A Two-Year Retrospective Analysis of Dual COVID-19 and Sepsis Infection Patients at UPMC McKeesport

by

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Abstract

Background: COVID-19 may be a new challenge requiring ongoing research, but sepsis has been a constant public health problem in hospitalized patients in the US. Literature reviews show the comparison and potential link between COVID-19 and viral sepsis. In this study, 13% of COVID-19 positive patients admitted to UPMC McKeesport over two-year span also developed concurrent sepsis. The goal of this study was to investigate the possible relationship between COVID-19 and sepsis and to determine prevention strategies to curb the severity of the dual infection.

Methods: Chart reviews were performed of patients with dual infection of COVID-19 and sepsis through electronic medical records. Data collected included: admit and discharge date, mortality, sex, language spoken, age, patient type, race, documented PCP, discharge disposition description, length of stay, vaccination status/type, and ventilator/intubation needs. Data was analyzed on Microsoft Excel and Stata 14.2.

Results: The mortality rate for patients with dual infection was 42%. Vaccinated mortality rate was 29% compared to unvaccinated mortality rate of 56%. There is a statistically significant difference between admission and discharge disposition when comparing patients who met Goal length of stay to Extreme length of stay. Vaccination status improved length of stay (LOS) outcome. Fully vaccinated patients had SSD of meeting Goal LOS compared to combined Medium and Extreme LOS (p=0.007).

Conclusion: The study results suggest a potential link between COVID-19 and sepsis, but future research with a larger sample size could provide further conclusions. Knowing if a link exists can lead to improved patient outcomes by identification of patients who could develop a dual infection.

Public Health Significance: COVID-19 and sepsis are very serious public health issues that burden hospital ICUs. It is important to study the link between the two diseases to target intervention and prevention measures and improve patient outcomes.

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Preface

I would first like to thank Clare Cowen and Dr. Mohamed Yassin for all their guidance and support throughout my practicum and essay writing process. This essay and research were only possible because of their knowledge and expertise in infection prevention and control. I would like to thank Dr. Toan Ha for being a great advisor and essay reader. I would also like to thank Crystal Pambacas and Daren Busch of the Quality Department at UPMC McKeesport for their work on sepsis and assistance with data. I would like to thank the finance and pharmacy departments at UPMC McKeesport for pulling and assisting me with data collection, specifically Chelsea Leake, Sydney Krizon, and Rebecca Morcheid. I would like to thank Amy Haugh, the UPMC St. Margaret's librarian for assisting me in my literature search.

I would also like to thank Dr. Linda Frank and Dr. Graham Snyder. Dr. Frank is the MPH-MIC Program Director and IDM Professor. Along with Dr. Yassin and Dr. Snyder, she created the infection prevention class and practicum which introduced me to the infection prevention and control field. I am very thankful for the opportunities this class and practicum has opened for me and the connections I have made.

1.0 Introduction

The prevalence and causes of a dual infection of COVID-19 and sepsis in hospitalized patients is not yet defined by previous research. One study found that sepsis was present in about 32% of COVID-19 hospitalizations, suggesting a link exists between the two (Shappell, 2022). Sepsis caused by a virus is often ignored, indicating a need for research (Liu, 2022). Viruses have a strong ability to disrupt the immune response and cause uncontrolled inflammation that can lead to sepsis (Ren, 2020). Another researcher suggests a possible cause of sepsis in COVID-19 patients is the immune response may be incapable of controlling the cytokine storm that SARS-CoV-2 causes (Zafer, 2021). This is one possible explanation for a potential link between COVID-19 and sepsis. Critical COVID-19 cases share the same clinical characteristics as classical bacterial sepsis (Wu, 2022). Mortality rates from severe COVID-19 are like those observed in sepsis (Vincent, 2021). The similarities between these two diseases have been characterized, but no definitive link has been identified.

1.1 COVID-19 Background

COVID-19, or coronavirus disease 2019, is caused by SARS-CoV-2 virus. This new virus was discovered in December of 2019 in Wuhan, China and quickly spread to pandemic levels. SARS-CoV-2 causes respiratory symptoms that mimic a cold or flu. The virus is part of the Coronavirus family that also includes SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome). The virus is spread quickly through droplets that are expelled when a person breathes, coughs, sneezes, or speaks. Most infected people have mild symptoms that include fever, dry cough, shortness of breath, and fatigue (CDC, 2022). Viruses are susceptible to genetic changes over time, which can affect how fast the virus spreads, the severity of illness, and the effectiveness of treatments against it. COVID-19 has had multiple variants due to these genetic changes (CDC, 2021).

A person who is infected with SARS-CoV-2 can have potentially five different outcomes that include an asymptomatic case, a mild case, a severe case, a critical case, or death (Scaglioni, 2020). Severe cases disproportionately affect people aged 60 and older and those with underlying health conditions (Herrman, 2021). Early studies showed a significant association between older age, heart disease, and a history of cancer with COVID-19 mortality (Alizadehsani, 2020). A different study showed that the fatality rate increased with age and the factors that were most associated with mortality were being age 75 or older, dyspnea, diabetes, hypertension, and chronic kidney disease (de Souza, 2020). Older adults are more likely to need hospitalization, intensive care, and a ventilator to help them breathe (CDC, 2022). COVID-19 infection increases a patient's risk of ventilator induced lung injury because infection often necessitates mechanical ventilation (Scendoni, 2022). SARS-CoV-2 causes immune dysregulation and the differences in immune response could have a significant impact of the severity of COVID-19. Age and comorbidities contribute to disease severity through immune mechanisms such as the expression of ACE2 which is the receptor the virus uses to enter the human cell. The expression of ACE2 varies with age and is linked to the immune/inflammatory response through a complex network. Patients with more severe disease show more impairment in the adaptive immune response compared to those with mild cases. The immune system plays a significant role in controlling the infection and the severity of disease (Costagliola, 2020).

There are factors other than older age and underlying health conditions that could influence the risk of getting sick from COVID-19. Vaccinations, past infections, and access to testing and treatment can help protect people from severe infection. People who are vaccinated and up to date with all recommended doses are less likely to be hospitalized or die from COVID-19. Most of the treatments for COVID-19 need to be started within the first few days of infections, so access to testing can increase the chances a person will receive needed treatment (CDC, 2022). People who are immunocompromised or have weakened immune systems are at risk for a more severe infection or a longer disease course. These individuals can take extra precautions, like staying up to date with vaccines and wearing a mask to ensure infection does not cause severe harm (CDC, 2022).

There are multiple ways to protect yourself and others from COVID-19. Basic health and hygiene practices like handwashing is one way. Other measures like vaccines help the body develop protection from SARS-CoV-2 and significantly lower the risk of getting sick, being hospitalized, or dying. Wearing a mask contains droplets and viral particles that are coughed, sneezed, or breathed out (CDC, 2022). Recommended precautions are taken to protect the population from severe disease.

COVID-19 vaccines were rolled out early in the pandemic, around December 2020. There were multiple vaccines available during this study. Pfizer-BioNTech and Moderna are mRNA vaccines, and Johnson & Johnson's Janssen (J&J) is a viral vector vaccine. The mRNA vaccines are created to teach cells how to make a protein or a piece of protein that will trigger the immune response. The mRNA is broken down and discarded from the body within a few days after vaccination. J&J, the viral vector vaccine, is made using a modified version of a different virus and not SARS-CoV-2. This vaccine delivers instructions to the cells on how to recognize and fight

SARS-Cov-2. People who are fully vaccinated and up to date with boosters have a lower risk of severe illness, hospitalization, and death from COVID-19 (CDC, 2022).

1.2 COVID-19 Disparities

Minority populations have been disproportionately affected by the COVID-19 pandemic. The impact of the pandemic has been felt differently depending on an individual's status in society. The pandemic has amplified the existing social inequalities tied to race, class, and access to healthcare (Reyes, 2020). Black, Hispanic, and Asian people have substantially higher rates of infection, hospitalization, and death when compared to White people. Racial and ethnic minority populations are more likely to live in crowded conditions, in multigenerational households, and have jobs that cannot be performed from home. These types of environments make social distancing difficult. These groups often have poorer access to health care and a higher number of comorbidities. The prevalence of hypertension, diabetes, and obesity are higher among low-income, minority populations. These populations predominantly live in low income, sometimes violent, neighborhoods, often lack health insurance, and are more likely to travel on public transportation (Lopez, 2021). Blacks, Hispanics, and other minority racial populations are more vulnerable to COVID-19 due to disproportionate socioeconomic and structural determinants of health disadvantages. These disadvantages lead to inequities in health care access and overall poorer health outcomes (Mude, 2021).

The Center for Disease Control and Prevention (CDC) created a health equity strategy to address these disparities. All people should have the opportunity to attain the highest level of health possible. This strategy focuses on efforts to address avoidable inequities, historical injustices, and eliminating disparities that exist in healthcare. The steps the CDC are taking to reduce healthcare disparities include increasing testing, contact tracing, isolation options, and disease management. The health equity strategy is working to reduce stigma and bias in healthcare while expanding cultural responsiveness and health equity principles (CDC, 2022). Underserved, minority populations are more vulnerable to COVID-19, but through increased health equity these disparities could decrease.

1.3 Sepsis Background

Sepsis is the leading killer of hospitalized patients and is responsible for 1 in 5 deaths every year. It is classified as the body's extreme response to an infection. Sepsis begins with an infection, which can be caused by a bacteria, virus, or fungus. Sepsis most commonly develops from pneumonia or urinary tract infections, but it could also occur as a result of severe COVID-19. It begins when immune cells start fighting the body's own tissues and organs, like an autoimmune response. The immune system can cause damage to multiple organs in the body including the heart, lungs, kidneys, or blood cells. Blood flow to the brain and other organs can become restricted which causes the blood pressure to go very low. This is considered septic shock and once it develops the mortality rate increases (Brandt, 2022). The current definition of sepsis is focused on the inflammatory basis of disease. Sepsis 3 criteria uses a sequential organ failure assessment (SOFA) score to identify sepsis and septic shock. This score contains evaluation parameters pertaining the six organ systems that include respiratory, coagulation, liver, central nervous system, renal, and circulatory system. A change in SOFA score by less than or equal to two points from baseline assessment is considered organ dysfunction. If no preexisting organ dysfunction has occurred, the baseline SOFA score is zero (KOÇAK TUFAN, 2021).

Sepsis symptoms are similar to other conditions like heart attacks, blood clots, or allergic reactions which makes detection very difficult. The current treatments are supportive only and no treatment exists to reverse the pathophysiological effects of sepsis. Interventions are aimed at keeping the patients alive with the expectation that organ function will recover after infection is cleared. Patients who recover from severe sepsis frequently have chronic organ dysfunction and there are no treatments to reverse the organ dysfunction caused by sepsis (May, 2021).

A majority of patients who are admitted to the intensive care unit (ICU) meet sepsis 3 criteria and present with an infection associated organ dysfunction (Karakike, 2021). Patients requiring ICU level care are more likely to develop infections that can lead to sepsis. Early identification and treatment with antibiotics and fluids improves a person's chance of survival. To be diagnosed with sepsis, the patients must have a probable or confirmed infection. Some clinical signs that can be identified are a change in mental status, a systolic blood pressure less than or equal to 100 mmHg, and a respiratory rate higher than or equal to 22 breaths per minute (Mayo Foundation, 2021). The source of the infection needs to be identified so prompt treatment can begin.

It is important to recognize sepsis early to decrease the chance of mortality. Risk factors for sepsis are part of the interplay of social influences like racism, poverty, and community dynamic. Older individuals with underlying chronic diseases like obesity and diabetes are more likely to die from sepsis. Factors like race, poverty, and access to health care can have an impact on sepsis survival (Brandt, 2022). Sepsis research shows the most underlying causes of death were related to chronic comorbidities and were not preventable through better hospital care. One study shows that sepsis is present in about 30% to 50% of hospitalizations that end in death (Rhee, 2019). Hospitalizations is one main factor that leads to sepsis. Some people are at higher risk for developing sepsis because they are at higher risk for contracting an infection. This includes the very young, the very old, those with chronic illnesses, and those with weakened or impaired immune systems (Sepsis Alliance, 2022).

Sepsis survivors are vulnerable to future health problems. Cognitive, physical, psychological, and medical impairments are common after sepsis. One study found that about 40% of patients discharged after having sepsis were rehospitalized within 90 days either with recurrent infection or an increase in chronic health problems. These adverse outcomes may not only affect those who had a severe disease course. Patients have an increased risk of mortality for at least two years following sepsis (Prescott, 2020). Sepsis is a serious health problem that leaves long lasting effects.

1.4 Infection Control for COVID-19

The COVID-19 pandemic has brought continuing changes to infection control in a hospital setting. As of September 23, 2022, the following are up the up-to-date recommendations according to the CDC. Vaccination status is no longer used to inform source control, screening testing, or post exposure recommendations. Screening testing of asymptomatic healthcare workers is up to the facility to decide. The new updates reflect the levels of vaccine and infection induced immunity and the availability of prevention tools. The CDC offers guidance for facilities to implement infection prevention and control practices based on the individual circumstances. Precautions can be influenced by the current levels of SARS-CoV-2 transmission in the community.

Recommended routine infection prevention practices during the pandemic include encouraging everyone to stay up to date with recommended vaccine doses, establishing a process to identify and manage people with suspected or confirmed infection, and taking actions to prevent transmission. It is important to implement source control measures. Source control is the use of respirators or facemasks to cover the mouth and nose to prevent spread of respiratory secretions. Source control for healthcare personnel include NIOSH approved particulate respirator with N95 filters or higher, a barrier face covering that meets the requirements, or a well-fitted mask. These source control options could be used for an entire shift unless it becomes soiled, damaged, or hard to breathe through. When community transmission is high, source control is recommended for everyone in healthcare settings, especially when encountering patients. If community transmission is not high, it is up to the healthcare facility to choose not to require universal source control (CDC, 2022).

Healthcare personnel caring for patients with COVID-19 should use standard precautions when entering the patient room, which includes hand hygiene and use of personal protective equipment (PPE) when needed. Transmission-based precautions, used when the patient is contagious, include the use of a N95 mask, gown, gloves, and eye protection. Procedures that could generate infectious aerosols should be performed cautiously and avoided if an alternative exists. Transmission based precautions should be maintained for patients who are hospitalized for SARS-CoV-2 and have severe to critical illness. Patients should wear PPE until symptoms resolve or until they meet criteria to end isolation. For patients who have mild illness, source control and isolation can be stopped after at least 10 days have passed since symptoms started and at least 24 hours have passed since last fever and symptoms have improved. Patients who are asymptomatic can stop isolation after at least 10 days since the first positive viral test. Patients who are critically or severely ill can stop source control after at least 10 days and up to 20 days since symptoms first appeared, at least 24 hours have passed since last fever, and symptoms have improved. Patients who are immunocompromised may produce replication competent virus further than 20 days after symptom onset (CDC, 2022).

For COVID-19, a mild illness is defined as individuals who have any of the signs and symptoms which includes fever, cough, sore throat, malaise, headache, muscle pain without shortness of breath, dyspnea, or abnormal chest imaging. A moderate illness is defined as individuals who have evidence of lower respiratory disease by clinical assessment or imaging, and a saturation of oxygen greater than or equal to 94% on room air at sea level. Severe illness is defined as individuals who have respiratory frequency greater than 30 breaths per minute, saturation of oxygen greater than 94% on room air, a ratio of arterial partial pressure of oxygen to the fraction of inspired oxygen (PaO2/FiO2) less than 300 mmHg, or lung infiltrates less than 50%. Critical illness is defined as individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction (CDC. 2022).

There is COVID-19 guidance that needs to be followed for skilled nursing facilities (SNF). When a patient is being discharged to a SNF, the person must be tested for COVID-19 before discharge. There are few exceptions to this guidance. Patients who are not currently exhibiting symptoms and who tested positive for COVID-19 within the last 90 days do not have to be tested before discharged to a SNF. Patients who are not exhibiting symptoms and who are fully vaccinated do not have to be tested. If the patient tested positive for COVID-19 before admission to the hospital, the hospital does not have to test again. If the patient is discharged within 72 hours of admission and tested at admission, a second test is not required. The results of the test must be communicated to SNF prior to discharge. Patients who test positive should only be discharged to a SNF with the ability to adhere to infection prevention and control recommendations. SNFs that meet criterion may not refuse to accept or readmit a patient with a positive COVID-19 result but may refuse to accept a patient if COVID-19 test has not been administered in accordance with guidance (Commonwealth of Pa, 2022).

1.5 McKeesport, Pennsylvania

McKeesport is in southwestern Pennsylvania and is part of Allegheny County. UPMC McKeesport is the main hospital and serves the residents of the Monongahela, Youghiogheny, and Turtle Creek valleys. It is located 15 miles southeast of Pittsburgh. UPMC McKeesport offers 200 beds for acute care, specialty care, and rehabilitation. Some of the main services offered are addiction medicine, rehab services, imaging services, and wound healing services (UPMC, 2022).

The population size, as of July 1, 2021, of McKeesport is 17,493. The population has decreased about 1.4% from the previous year based on estimates from April 1, 2020. 19.9% of the population are aged 65 years and over. 23.1% are persons under 18 years of age. 55% of the population is White race alone. Black or African American race makes up 37.9% of the population. 87.7% of the population in McKeesport is a high school graduate or higher; 13.9% have a bachelor's degree or higher. 7.2% of the population is without health insurance and 19.6% that are under 65 years of age have a disability. 53.2% are in the civilian labor force and the mean travel time to work is 28 minutes. The median household income is $28,881, which is classified as lower class (U.S. Census Bureau, 2022). The average cost of COVID-19 positive admission at UPMC McKeesport was $9,800 compared to the average cost of general patients at $3,900. The cost of care could be a burden on the low-income families in this area of Pennsylvania.

McKeesport has unique patient geographical location and population served compared to state averages. 19% of the Pennsylvania population are over 65 years of age. Regarding race, 81% of Pennsylvania's population is White, while 12.2% identify as Black or African American. 91% of Pennsylvania residents are high school graduates or higher and 32.3% have a bachelor's degree or higher. 6.6% of the population is without health insurance and under 65 years of age. 9.8% of the population under 65 has a disability. 62.7% work in the civilian labor force. The mean travel time to work for Pennsylvania residents is 27.1 minutes. The median household income for Pennsylvania residents is $63,627 which is considered middle class. 12.1% of the population live in poverty (U.S. Census Bureau, 2022).

1.6 Analysis Aims

Through this two-year descriptive retrospective analysis, we aim to study UPMC McKeesport patients who tested positive for COVID-19 to investigate a potential link between COVID-19 and sepsis. We aim to study severity measures and patient's outcomes for those who have both COVID-19 and sepsis. Using descriptive statistics, we will analyze mortality rates, ventilator usage, length of hospital stays, and admission to the intensive care unit. Through this analysis, we also aim to investigate vaccine compliance and the influence vaccines have on patients who are dually infected. Through this we hope to determine prevention strategies to curb the severity of COVID-19 and sepsis dual infection.

1.7 Public Health Significance

COVID-19 and sepsis continue to be significant public health issues. COVID-19 has taken a toll on the healthcare system worldwide. This has led to an increase in mortality and the pandemic has had a negative effect on the prognoses of critically ill non COVID-19 patients (Unterberg, 2022). Sepsis causes 20% of global deaths, particularly in children and vulnerable populations (Kawale, 2022). A dual infection of COVID-19 and sepsis creates worse patient outcomes. Linking the two diseases could lead to improved patient outcomes by identifying risk factors. A considerable proportion of patients in a previous study with severe COVID-19 met sepsis 3 criteria (Assimakopoulos, 2022). Knowing these two diseases are linked creates potential to develop interventions and deploy prevention measures into the population to decrease COVID-19 severity. Reducing the incidence of COVID-19, either by vaccinations or other prevention measures, could reduce the chances of viral sepsis and decrease mortality. Identifiable risk factors of a dual infection could help clinicians prevent severe patient outcomes.

2.0 Methods

This single-center study is a retrospective descriptive analysis of COVID-19 positive patients admitted and treated at UPMC McKeesport from April 4, 2020, to April 29, 2022.

2.1 Sample Selection and Data Collection

The total sample for this analysis consists of 881 COVID-19 positive patients who were admitted to MCK between 2020 and 2022. The dataset was pulled from the Hospitalizations dashboard in QlikSense and compiled on a Microsoft Excel spreadsheet. This patient dataset included FIN number as patient identifier, sex, language, DOB, age, hospital finance FC group, patient type, admission and discharge date, 90-day readmission flag, diagnosis description, race, risk of mortality, mortality, IP PCP physician name, discharge disposition description, ICU flag, length of stay, chief complaint, discharge location, zip code, and readmission risk. Data on vaccination status was collected and included vaccine date, vaccine type, vaccine 2 date, vaccine 2 type, full vaccination, vaccine 3 date, vaccine 3 type, COVID-19 positive date, and if patient required a ventilator/intubated. MCK treated 881 adult patients diagnosed with COVID-19 over a two-year span.

This sample consists of MCK COVID-19 positive patients and is not dependent on diagnosis description or chief complaint. All the patients in the dataset were COVID-19 positive during the hospital stay. The variable patient type included observation, inpatient, inpatient rehab, inpatient mental health, and inpatient hospice. For risk of mortality, a lower score (1) indicated a minor risk of mortality, and the higher score (4) indicated an extreme risk of mortality. Readmission risk included the descriptors of lowest, lower, medium, higher, and highest to describe the risk of readmission after discharge.

Patient electronic health records (EHRs) were accessed via Core PowerChart. Data on vaccination status, ventilator use, and COVID-19 positive date were collected from EHRs and added to the Microsoft Excel data spreadsheet. Vaccine data was collected on patients admitted between February 2021 to April 2022. Optum Enterprise CAC CDI was used to search through EHRs by key terms to find vaccination status and ventilator usage. For patients whose vaccination status was unknown, the PA SIIS website was used. This resource gave information on vaccine type, date, and status for patients when name and DOB was entered. Electronic health records also gave indication of COVID-19 positive date. The FIN number was used as patient identifier. Each patient is given a FIN number for each hospital encounter. Data was pulled using the patients FIN number to search the EHR. This allowed for us to see repeat COVID-19 infections and get specific information for the hospital visit that was due to COVID-19 infection.

2.2 Study Design

116 patients from the COVID-19 positive sample were diagnosed with sepsis. The same variables listed above were examined for the dual infection patients. Four variables were considered to indicate severity of disease: mortality, LOS, ventilator usage, and ICU admission.

2.3 Statistical Analyses

Pivot tables were used to examine mortality, LOS, ventilator usage, and ICU admission. Stata 14.2 was used to perform statistical analyses and indicate any statistically significant findings.

3.0 Results

3.1 COVID- 19 Positive Patient Demographics

A majority of the COVID-19 positive patients admitted to UPMC McKeesport between April 2020 to April 2022 were from the zip code 15132 which designates McKeesport, Pennsylvania. 39% of this sample were in the age range 18-64. 61% were considered seniors meaning they were aged 65 and up. Almost all the patients spoke English (97%). Two of the patients spoke Spanish, one patient spoke Vietnamese, and 27 patients had an unknown primary language, and it was not documented on the chart. 52% of the patients were female sex and 48% were male sex. Most of the patients were classified as White (72%), followed by Black race (26%). One patient was Indian, five patients were Native American/Alaskan Indian, one patient was Vietnamese, and 12 patients did not disclose their race on the chart. Of the 881 COVID-19 positive patients, 78% were not vaccinated and 22% were fully vaccinated. Most of the patients were classified as inpatient (86.49%), followed by observation (10.44%), inpatient mental health (1.7%), inpatient rehab (1.14%), and inpatient hospice (0.23%).

3.2 Primary Findings for Dual Infection Patients

116 (13%) patients from the original sample also developed sepsis. 43% of these patients were not vaccinated, 21% were fully vaccinated, and 36% were admitted before vaccines were available. The overall mortality rate of dual infection of COVID-19 and sepsis was 42%. Zip code

15132 had more mortalities than any other zip code examined. Mortality and case counts were tracked over the two-year period. Mortality rate was shown to increase over the two-year period (**Figure 1**). Mortality based on vaccination status was examined. Before vaccines became available to the public, the mortality rate was 33%. After vaccines became available, the mortality rate was 47%. Once vaccines became available, 29% of the patients who were fully vaccinated ceased to breathe while 71% did not die. 56% of the unvaccinated patients died and 44% survived. Data for vaccine type was examined in regard to mortality. Eight patients were vaccinated with Moderna; of this 8, 25% died and 75% survived. 15 patients were vaccinated with Pfizer; of this 15, 27% died and 73% survived. One patient was vaccinated with J&J and ceased to breathe.

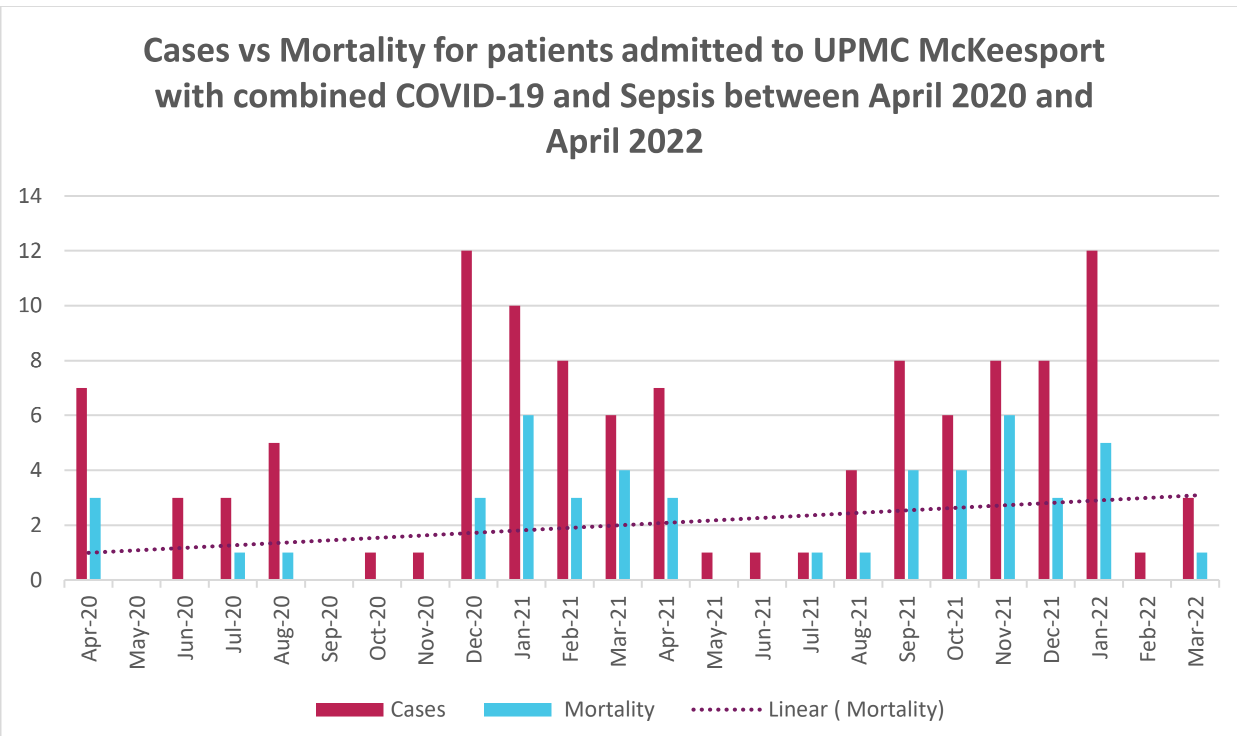

Figure 1. Cases and Mortality Counts Over Time for Dual Infected Patients

Seventy-three (63%) of these patients were on a vent while admitted to UPMC McKeesport. Mortality with the need of a ventilator compared to no need for a ventilator was a statistically significant finding. There is statistically significant evidence that mortality is more likely when patient is in need of ventilation compared to no need for ventilation. Of those who died (49 patients), 94% were on a vent at some point in their hospital stay ($p<0.00001$). Thirty-eight percent of patients fully vaccinated with Moderna required ventilation/intubation. Fifty-three percent of patients fully vaccinated with Pfizer required ventilation/intubation. Sixty-six percent of patients who were not vaccinated required ventilation/intubation. Only one patient was vaccinated with J&J and required ventilation/intubation.

When breaking down mortality by age group and vaccination status, the mortality rate for patients aged 65 and up before vaccines became available was 79%. After vaccines became available, the mortality rate for unvaccinated patients aged 65 and up decreased to 57%.

Length of stay in the hospital was used to indicate disease severity. A comparison was made looking at LOS for patients admitted for non-COVID-19 reasons, patients with COVID-19 only, and patients with the dual infection (**Figure 2**). The average LOS for those without COVID-19 was 5.07 days. The average LOS for COVID-19 positive only patients was 8.51 days. The average LOS for dual infected patients was 10.7 days. There was a statistically significant difference between the LOS of the non-COVID-19 patients when compared to the LOS of the dual infected patients ($p<0.0001$). There was also a significant difference between the non-COVID-19 patients when compared to the LOS of COVID-19 positive patients. No significant difference exists between average LOS for COVID-19 positive patients and dual infection patients.

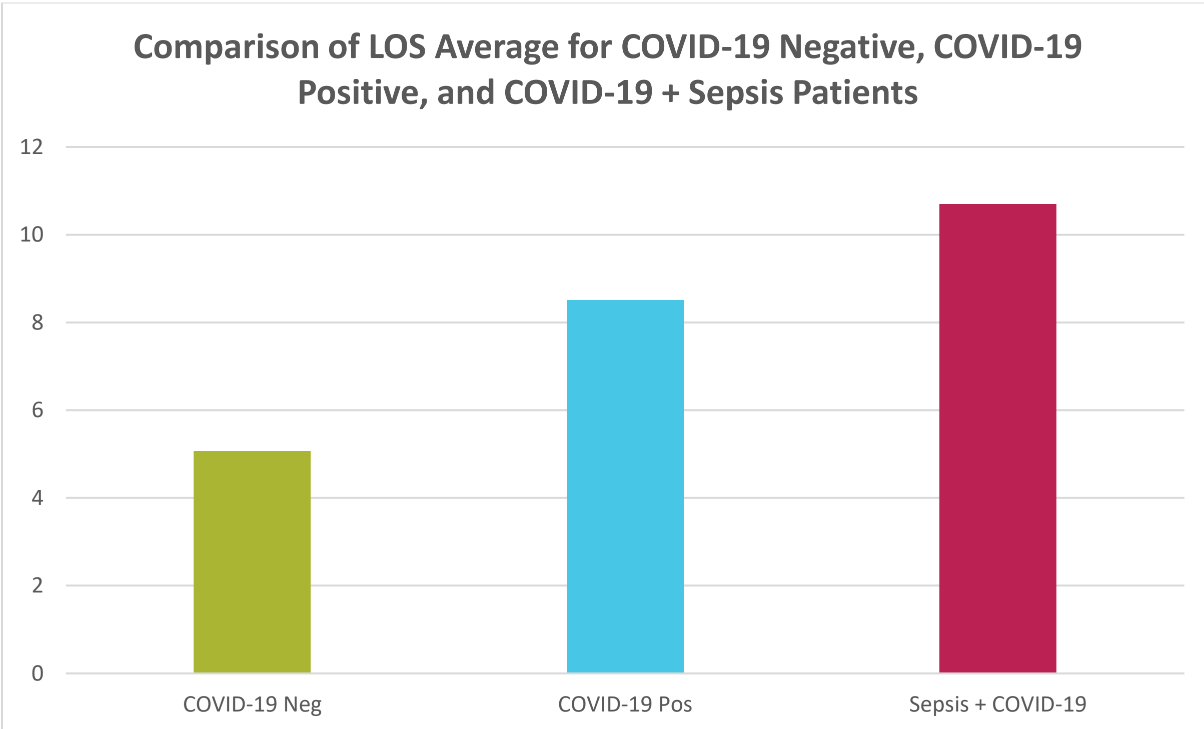

Figure 2. Average LOS for Non-COVID-19 Patients, COVID-19 Patients, and Dual Infection Patients

Only 16% of patients who were admitted to UPMC McKeesport and developed COVID-19 and sepsis were discharged home, and without any care needs. For this study the focus was on patients either discharged to home or a skilled nursing facility (SNF). LOS was defined as goal, medium, and extreme. A goal LOS ranged from 0 to 5 days. A medium LOS ranged from 5.1 to 9.9 days. An extreme LOS was defined as 10 or more days in the hospital. **Figure 3** and **Figure 4** highlight the differences in LOS for those discharged home versus those discharged to a SNF. 60% of patients discharged to a SNF were categorized as having an extreme LOS. 42% of patients who were discharged to home/self-care met the goal LOS. There were no significant differences when combining the medium and extreme LOS versus goal LOS, but there was a strong trend. It is likely that if the patient study population were bigger there would be a statistical difference. There is a statistically significant difference between admission and discharge disposition when comparing patients who met the Goal LOS to Extreme LOS (p=0.001).

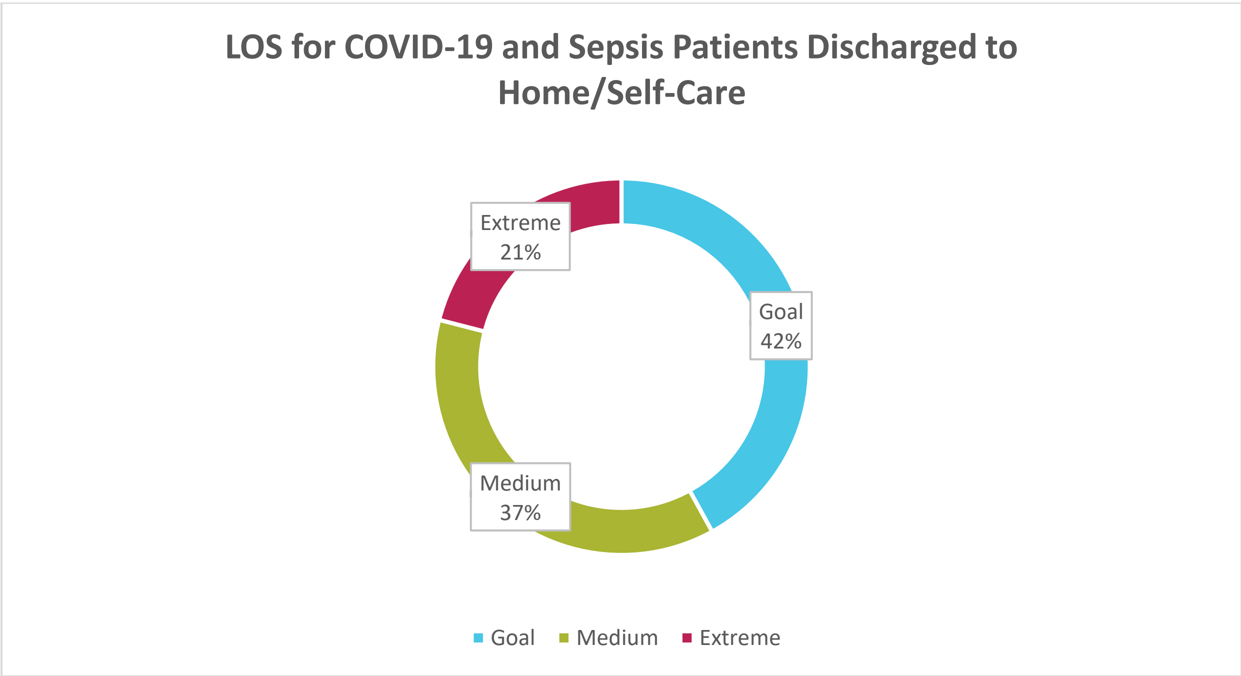

Figure 3. LOS for Patients Discharged to Home Characterized by Goal, Medium, and Extreme

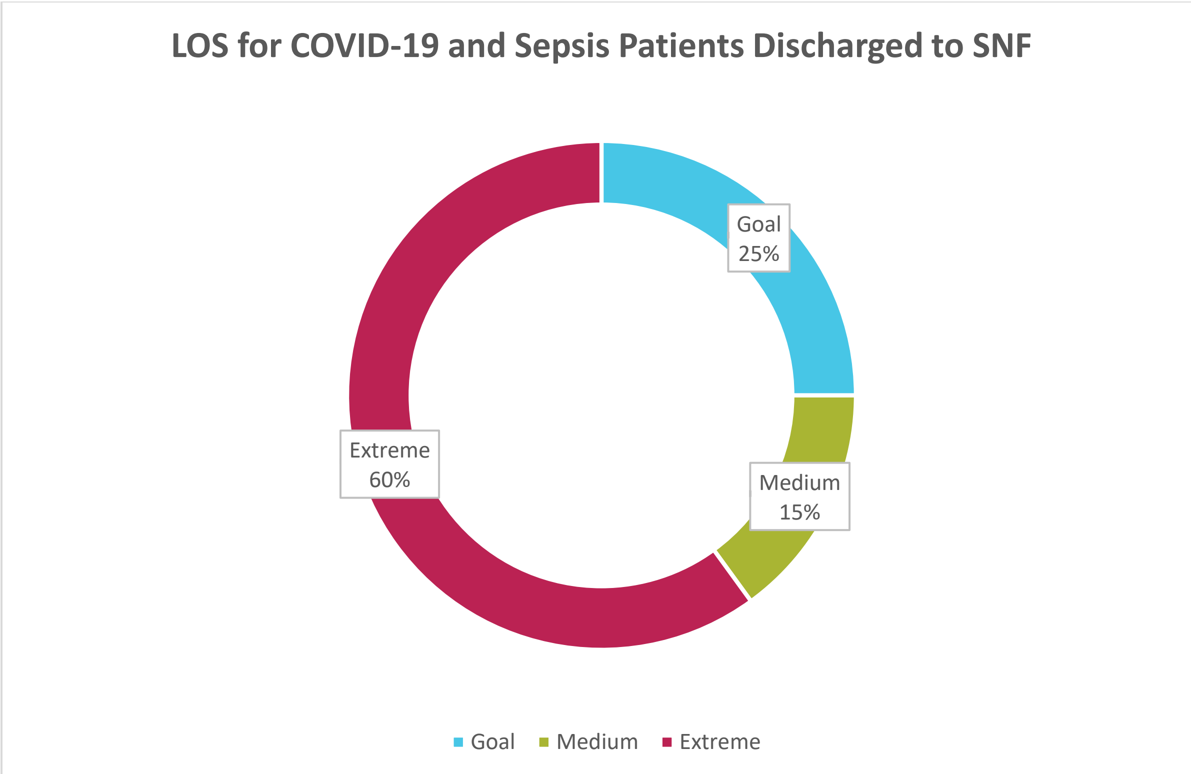

Figure 4. LOS for Patients Discharged to a SNF Characterized by Goal, Medium, and Extreme

Vaccination status was another variable examined regarding LOS. 62% of patients who were unvaccinated had an Extreme LOS while 46% of vaccinated patients had an Extreme LOS. 29% of patients who were fully vaccinated had a Goal LOS compared to the 14% of unvaccinated patients who met the Goal LOS. Fully vaccinated patients had a statistically significant difference of meeting the Goal LOS compared to the combined Medium and Extreme LOS (p=0.007). When combining before vaccines were available patients with unvaccinated patients there is also a statistically significant difference between those patients and the vaccinated patients when comparing Goal LOS to Medium/Extreme LOS (p=0.007). When comparing vaccine type and LOS outcomes, there was no statistically significant difference. Of the patients vaccinated with Moderna, 37.5% met the Goal LOS, 25% met the Medium LOS, and 37.5% met the Extreme LOS.

For patients vaccinated with Pfizer, 27% met a Goal LOS, 27% met the Medium LOS, and 46% met the Extreme LOS.

34 patients (29%) were admitted to the ICU at UPMC McKeesport over this two-year period. 50% of those who were admitted were not vaccinated, 21% were vaccinated, and 29% were admitted before vaccines became available. There are no statistically significant differences in being admitted to the ICU based on vaccination status.

3.3 Secondary Findings for Dual Infection Patients

A majority of dual infection patients admitted to UPMC McKeesport between April 2020 to April 2022 were not vaccinated even after vaccines became available to 18 and older adults in February 2021. Only 21% of patients were fully vaccinated. 43% were unvaccinated and the remaining 36% were admitted before vaccines were available to the public. When vaccination status, broken down by age and mortality, was examined it seems like the mortality of patients age 65 and older decreased when vaccines became available. 23% of the patients in the age group 18-64 were fully vaccinated compared to 19% of the patients in the age group 65 and older. 44% of the patients in the age group 18-64 were not vaccinated compared to 38% of the patients in the age group 65 and older.

It was also found that the patients in the 65 and older age group were more likely to have a PCP prior to COVID-19 vaccine availability. 73 patients (63%) were categorized as seniors, meaning they were either 65 years old or older. 43 patients (37%) were categorized in the age range 18-64. 90% of the patients who were age 65 or older with the dual infection had a PCP. 86% of patients in the age range of 18-64 with the dual infection had a PCP. A majority of patients

(89%) had a PCP when admitted to UPMC McKeesport. 19% of those patients who had a PCP were vaccinated, 42% were not vaccinated, and 39% were admitted before vaccines became available. For the 13 patients who did not have a PCP, 31% were fully vaccinated, 54% were not vaccinated, and 15% were admitted before vaccines were available.

To further investigate the role vaccination status had on severity of disease, discharge disposition was examined with focus on patients discharged to home/self-care, a skilled nursing facility (SNF), and a long-term acute care facility (LTAC). For the 19 patients discharged to home/self-care, 21% were fully vaccinated, 47% were not vaccinated, and 32% were admitted before vaccines became available. For the 20 patients who were discharged to a SNF, 30% were fully vaccinated, 15% were not vaccinated, and 55% were admitted before vaccines were available. For the 6 patients discharged to a LTAC, 17% were fully vaccinated, 17% were not vaccinated, and 66% were admitted before the vaccine became available.

This study also examined where patients were admitted from for patients discharged to acute care, including hospice, LTAC, rehab, or a SNF. Of the patients who were discharged to an acute care facility (34 patients), 59% were admitted from home. 15% of these patients were admitted to the hospital from a SNF and 26% were admitted to the hospital from a personal care home (PCH). For the patients admitted to the hospital from home (20 patients), 50% were discharged to a SNF, 20% were discharged to a rehab facility, 20% went to a long-term hospital, and 10% went to hospice. Of the patients admitted to the hospital from a PCH, 22% were discharged to an LTAC, 22% were discharged to a rehab facility, and 56% were discharged to a SNF.

Table 1. Secondary Findings Based on Age for Patients Admitted with COVID-19 and Sepsis

Age Group	Fully Vax	Not Vax	Before Vax	Has PCP	N PCP	Mortality
18-64	23%	44%	33%	86%	14%	30%
65+	19%	42%	38%	90%	10%	49%

3.4 Tertiary Findings

The data shows that Black males in the McKeesport area could potentially be a population of interest to focus intervention efforts to reduce severity. When looking at race and mortality, 48% of the Black population died while 40% of the White population died. Black males had a slightly higher chance of having a dual infection of COVID-19 and sepsis. Of the male population with a dual infection, 58% were Black and 42% were White. Regarding vaccination status, 56% of Black males were not vaccinated, 17% were fully vaccinated, and 27% were admitted before vaccines were available. 40% of White males were not vaccinated, 16% were fully vaccinated, and 44% were admitted before vaccines became available. The likelihood of having a PCP was compared across the races and sexes of this population. 78% of Black males had a PCP before being admitted to the hospital compared to 91% of White males. 85% of Black females had a PCP, compared to 95% of White females. When dividing the populations by age, 78% of Black males and 72% of White Males were aged 65 and up. 46% of Black females and 50% of White Females were aged 65 or older. 72% of the Black male population required a ventilator at some point in their hospital stay, compared to 69% of Black females, 60% of White males, and 60% of White females. 33% of Black males were admitted to the ICU, compared to 23% of Black females, 30% of White males, and 30% of White females.

Table 2. Tertiary Findings Based on Race and Sex for Patients Admitted with COVID-19 and Sepsis

Race/Sex	Vax	Not Vax	Before Vax	Has PCP	On Vent	ICU	Aged 65+
Black M	17%	56%	27%	78%	72%	33%	78%
Black F	24%	38%	38%	85%	69%	23%	46%
White M	16%	40%	44%	91%	60%	30%	72%
White F	28%	42%	30%	95%	60%	30%	50%

4.0 Discussion

After a retrospective review of dually infection patients, a potential link exists between COVID-19 and sepsis based on patient outcomes. 13% of the COVID-19 positive patients admitted to UPMC McKeesport also developed sepsis. A previous study found the incidence of sepsis in COVID-19 patients to be 11% which supports our findings (Abumayyaleh, 2021). Only 16% of these patients were discharged home without any further care needs. The other 84% of patients either required some sort of long-term care or ceased to breathe, showing the severity of a dual infection of COVID-19 and sepsis. Over the two-year period, the mortality rate increased despite vaccinations being available (**Figure 1**). Vaccinated patients were still developing COVID-19 and sepsis but looking at the difference in mortality rates between vaccinated (29%) and unvaccinated (56%) patients shows that vaccines offered protection.

Intubation and ventilator usage is a good indicator of how severe a dual infection of COVID-19 and sepsis can be. Of the patients who were intubated, 94% of them ceased to breathe. There was a significant difference between mortality for patients who required a ventilator compared to the patients who did not require a ventilator. One study found that COVID-19 mortality rates are strongly associated with ventilation, especially when critically ill and in need of intensive care (Cidade, 2022). Early research on ventilator associated mortality in COVID-19 patients suggests a lower rate, but differences could be due to specific physiological changes the patient endures during ICU stay (Auld, 2020; Moitra, 2017). There is an increased chance of mechanical ventilation the longer a patient stays in the ICU (Moitra, 2017). Looking at vaccination status in those who required intubation, only 50% of the vaccinated population required intubation compared to the 66% of the unvaccinated population. This hints at vaccines protecting the patient from more severe outcomes, but no conclusion can be made here.

Length of stay (LOS) was the main severity measure that indicated a potential link between COVID-19 and sepsis. The average LOS for dual infection patients was significantly higher than non-COVID-19 patients (**Figure 2**). This indicates that patients with a higher severity of disease need a longer stay in the hospital. One study found that the median hospital stay for dual infected patients was 17 days and 28 days for non-COVID-19 septic patients (Heubner, 2022). In theory, those patients who were discharged home should have a shorter LOS and less severe disease. Patients with COVID-19 only have a significant difference in LOS when compared to patients admitted to the hospital for non-COVID-19 reasons. This suggests that even alone COVID-19 can be a severe disease. One study on COVID-19 found that newly emerged care needs were a complication of the infection; 27% of their population who were previously self-sufficient were not able to return to their home after discharge (Herrman, 2021). The patients who were discharged home or to self-care from UPMC McKeesport had a higher chance of meeting the Goal or Medium LOS (**Figure 3**). The patients who were discharged home were more likely to be in the hospital 5 days of less. There is a significant difference between admission and discharge disposition when comparing patients who met the Goal LOS to Extreme LOS. Those who were discharged to a SNF were more likely to have an Extreme LOS meaning they were more likely to be in the hospital 10 or more days (**Figure 4**). This suggests that patients with a more severe disease course will have a longer LOS and be more likely to require secondary care after discharge. In a previous study regarding ICU LOS, patients who were in the ICU for more than two weeks were less likely to be discharged home and were more likely to required secondary care (Moitra, 2017).

Vaccinated individuals were less likely to have a Medium or Extreme LOS compared to the unvaccinated patients. Fully vaccinated patients had a significant difference of meeting the Goal LOS compared to the combined Medium and Extreme LOS. This suggests that vaccinations can provide protection against the more severe disease course that a dual infection can have. Vaccination status influenced a patient's likelihood of having a shorter LOS compared to unvaccinated patients. The numbers for vaccine type were too small to make significant conclusions, but when comparing Moderna and Pfizer vaccines in our population, those patients vaccinated with Moderna had a higher percentage with Goal LOS. This means that patients who were vaccinated with Moderna were more likely to be in the hospital five or less days. Patients vaccinated with Pfizer had a slightly lower percentage of patients who met the Goal LOS and slightly more patients in the Extreme LOS meaning that patients vaccinated with Pfizer were more likely to be in the hospital more than 10 days. Due to the small sample size, differences between vaccine type and protection in regard to LOS could not be concluded to be statistically significant.

A majority of patients who died from combined COVID-19 and sepsis infections were not vaccinated, even after vaccines became available to 18 and older adults in February 2021. The results suggest that the mortality of patients aged 65 and older decreased when vaccines became available, showing vaccines did improve patient outcomes. Vaccinations may have helped the aged 65 and up population survive based on the unvaccinated mortality decreasing from 79% to 57%. Regardless of vaccination status, age and comorbidities are risk factors for poor outcomes in patients who are infected with SARS-CoV-2 (Busic, 2022). Research in the 65 and older population showed that these patients were more likely to have a primary care physician (PCP) before vaccines became available to the public (**Table 1, Column 5**). This may have contributed to their willingness to get vaccinated, but it cannot be proved in this study. Primary care delivers quality healthcare which improves health outcomes in the population (Caswell, 2022). Having a primary care physician can improve the likelihood of a patient receiving regular care that could lead to better health outcomes.

Minority groups have been disproportionately affected by the COVID-19 pandemic (Reyes, 2020). This research suggests that Black males could be a population of interest to focus intervention efforts. Black males were the demographic with the highest percentage of the population that were not vaccinated and the lowest percentage that had a primary care physician. A majority of the Black male population studied were over 65 years old. The Black male population had the highest usage of ventilators when compared to other races and sexes (**Table 2, Row 2**). There were no statistically significant differences between race or age and outcome, but this could be due to the small sample size. Minorities face greater difficulties accessing primary care compared to White populations (Shi, 2012). African Americans historically have been disproportionately diagnosed with comorbidities, which is a known risk factor for more severe outcomes in COVID-19 (Reyes, 2020). There is potential for future research in these populations for prevention efforts to improve patient's outcomes.

4.1 Limitations

The study has several limitations. First, the sample size of 116 COVID-19 and sepsis patients is small and could not offer many significant conclusions. The LOS variable could be confounded by the facility's requirements around COVID-19 admissions. The study found no significant differences between COVID-19 patients average LOS and combined COVID-19 and

Sepsis average LOS (p=0.08). It cannot be concluded that a longer LOS is more likely for dual infection patients when comparing to COVID-19 positive patients.

4.2 Future Directions

This study provides basic data on a potential link between COVID-19 and sepsis. Larger, multi center studies could provide additional evidence of a link between the two diseases. Future research into COVID-19 and sepsis that could identify risk factors for viral sepsis caused by SARS-CoV-2 can lead to better detection methods and control of disease in clinical practice (Tang, 2021). It seems that vaccinated individuals had a less severe illness and less mortality compared to unvaccinated individuals, but vaccinated individuals were still developing COVID-19 and sepsis. Research on COVID-19 vaccines show that unvaccinated individuals are at greater risk for dying than unvaccinated individuals (CDC, 2022). It is possible patients had less of a chance of dying from the dual infection if they were fully vaccinated and a fifty/fifty chance of dying if unvaccinated. Research shows that patients who are vaccinated against COVID-19, regardless of type of vaccine, had a lower mortality rate and less frequently required mechanical ventilation when compared to unvaccinated individuals (Busic, 2022). The number of vaccinated patients was too small to suggest significant differences between vaccinated and unvaccinated individuals. Only 24 patients were fully vaccinated in the population. The study patient population was not big enough to make a conclusion about vaccine type, whether one brand was more effective at protecting the population over the others. More data is needed to determine prevention strategies, including vaccinations. The sample size is too small to confirm if vaccinations improved any outcomes other than LOS. A larger sample size and longer period of study could offer better conclusions for the link between COVID-19 and sepsis.

5.0 Conclusion

There is a potential link between COVID-19 and sepsis based on this research. Ongoing research is needed to confirm the link. Severe COVID-19 and sepsis have similar characteristics and prognoses. Linking these two diseases could lead to improved patient outcomes by early identification of potential severe disease. Efforts to prevent mortality from the dual infection can be started at the beginning of hospital admission instead of waiting until sepsis develops if hospital staff could identify those COVID-19 patients who are more likely to develop sepsis. Definitive evidence of a link between sepsis and COVID-19 can lead to targeted intervention efforts and more informed prevention measures.

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