0.225
	30-39	66(95.7)	3(4.3)	1.41(0.96-2.07)	2.13(1.27-3.58)	0.004*
	40-49	36(87.8)	5(12.2)	0.99(0.63-1.53)	1.49(0.85-2.61)	0.154
	>50	44(84.6)	8(15.4)	**1**	**1**	
Comorbidity	Yes	30(73.2)	11(26.8)	**1**	**1**	
	No	211(91.3)	20(8.7)	1.89(1.28-2.78)	1.87(1.16-3.01)	0.010*
Positive contact	Yes	41(80.4)	10(19.6)	0.63(0.44-0.88)	0.73(0.50-1.07)	0.111
	No	200(90.5)	21(9.5)	**1**	**1**	
Public Transport	Yes	186(86.1)	30(13.9)	0.67(0.50-0.91)	0.45(0.32-.65)	0.000*
	No	55(98.2)	1(1.8)	**1**	**1**	
Smoking status	Yes	11(55)	9(45.0)	0.32(0.17-0.59)	0.44(0.22-0.86)	0.018*
	No	230(91.3)	22(8.7)	**1**	**1**	
Education	Informal	26(74.3)	9(25.7)	**1**	**1**	
	Primary	76(81.6)	7(8.4)	1.56(0.99-2.44)	1.17(0.71-1.92)	0.530
	Secondary	66(89.2)	8(10.8)	1.50(0.95-2.37)	1.31(0.74-2.30)	0.343
	Higher	73(91.3)	7(8.7)	1.71(1.08-2.67)	1.66(0.95-2.93)	0.074
Prior infection	Yes	41(97.6)	1(2.4)	3.73(2.59-5.36)	2.11(1.37-3.22)	0.001*
	No	200(87.0)	30(13.0)	**1**	**1**	
Using mask	Yes	119(93.7)	8(6.3)	**1**	**1**	
	No	122(84.1)	23(15.9)	0.37(0.28-0.48)	0.39(0.28-0.55)	0.000*
Cough	Yes	101(80.2)	25(19.8)	**1**	**1**	
	No	140(95.9)	6(4.1)	1.77(1.36-2.30)	1.29(0.95-1.73)	0.092
Fatigue	Yes	98(83.8)	19(16.2)	**1**	**1**	
	No	143(92.3)	12(7.7)	1.77(1.36-2.30)	1.48(1.08-2.04)	0.014*
Headache	Yes	112(82.3)	21(17.8)	**1**	**1**	
	No	129(92.8)	10(7.2)	1.40(1.09-1.81)	1.17(0.87-1.56)	0.218
Sore throat	Yes	102(87.2)	15(17.8)	**1**	**1**	
	No	139(86.7)	16(13.3)	1.52(1.17-1.97)	1.25(0.92-1.71)	0.145
Dyspnoea	Yes	14(66.7)	7(33.3)	**1**	**1**	
	No	227(90.4)	24(9.6)	2.49 (1.44-4.28)	1.71(0.95-3.08)	0.071
Loss smell	Yes	36(80.0)	7(20.0)	**1**	**1**	
	No	205(89.5)	24(10.5)	1.67(1.16-2.38)	1.12(0.72-1.75)	0.605
Loss taste	Yes	70(84.3)	13(15.7)	**1**	**1**	
	No	171(90.5)	18(9.5)	1.35(1.02-1.78)	1.13(0.81-1.58)	0.455

Table 5.7 (Continued)

Variable	Category	Recovery status		CHR (95% CI)	AHR (95% CI)	P-value
		Recovered, n (%)	Censored, n (%)			
Fever	Yes	118(90.8)	12(9.2)	**1**	**1**	
	No	123(86.6)	19(13.4)	0.82(0.63-1.05)	0.87(0.65-1.17)	0.371
Hand hygiene	Yes	68(93.2)	5(6.8)	**1**	**1**	
	No	173(86.9)	26(13.1)	0.64(0.48-0.85)	0.72(0.53-0.99)	0.044*
Occupation	Marchant	6(85.7)	1(14.3)	0.97(0.41-2.27)	1.47(0.56-3.84)	0.429
	Office Worker	121(89)	15(11.0)	1.270(.91-1.75)	0.88(0.58-1.33)	0.556
	Self employed	33(89.2)	4(10.8)	1.14(0.73-1.76)	1.10(0.61-1.79)	0.886
	Student	18(90)	2(10.0)	1.18(0.68-2.02)	1.11(0.58-2.09)	0.747
	Retired	12(92.3)	1(7.7)	0.97(0.51-1.82)	0.61(0.26-1.39)	0.240
	Housewife	51(86.4)	8(13.6)	**1**	**1**	
BMI	Overweight	60(90.9)	6(9.1)	0.89(0.65-1.17)	0.67(0.48-0.95)	0.025*
	Underweight	6(85.7)	1(14.3)	0..65(0.28-1.47)	0.38(0.15-0.96)	0.043*
	Obese	10(83.3)	2(16.7)	0.58(0.30-1.09)	0.52(0.25-1.08)	0.082
	Normal	165(89.2)	22(10.8)	**1**	**1**	
Viral load	<25	214(88.4)	28(11.6)	0.61(0.35-1.06)	1.23(0.67-2.26)	0.500
	25-35	13(92.9)	1(7.1)	0..67(0.31-1.43)	1.58(0.65-3.81)	0.304
	35+	14(87.5)	2(12.5)	**1**	**1**	

6. Discussion

While Home-Based Isolation and Care (HBIC) has been effective for managing COVID-19 patients, gaps remain in understanding recovery timeframes and associated factors. This study investigated recovery times and associated factors among COVID-19 patients under HBIC in Addis Ababa using multivariable Cox regression analysis. The findings will help set realistic recovery expectations for patients, inform clinical decisions, and aid in developing evidence-based HBIC guidelines.

In this study, the median recovery time for COVID-19 patients under HBIC was seven 7 days with an interquartile range (IQR) of 6-9 days. This finding aligns with a similar report from Mexico among hospitalized COVID-19 patients (82). It was shorter than the 15 days median recovery time in India and the 13.8 days average recovery time reported from Pakistan for patients opting for home isolation (83,84). It was also shorter than 9-18 days median recovery time reported from facility-based care in various regions of Ethiopia (22,25,26,28,30,81). This implies that Home-Based Isolation and care is effective in reducing isolation and median recovery time among for COVID-19 patients (15). Nonetheless, it was higher than 5 and 4 days of median recovery times reported Ethiopia and Iran, respectively (29,32). This disparity may be due to access to healthcare services, sociodemographic variability, and difference in length of follow-up time across the study settings (30,31,49).

Vaccinated patients exhibited shorter median recovery time (7 days, IQR 5-8) compared to unvaccinated individuals (8 days, IQR 7-10). This indicates that vaccinated individuals have at least one day earlier recovery compared to unvaccinated individuals, this might be due to vaccine contribution to faster recovery from COVID-19 illness (34,85). The narrow disparity in the median time to recovery between the two groups could due to viral variant (omicron in this case), previous infection and vaccination doses (49,56). This finding was in line with reported from California and Saudi Arabia where vaccinated patients had 6.5 and 7 days recovery time respectively (86,87). On the other hand the median time of recovery in this finding was shorter than 10 days and 14 days median time of recovery among vaccinated groups reported from India and Republic of Korea (35,88). This variation could due to length of follow up time, viral variant type, severity of the disease, and sociodemographic variability (30,38,56).

The study found an overall recovery incidence density rate of 11.64 per 100 person-days (PDs), which aligns with the 11.99/100 PDs rate reported from Southwestern Ethiopia (30). However, it was lower than 13.79/100 PDs from Assosa (81). However, it was higher rate than 4.38 and 7.84 rates per 100 PDs reported from other parts of the country (22,28), indicating potentially faster recovery rate among COVID-19 patients under HBIC. Disparity in the recovery incidence density rate between the current and previous studies could be possibly due to the difference in viral variants, study setting, study design, vaccination and length follow up time (79,89,90).

Vaccination also appears to have significant impact on recovery incidence density rate. Vaccinated patients had recovery incidence density of 13.19 per 100 person-days, whereas the rate was 10.34 per 100 PDs among unvaccinated patients. This finding affirmed substantial benefit of vaccines in increasing recovery rates for COVID-19 patients. This underscores the critical role of vaccination to mitigate the adverse effects of COVID-19 (34,91). Interestingly, this finding was higher than 11.15 incidence density per 100 PDs reported among vaccinated patents in Mexico (92). This disparity could be due to the differences in study population, hybrid-immunity from prior infection, disease severity, and study setting (25,49,76).

Vaccinated individuals had 62% higher hazard of recovery than unvaccinated counterparts, even after accounting for other variables. This evidence demonstrates the crucial role of vaccination in accelerating COVID-19 recovery, aligning with previous studies which demonstrate benefits of vaccination in reducing COVID-19 severity and accelerating recovery (76). In China, vaccination was associated with 29% reduced risk of long COVID disease, while in Saudi Arabia, vaccination was identified as predictor of mild COVID-19 illness (34,85). Moreover, vaccinated patients in California experienced about a 70.6% substantial decrease in risk of ICU admission. In Pakistan, vaccinated patients demonstrated 35% lower risk of prolonged hospitalization compared to unvaccinated counterparts (86,93). Therefore, the finding from our study signifies relevance of vaccination in improving recovery outcomes among COVID-19 patients and effectively mitigate the impact of the virus related with delayed recovery.

In this study, age was also significant predictor of recovery time. Individuals aged 30-39 years had a 2.13-fold higher hazard of recovering from COVID-19 compared to individuals aged 50 years and above. Studies in Ethiopia also reported younger age groups as significant predictor of shorter time of recovery from COVID-19 disease (22,30,43,94). Finding from this study suggests that younger age groups may have more robust immune systems or better resilience against the disease, leading to quicker recovery. This may be due to age-related changes observed in both innate and adaptive immune response systems (95). The age category (30-39) may represent population with relatively fewer age-related comorbidities as compared the older age categories. Conversely, there are reports showing absence of significant disparity in the recovery time between different age groups (25,27,96). Therefore, understanding age related variations during COVID-19 disease progression can inform tailored approaches to patient management and resource allocation for case management.

In this study, individuals without comorbidities exhibit 87% higher hazard of recovery than those with one or more comorbidities. This could be linked to the fact that individuals with underlying conditions often experience weakened immune systems due to dysregulated immune responses, impaired organ function (97,98). This hazard was lower than reported by prospective cohort study in Ethiopia, a 98% among individuals without comorbidities (99). However, it was higher than reported by previous studies in the southern (62%) and northern (44.1%) of Ethiopia (25,28). Additionally, it was higher than the 63% rate reported from a study in India (83). The disparity in those reports could be attributed to variations in access to healthcare service, treatment protocols followed, vaccination status, length of follow up time and patient characteristics (30,32,49,56,76). Therefore, the finding from this study highlights the importance of considering underlying health conditions in COVID-19 management under HBIC, indicating the need for tailored interventions by identifying specific underlying health conditions.

Regular public transport users experienced 55% decrease in the hazard of recovery compared to non-users. This signifies risk of public transport as potential facilitator of viral transmission and excessive exposure to viral doses. The increased exposure to the virus during public transport may lead to higher viral loads, which may contribute to the reduced recovery rates observed in this study (67). Hence, the lower hazard of recovery in this study may be linked to excessive exposure to the virus during regular commuting. According to study from India, high-risk travel exposures such as close contact to an infected individual in common conveyance for more than six hours resulted in secondary attack rate of 79.3% by the SARS-CoV-2 virus (68). Similarly, study from Norway found an increase in the odds (OR,1.50) of COVID-19 cases among public transport users before and after lockdowns was attributed to travel exposure risk (100). Therefore, enhanced ventilation, rigorous cleaning protocols, and the promotion of alternative transportation modes should be instituted to help decrease the likelihood of high viral exposure in public transit settings.

Smokers had significantly lower hazard (56%) of recovery compared to non-smokers in this study. This aligns with existing evidence highlighting smoking as a risk factor that can worsen COVID-19 recovery (42). A study in southwest Ethiopia found 29% increment in the hazard of severe COVID-19 disease among smokers, potentially contributing to prolonged recovery times (43). Studies conducted in Wuhan and Changsha cities of China have reported that smoking is predictor of unfavorable outcomes of COVID-19 patients (44,45). The lowered hazard of the event may attributed to impaired lung functions due to smoking induced inflammation, increased mucus production, tissue damage, airway thickening and emphysema, lower respiratory system (46). Therefore, it is imperative for smokers to cease smoking in order to enhance their successful recovery from COVID-19 disease. Furthermore, this study underscores the critical importance of addressing smoking as a modifiable risk factor for adverse COVID-19 outcomes including delayed recovery.

In the current study, individuals with a previous infection with SARS-COV-2 virus had higher hazard (aHR, 2.11) of recovery compared to those without previous infection. The higher hazard of recovery could be due to potential immune mediated mechanisms from previous infection. This finding was supported by population-based study from Japan, in which prior infection was found protective against Omicron reinfection (48). Another meta-regression systematic review found that prior infection was 82.5% effective in protecting against severe COVID-19 disease outcomes (49). A study in Australia found that prior infection with SARS-CoV-2 led to faster viral clearance during breakthrough infections (47). The observed association between prior infection and faster recovery from current study may be attributed to protective immunity from previous infection, potentially leading to milder illness and faster recovery (47). Therefore, recognizing the role of previous infection in shaping Covid-19 recovery trajectories signify importance of incorporating natural immunity into public health policy and practice.

This study revealed that individuals who did not comply to regular hand hygiene practice exhibited a 28% lower recovery hazard than who did practice proper hand hygiene. The protective effect of hand hygiene observed may be linked to the evidence that consistent handwashing can reduce viral load and inoculum size, thereby facilitating faster recovery (60). In Australia, strict adherence to thorough hand washing has been correlated to 51% decrease in COVID-19 incidence and reduction in mortality rate from COVID-19 (61,62). Study from Hong Kong reported 42% decrease in the risk of SARS-CoV-2 infection through consistent adherence for hand washing and disinfection practices(63). Additionally, another meta-analysis study reported tenfold increase in hand washing frequency correlated with a 28% daily reduction of infection risk by SARS-CoV-2 (64). Based on the current finding, implementing robust hand hygiene practices could improve patient outcomes and potentially reduce home isolation time. Therefore, promoting recommended hand hygiene practice is crucial for mitigating COVID-19 disease severity, leading to faster recovery.

In this study, patients with BMI category of overweight and underweight had significantly reduced hazard of recovery by 33% and 62% respectively relative to normal BMI. Similar finding was reported from Ethiopia (96). Similarly study from China reported abnormal BMI as independent predictor of severe COVID-19 disease progression (39). A study in United Kingdom reported increased odd of hospital admission among overweight COVID-19 patients relative to normal (40). The metabolic dysregulation, chronic inflammation and impaired immune function resulted from higher BMI among overweight individuals may responsible for the prolonged illness duration in this study (41). Similarly, significant association between underweight and reduced recovery rate could be due to compromised nutritional status, weakened immune response and susceptibility for infection (101) which may contribute to delayed viral clearance. This finding was further supported by evidence from United Kingdom, where underweight individuals had higher odds of hospital admission for COVID-19 disease compared to individuals with normal BMI (40). Another study conducted in Wuhan found that underweight individuals were at an increased risk of severe COVID-19 illness (102). Therefore, the significant associations between hazard of recovery and abnormal BMI in this study showed the importance of integrating nutritional assessment and metabolic risk stratification into existing COVID-19 clinical management strategies. Moreover, advocating measures lifestyle modification such as healthy eating habits, physical activity and weight reduction could mitigate the risk of severe COVID-19 outcomes and enhance resilience against respiratory infection in the HBIC (103).

This study, individuals who did not wear mask in an indoor event exhibited a 61% lower hazard of recovery relative to those who did wear mask. This finding aligns with observations from other previous studies. Study from Tunisia (65) reported faster likelihood of recovery among individuals who did wear masks consistently. These preventive effect of face mask is likely due to their ability to lower viral load from immediate environment and minimizing risk of high-dose inoculation of the virus thereby contributing to earlier recovery (104–106). Study conducted among orthopedic surgeons in Wuhan reported that consistent wearing of any respirator masks was associated with an 85% SARS-CoV-2 infection reduction (66). Another study from India reported that mandatory mask wearing resulted with asymptomatic manifestation and earlier seroconversion among infected individuals which facilitate faster recovery. Similarly different studies show consistent use of masks raised proportion of asymptomatic patients up to 45% during later periods of the pandemic which was 15% during earlier period (106,107). The evidence from this study suggests regular and consistent mask usage can collectively reduce risk of delayed recovery COVID-19 disease. Therefore, promoting widespread adoption of face mask at high-risk area as preventive measure remain crucial.

7. Strength and limitation of the study

7.1 Strength

Although the retrospective nature of the study limits its ability to establish causal relationships, it offers valuable insights into COVID-19 recovery under the home-based isolation and care setting. The inclusion of variables such as vaccination status, prior infection, hand hygiene, public transportation usage, and mask usage provides comprehensive understanding of the interplay of factors influencing recovery outcomes in HBIC setting. This study is the first of its kind to investigate the experiences and outcomes of COVID-19 patients under home-based isolation and care particularly in Addis Ababa and across Ethiopia. Its clear structure and effective communication of findings enhance accessibility and scholarly impact of this study. The study's transparent acknowledgment of limitations highlights areas for future research, strengthening its academic credibility and potential to impact healthcare practices in similar contexts.

7.2 Limitation of the study

While the study had notable strengths, it is imperative to acknowledge and address its limitations for drawing accurate conclusions. The study had some limitations, including its retrospective design, small sample size, focus on the Omicron variant, and lack of data on specific comorbidities, pregnancy status, and marital status which may limit its generalizability to those subpopulations. This study relies on self-reported data with remote health professional consultation, which may introduce some biases in outcome measurement. Future research should address these limitations with larger, more diverse and prospective studies to provide more comprehensive understanding of COVID-19 recovery and inform effective home-based interventions.

8. Conclusion and Recommendations

8.1 Conclusion

The findings of this study illustrate the recovery trajectories of COVID-19 patients under home-based isolation and care, revealing median recovery time of just seven days. Vaccinated individuals demonstrated significantly shorter recovery periods compared to their unvaccinated counterparts, underscoring the pivotal role of vaccination in expediting recovery. Moreover, this study identifies varying recovery rates and recovery time influenced by factors such as prior infection and vaccination status, highlighting nuanced nature of COVID-19 recovery under home-based isolation and care.

These insights emphasize importance of tailored management strategies that consider individual characteristics. Overall, our results advocate for the adoption of home-based isolation and care for mild COVID-19 cases and underscore the profound benefits of vaccination in enhancing recovery outcomes. These findings have practical implications for clinical decision-making and the development of effective disease management protocols amidst the ongoing pandemic. However, further research is needed to gain comprehensive understanding of the interplaying mechanism of factors affecting recovery outcomes.

8.2 Recommendations

Public, Patients and caregivers: Vaccination remains the cornerstone in improving recovery, stay up-to-date with booster shots as recommended by health authorities. Maintain strict adherence to isolation guidelines, hand hygiene, and other protective measures to minimize the risk of disease transmission and complications under home-based isolation and care.

Clinicians and Public Health officers: Actively promote vaccination and boosters to patients. Should implement thematized in interventions to individuals based on factors influencing rate and recovery time with maximum efforts paved to consider risk factors for delayed and faster recovery identified in this study. Collaborate with policymakers and program planners to integrate home-based COVID-19 care into the broader healthcare system and pandemic response strategy.

Policymakers and program planners: Focus on increasing vaccination access and equity. Allocate resources and funding to support the development, implementation, and scaling of home-based COVID-19 care programs, particularly in areas with limited healthcare infrastructure. Collaborate with clinicians and researchers to continuously evaluate and refine home-based care protocols and policies based on emerging evidence and evolving pandemic conditions.

Researchers: Conduct further studies on COVID-19 disease focusing on the long-term effects and the role of social determinants to improve recovery of COVID-19 outcomes among HBIC patients. Collaborate with clinicians and policymakers to translate research findings into actionable recommendations for program implementation and policy development, ensuring the seamless integration of home-based care into the broader healthcare system.

9. References

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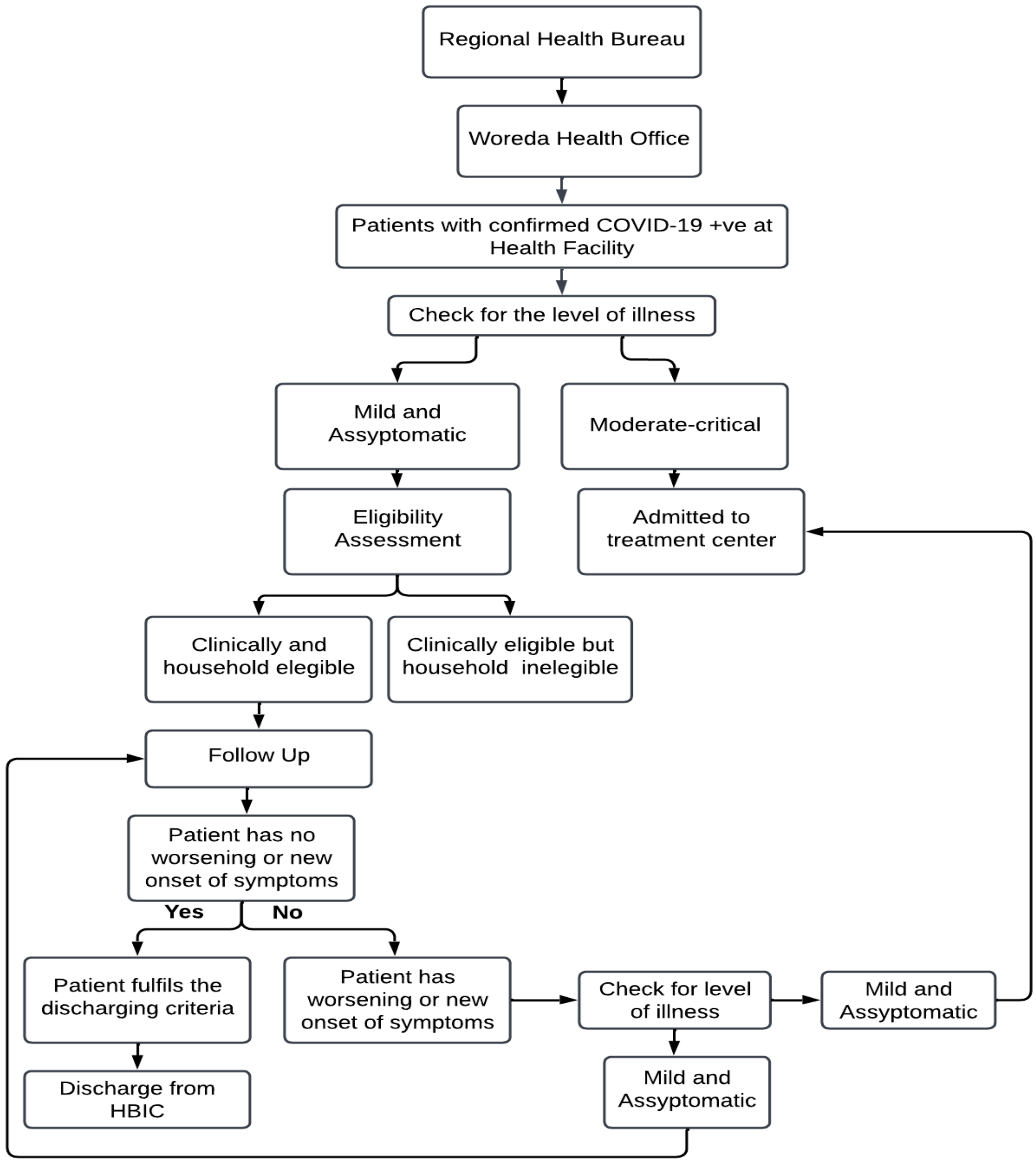
10. Annex

Annex I: Patient flowchart diagram for home based isolation and care, adapted from the national HBIC interim guide, Ethiopia.



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To whom it may concern

Addis Ababa

Subject: - Permitting to use secondary study data

Dr. Ayele Bizuneh, who is a permanent staff of AHRI, is currently pursuing his Master of Public at Addis Ababa University, School of Public Health with specialty in Epidemiology and Biostatistics. On September 10, 2023 he requested a letter of permission to use secondary data from previous study, **"COVID-19 vaccine effectiveness and vaccination breakthrough outcomes among COVID-19 case in Addis Ababa and Adama, Ethiopia"** for his planed research work. The general objective of his study is *'to determine the time to recovery, recovery incidence rate and associated factors among COVID-19 patients under home-based isolation and care services'* in Addis Ababa. Based on this we are grateful to give him permission to do and publish his research work using secondary data with clear and separate objectives from the original study in discussion with the directorate.

Sincerely

Dereje Nigussie (PhD)
Vaccines and Diagnostics Production Directorate
Director

C/C

To Dr. Ayele Bizuneh

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ADDIS ABABA UNIVERSITY
College of Health Sciences
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Ethical Clearance Form

Version January, 2024

Date: /19/01/2024/
Ref. No. SPH/296/2024

Project number /_____001_____/

Date of approval (D/M/Y) /19/01/2024	
Project Title: **Survival modelling for covid-19 patients receiving home based isolation and care services in Addis Ababa, Ethiopia.**	
Name of PI **Ayele Bizuneh Gizaw**	**Phone Number**
Institution	**School of Public Health**
Department	
Decision of Research and Ethics Committee:	☑ **Approved** ☐ **Approved with Recommendation** ☐ **Resubmission** ☐ **Disapproved**
Valid until	**January, 2024 - June, 2024**

Dean, School of Public Health

Signature __________

Date /19/01/2024/