# DETERMINANTS OF COVID-19 SEVERITY AND OUTCOME AMONG NORTHERN SASKATCHEWAN FIRST NATIONS

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## Abstract

**Background:** Severe acute respiratory syndrome due to Coronavirus-2 (SARS-CoV-2) remains a global public health concern. Demographic and medical factors like vaccination status have been reported to influence the disease burden and outcome. Indigenous populations have been reported to be disproportionately affected by COVID -19; however, the impact of COVID-19 on Indigenous people in Canada remains understudied. The objectives of the study are to: 1) describe the characteristics of COVID-19 cases among on-reserve northern Saskatchewan First Nations people for the period March 2020 to December 2022; and 2) determine the association of demographic and medical factors with various indicators of COVID-19 severity and outcomes.

**Methods:** We accessed de-identified data of 8,428 laboratory-confirmed COVID-19 cases during the period March 2020–December 2022. We conducted univariate, bivariate, and multivariate analyses to describe COVID-19 in this population and to determine the of association between various characteristics and COVID-19 severity. Characteristics of interest were demographic, clinical, and vaccine related. Three indicators of severity were included: hospitalization, admittance to an intensive care unit, and death.

**Results:** Even though they account for <5% of the population, northern Saskatchewan First Nations on-reserve reported 5.6% of the total number of COVID-19 cases in the province. Over 90% of cases were under 65 years old. More than 53% of cases had no COVID-19 vaccination history at the time of infection. The most common clinical symptoms reported among COVID-19 patients in the study were cough, fever, loss of taste, and loss of smell. We observed that people 65 years and older were more likely to be hospitalized with severe COVID-19, despite having less than 10% of the infection rate of younger individuals. This finding is similar to other studies in Canada and other parts of the world. More hospitalization and deaths were associated with males than females. Hospitalization, ICU admission, and death were higher among unvaccinated persons when compared to those who were vaccinated. Similarly, hospitalization was higher among individuals who were vaccinated for >12 months before onset of infection. Like in other studies, the presence of symptoms, and co-existing medical conditions were significantly associated with increased odds of hospitalization. The risk of dying from COVID-19 was higher in people >65 years, males, and those with co-existing medical conditions. The risk of dying from COVID-19

was lowered following vaccination with two or more doses of COVID-19 vaccine when compared to those who received one dose of the vaccine or those who were not vaccinated.

**Conclusion:** The implication of this study finding is that prioritizing vulnerable populations during COVID-19 and in subsequent public health emergencies and providing them with relevant interventions will reduce the burden of disease among these groups of individuals.

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| | |
|---|---|
| CI | Confidence Interval |
| COVID-19 | Coronavirus Disease 2019 |
| DM | Diabetes Mellitus |
| ICU | Intensive Care Unit |
| FNCZ | Far North central Zone |
| FNEZ | Far Northeast Zone |
| FNWZ | Far Northwest Zone |
| NCDs | Non-Communicable Diseases |
| NCZ | North central Zone |
| NEZ | Northeast Zone |
| NITHA | Northern Inter-Tribal Health Authority |
| OR | Odds ratio |
| rRT-PCR | Real time Reverse Transcription Polymerase Chain Reaction |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome due to Coronavirus Type 2 |
| SDoH | Social Determinants of Health |
| SE | Standard error |
| US | United States |
| VoC | Variant of Concern |
| WHO | World Health Organization |

# Chapter 1: Introduction

## 1.1. Background

Respiratory illness associated with severe acute respiratory syndrome due to Coronavirus-2 (SARS-CoV-2) also referred to as Coronavirus disease 2019 (COVID-19) has caused over 6.7 million deaths globally, representing over 1% of total mortality as of January 22, 2022 (1). Morbidity and mortality reports in Canada indicate that as of December 31, 2022, over 49,000 persons have died due to COVID-19 outbreak. This represents slightly over 1% mortality rate since the beginning of the outbreak in 2020 (2), a picture that is similar to the global trend of the pandemic. The COVID-19 pandemic has been identified as a major contributor to morbidity and mortality in several countries when compared to other viral infections (3–6). In the United States, Mexico and many European countries, COVID-19 was singled out as the number one cause of death especially at the initial phase of the pandemic (3,7–9).

The severity and outcome of COVID-19 infection are influenced by demographic factors and previous medical history of infected individuals. Studies have shown that the risk of COVID-19 infection was more than >3 times higher among persons with underlying illnesses including obesity, diabetes, chronic kidney disease, hypertension, and asthma. These studies recommend that persons with a higher risk of infection should be prioritized for preventive and therapeutic interventions (10–13). Demographic factors and medical history have been reported to impact the severity of COVID-19 infection among adults, including those who have completed a primary vaccination series in the United States (14). Beyond morbidity and mortality concerns, studies in different parts of the world have highlighted the concern of COVID-19 related hospitalization and length of hospital stay—a component of the pandemic that has become important due to pressure on health care systems and increased health spending. In Canada (excluding Quebec), hospitalization cost was reported to be over $317 million between January and November 2020 (15). Common findings across studies show that factors like sex, age, and pre-existing immunosuppressive comorbidities play a significant role in determining the severity of COVID-19 infection, impacting the necessity to hospitalize and prolonged hospital stay among hospitalized cases (16–23). Separate systematic reviews involving over 100 publications have also corroborated the finding that sex, age and pre-existing medical conditions affected hospitalization and length of hospital stay for COVID-19 cases (24–26).In Canada, a 2021 population-based cohort study

conducted in British Columbia found that pre-existing medical conditions along with age and immunization status impacted the hospitalization rate due to COVID-19 infection. This study also reported that vaccine uptake played a critical role in reducing the risk of hospitalization across the various age groups that were studied (27). A 2020 national cohort study conducted across 32 hospitals in Canada to characterize COVID-19 cases over a seven months period found that age was a significant determinant of COVID-19 related deaths in the study population (28). Another study that looked at length of hospital stay in Quebec and Ontario from March 2020–June 2021 identified the role of age in determining the length of hospital stay. This study also observed that those who died in hospital spent fewer days after admission (29). A November 2019–June 2020 hospital-based study conducted in Toronto compared the severity and outcome between COVID-19 and influenza; it showed a higher death rate, hospitalization/intensive care (ICU) use, and longer length of hospital stay in COVID-19 cases compared to influenza patients (30).

Among Indigenous populations in Canada and in other parts of the world, COVID-19 further exposed existing health disparities due to the inequalities in the social determinants of health (SDOH) (31,32). Social determinants of health including environment and economic stability have been reported to affect morbidity, recovery, and mortality from COVID-19 infection (33,34). Health inequalities and disparities that exist in accessing COVID-19 prevention and treatment services among people in different socioeconomic strata have been identified to be a major contributor to the negative impact of COVID-19 among Indigenous populations (35,36). Additionally, Indigenous populations in Canada have been reported to have higher risk of COVID-19 infection due to the inequalities associated with transgenerational trauma and racial discrimination which may affect their access to health care services and other amenities that further increase their vulnerability to infections and outbreaks (37–41).

The SDOHs among Indigenous populations in Canada are exacerbated by the intersections with structural health inequities arising from the effects of colonization, residential school history, loss of access to land-based traditional practices, and loss of language and culture (42,43). These intersections affect life-course of the Indigenous people with further impact on reported health issues affecting them (44,45).Despite the availability of thriving conditions for COVID-19 infections in minority populations, including Indigenous populations (31,37,38), the severity and outcome of the pandemic and how it affected the livelihood of this minority group has not been

adequately studied (46). Studies on the severity and outcome of COVID-19 in Indigenous populations have been reported in the US and Mexico among American Indians and Native Alaska (AI/NA) (47–49). A study among AI/NA showed that despite having lower comorbidity risk, the AI/NA were more likely to die in the hospital due to COVID-19 infection compared to patients in the general population (47,48). Serván-Mori and colleagues similarly reported in 2022 that Mexican Indigenous population were more likely to be admitted in the hospital and more likely to die from COVID-19 compared to non-Indigenous populations (49). Comparative studies on the basis of race have documented differences in the severity and outcome of COVID-19 across different racial backgrounds, including Indigenous and non-Indigenous populations (46,49–51). In Canada, limited documentation exists on the COVID-19 outcome in Indigenous populations who are disproportionately affected by health inequalities (52). This study, therefore, aims to describe and identify the determinants of COVID-19 severity among Northern Saskatchewan First Nations on-reserve communities. In countries like Australia, issues of disparities in the determinants of health. A study that compares the risk perception of COVID-19 between rural First Nations Australians and non-First Nations respondents indicated that rural First Nations Australians demonstrated higher risk perceptions as a result of inequitable risk communications compared to non-First Nations respondents (53). Disparities in food security, health information, economic and other disparities of social determinants of health that exist among Indigenous peoples in Australia and across the globe (54–56).

### 1.3. Objective and Research Questions

#### 1.3.1. Objective

The objectives of the study are to: 1) describe the characteristics of COVID-19 cases among on-reserve northern Saskatchewan First Nations people for the period March 2020 to December 2022; and 2) determine the association of these characteristics with various indicators of COVID-19 severity and outcome.

#### 1.3.2. Research Questions

Among on-reserve northern Saskatchewan First Nations people with confirmed COVID-19 for the period March 2020 to December 2022,

1. What are the demographic, clinical, and vaccination-related characteristics of these individuals, both (a) overall and (b) among those with severe (i.e., hospitalized) COVID-19?
2. What demographic, clinical, and vaccination-related characteristics are associated with COVID-19 severity as indicated by hospitalization, ICU admission, and death?

### 1.4. Statement of the Problem

The COVID-19 pandemic has been described as one of the biggest disease outbreaks affecting humans. With high numbers of mortalities, it plunged the world into health and economic crises. Two of the pandemic's visible outcomes—hospitalization and mortality—have been described as dependent on several factors including age, sex, race, presence of co-existing medical conditions, and vaccination status.

A US study indicated that the majority of the people hospitalized were over 60 years old, were ethnic minorities (Black and Hispanic), and had co-existing medical conditions (57). Comparison between vaccination and hospitalization rates showed that unvaccinated people were 3.5–17.7 times more likely to be hospitalized than vaccinated individuals. Hospitalization was also higher among unvaccinated persons, even with the emergence of the omicron variant (58).

In Canada, about 8% of reported COVID-19 cases require hospitalization (52). A population-based cohort study during the first three waves of the pandemic showed that the odds of hospitalization and death were higher during the first wave of the pandemic, which happened before the introduction of vaccines (29). Another study reviewed one public health database in Ontario and showed that being male, older than 90 years, and living in a rural area presented higher odds of COVID-19 fatalities compared to being 20 years or younger, female, and living in urban areas respectively (59). A similar trend was reported in Alberta where COVID-19 deaths were reported to be higher in adults older than 54 years compared to younger people (60).

In Saskatchewan, the COVID-19 hospitalization rate was 3.1% as of September 2021 (61). The hospitalization rate had increased since March 2020 when the rate was 2.2%, and the increasing hospital admission rate was identified by the Province's Premier to be pushing the intensive care units within the province to their capacity limits (61,62).

COVID-19 mortality  higher among the poor, and among older males (63). Between March 2020–October 2021, Saskatchewan reported the second highest number of COVID-19 deaths in the country (after Quebec) from, with most of the deaths occurring between November 2020 and February 2021 (64). Contrary to reports about the impact of age and comorbidities on the severity and outcomes of COVID-19, studies in Saudi Arabia, India and Uganda found out that age and presence of comorbidities were not significant predictors of COVID-19 severity and length of hospital stay (18,65,66)—a position that was confirmed by Liu et al. (2020) for age and other comorbidities besides hypertension (68).

### 1.5. Purpose of the Study

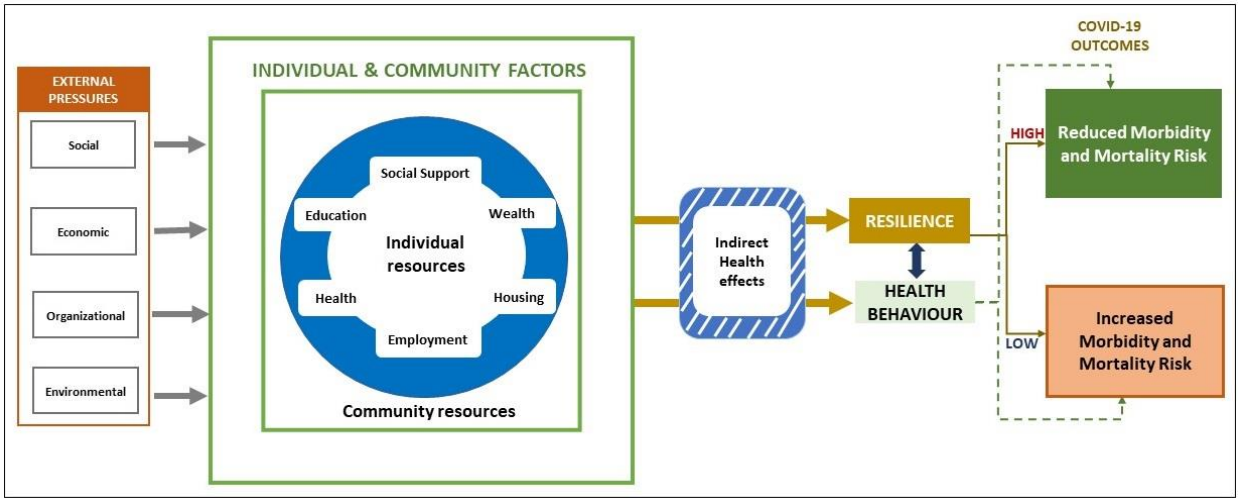
Researchers have posited the role of demographic factors, comorbidities, and vaccination in determining the course of COVID-19 across different racial backgrounds. It is important to also understand the role of these factors on the severity and outcomes of COVID-19 infection among northern Saskatchewan Indigenous populations living on-reserve. The dearth of information about the pandemic in Indigenous populations and paucity of information on Indigenous population in Canada make valid assumptions about COVID-19 in Canadian Indigenous populations difficult. In 2021, Waldner and colleagues suggested that more studies should be conducted to understand the epidemiology of the SARS-CoV-2 in Indigenous and other minority populations (52). Even though there is a high recovery rate associated with COVID-19 infection, sequelae including post-traumatic disorder, anxiety, and reduced exercise tolerance may persist after recovery from COVID-19 infection (69). Therefore, understanding the severity of COVID-19 infection among Indigenous populations will have implications on planning and implementation of appropriate public health interventions. Knowledge of the impact of the pandemic among on-reserve northern Saskatchewan First Nations will play a significant role in preparing for subsequent public health emergencies, which requires better collaboration, strengthening of existing health architecture, funding, and incorporating lessons learned from the current pandemic (70).

### 1.6. Conceptual Model for COVID-19 Infection Outcomes

The concept for this study is adopted and modified from the model of Saban and colleagues. The model states that availability of resistant resources, or deficit thereof, could lead to either worsened or better health through a sense of coherence and resilience building (71). This model is built

around the social determinants of health and the principle of salutogenesis. According to the model, in the event of health crises—such as those initiated by the COVID-19 pandemic, external pressures, or individual and community factors—working with indirect health effects could contribute to resilience building and health behaviours that may affect morbidity and mortality. The schematic representation of this conceptual model is represented in Figure 1.

Figure 1- The Conceptual Model for COVID-19 Outcomes




1.6.1. External Pressure

In outbreak situations, external pressures from policies initiated by government to curb disease transmission may impact people's inherent factors, and subsequently affect their resilience and health behaviours. In this way, such policies can have an overall effect of the disease outcome. Social policies around isolation and social distancing played a significant role in reducing the spread of SARS-CoV-2 and mitigating the impact of COVID-19 pandemic (72). Acceptance or rejection of these social policies played a role in interrupting or influencing the transmission of the virus; however, resultant psychological underpinnings impacted people's decisions to accept or reject the measures (73,74). The impact was further complicated by inequities in the social determinants of health, including equitable distribution of housing, education, and health care services between peoples across geographical and economic spaces. Experiences of fatigue also accompanied these policies over time.

The COVID-19 pandemic affected economies across the world, including high rates of job losses, tax income losses, disruption in transportation and global trade (75). This further negatively

impacted the already stretched economies. Organizational and political policies, according to Saban et al. included restriction of movement through lockdowns which were for a short term, but prolonged in some countries (71) depending on the dynamics of the pandemic in these countries.

Environmental policies were impacted during COVID-19, influencing individual and community factors, which in turn influenced COVID-19 morbidity and mortality. These environmental factors comprised changes in traffic, climate, environmental pollution (including changes in waste level and the recycling systems which impact on physical and water spaces), and access to green areas (71,76). While movement was restricted to prevent spread, active community transmission continued within closed environments, setting back the gains made with transportation and environmental pollution.

1.6.2. Individual and Community factors

Individual attributes were distorted by the COVID-19 pandemic and the external factors associated with the policies changes to control the spread of the pandemic. Closure of schools, and other educational and recreational facilities resulted in loss of study and social interaction time, particularly at the beginning of the pandemic. The introduction of virtual academic sessions provided an alternative, but this could not replace the additional value that is associated with physical class attendance such as physical contact, rapport building and physical activity including sports; extracurricular activities and games that produce a far reaching effect on health status (77). The effect of COVID-19 on housing resulted from the fact that more people were required to remain at home due to movement restriction, and thereby exposing the housing challenge as more people had to stay within enclosed spaces for longer periods. This further increased the chances of infection transmission especially in the face of increasing housing shortage (78).

According to Saban et al, several factors impacted livelihoods during the pandemic: health (due to closure of health facilities, prioritizing of health services, shortage of facilities within the facilities and manpower within the health care sector generally); employment (as a result of massive job losses, slow pace operations due to the transition to electronic transactions); wealth (reduced access to finances and lack of employment or trading); and, social support (both direct and indirect due loss of family and friend networks, and inadequate government support) (71,77). This had an overall effect on the number of COVID-19 cases.

### 1.6.3. Indirect health effects

Mental health, acute and chronic non-communicable diseases (NCDs) became topical issues of concern since the onset of the COVID-19 outbreak; they are indirect consequences of the external pressures that impacted individual factors. Cases of depressions, increased alcohol consumption, substance use, and other mental health issues became exacerbated due to the impact of these external factors (79–81). The risk of non-communicable diseases such as obesity, diabetes, hypertension, and other cardiovascular disease increased among individuals with low resilience due to reduced physical activity and increased sedentary lifestyle (82–84). This further highlights the relationship between the indirect health effects and resilience: lifestyle changes increased vulnerability and reduced resilience against contracting severe COVID-19, sometimes with fatal outcomes. Poor mental health and NCDs were reported as significant predictors for the occurrence of severe COVID-19 outcomes. A study in the United States posited the relationship between individual factors (income and health disparities, and racial background), indirect health effect and resilience, with individuals who had better mental health being more resilient and optimistic (85).

### 1.6.4. Resilience and health behaviour

Resilience is a positive psychological change, also known as post-traumatic growth. It involves a combination of personal characteristics and dynamic processes by which people adjust and move ahead in response to traumatic or challenging situations (86). A cross-sectional study in Saudi Arabia reported highlighted resilience as a significant protector against the COVID-19 pandemic fatigue, which was measured by declined adoption of protective measures against COVID-19 (87). Adults in the US were reported to have higher resilience in the presence of social support, and physical activity (88). In Canada, a study on potential risk factors and resilience further highlighted their relationship within two weeks after introduction of the COVID-19 preventive measures (89). The relationship between resilience and COVID-19 related health behaviour like face mask use, handwashing with soap or hand sanitizing, and social distancing in public places has been reported (86,87,90). Zarowsky and Rashid reported that social support, including the strengthening and optimizing of familial relationship were critical in building resilience and wellbeing as the pandemic control measures remain in place (91). A multi-country study that included countries from Asia, America, Europe and the Middle East further affirmed these findings of the role of resilience in COVID-19-associated health behaviour (82).

1.6.5. Morbidity and mortality

Resilience and health behaviour have been reported to impact COVID-19 severity and outcomes (morbidity and mortality). A cross-sectional study in Turkey reported that increased health perception was significantly associated with increased resilience (92). A longitudinal study in Canada among individuals with multimorbidity found increased resilience to be protective against the pandemic impact (93). These findings corroborate the submission by Saban and colleagues who postulated in their model that reduced morbidity and mortality were associated with the interplay between increased resilience and improved health behaviour (71).

## 1.7. Definition of terms

***Severity –*** Severity was defined to be based on the patient's critical desire for help by underscoring the degree of poor health (94). In this study, severity was defined using site of care as proxy which include outpatient (indicated by home isolation and management), inpatient general ward, and ICU admission (95).

***Outcome –*** Outcome refers to the variable used to document the impact of exposure (COVID-19) on the health of infected person. It is also referred to as endpoint (96), and categorized in this study as either cure/discharge or death.

***Confirmed cases –*** Confirmed cases was defined as individuals who have been verified to be infected with SARS-CoV-2 through laboratory diagnosis using real time reverse transcription polymerase chain reaction (rRT-PCR).

***Hospitalization –*** In this study, a hospitalized case was defined as person infected with COVID-19 who was admitted to the in-patient general ward or ICU for a period of longer than 24 hours for the purpose of treatment or observation/monitoring.

***Indigenous population*** – These are referred to as a group of people  certain ethnicities who are the original or earliest settlers in a geographic location (54).

## Chapter 2: Literature Review

This chapter presents an overview of COVID-19, beginning with the origin and cause of COVID-19. The chapter then describes COVID-19 in terms of mode of transmission, clinical symptoms, diagnosis, treatment, and prevention. The burden of the disease globally, in Canada, and among Indigenous populations is then highlighted. The final sections describe the waves of COVID-19 and risk factors for severe outcomes.

### 2.1. The origin and cause of COVID-19

The Severe Acute Respiratory Syndrome due to Coronavirus-2 (SARS-CoV-2) was first reported by the World Health Organization (WHO) on 31st December 2019, after being notified of a cluster of respiratory illness in Wuhan, China. The first case was documented to have started earlier in December, 2019 and was already circulating prior the notification of WHO later in the month (68,97,98). The origin of the disease was reported to be associated with seafood market posing assumptions of animal-to-human, and subsequently human-to-human transmission (99,100).

The cause of the outbreak was revealed as the beta subgroup of the *Coronaviridae* family (100), which became first known as the 2019-novel Coronavirus (2019-nCoV), and later named as the Coronavirus disease 2019 (COVID-19). It was subsequently referred to as severe acute respiratory syndrome due to Coronavirus-2 (SARS-CoV-2). By the end of January 2020, the WHO describe the outbreak as a public health emergency of international concern (PHEIC). The WHO later declare the outbreak as pandemic on March 11, 2020 because of the vast global spread and large number of cases (101), with over 121,000 cases across 110 countries and 4,373 deaths (102,103) in its first 100 days. The spread of the virus was so fast that by the fifth week of the outbreak, over 40,000 cases and about 900 fatalities had been reported in 25 countries globally (104). By the end of February 2020, there were over 78,000 cases with over 2,700 reported deaths in more than 40 countries (102). During this period, the characteristics of the cases showed that the average age of those affected was 51 years with majority of the cases in those 30–69 years old (105).

### 2.2. Transmission and clinical symptoms

Transmission of COVID-19 from among humans is through infected respiratory droplets, with some suggestions of possible spread via the faeco-oral route (100,106). The virus was reported to

have an incubation period of about 5 days and up to 14 days (104). Transmission has been documented to occur from asymptomatic persons who have the capacity of infecting approximately 3 persons each during the period of infectivity (106).

The clinical symptoms of SARS-CoV-2 infection have been shown to include fever, dyspnea (breathing difficulty), anosmia (loss of smell), and headache (107). In another study, O'Brien et al reported that cough, chills, weakness and pain were the four most common clinical symptoms of COVID-19 which occur at a similar rate in male and female patients (108). Accordingly, fever was reported more in male patients while sore throat, runny nose, shortness of breath, nausea, diarrhea and headache were reported more among female patients (108). In describing the COVID-19 pandemic, the World Health Organization (WHO) identified fever, cough and fatigue as the most common symptoms (105). These symptoms have been reported in infected persons within 5–6 days post infection, and over 80% of cases develop mild to moderate symptoms (105).

### 2.3. Diagnosis of COVID-19 infection

Nasopharyngeal and oropharyngeal swabs and washes have been recommended as the ideal samples for the diagnosis of COVID-19 using laboratory techniques. These samples are tested using molecular techniques like RT-PCR, real-time RT-PCR (rRT-PCR), reverse transcription loop-mediated isothermal amplification. Finally, quantitative RT-PCR (for earlier identification of COVID-19 infections) has been identified as the gold standard for laboratory diagnosis of COVID-19 (109–111).

For COVID-19 surveillance intensification, countries adopted the rapid diagnostic screening tests which has quicker turn-around time, is cost effective and requires minimal expertise for utilization and interpretation of results. These tests were deployed for screening and mass testing to limit community spread of COVID-19 (110,112). Lung computed tomography have also been used for COVID-19 diagnosis with a sensitivity of over 90% (113,114).

Presumptive diagnosis—with the help of clinical symptoms such loss of smell and taste following the occurrence of fever, cough, and/or sore throat (115)—has been reported to be helpful for initial identification of cases.

## 2.4. Treatment and management of COVID-19

About 50% of COVID-19 cases may not show signs of infection (116,117). However, in the event of clinical disease supportive, symptomatic, and even full clinical management involving the use of antiviral drugs may be necessary (118). Generally, Hafeez et al. recommended rest with adequate food and water for energy and hydration. Symptomatic treatment involves management of fever through the use of antipyretics and application of sedatives to children who may have convulsion or seizure (118).

Clinical management of COVID-19 cases may require the use of oxygen therapy due to increased risk of hypoxia following the virus's attack on the lung tissues (118). The use of high-flow oxygen through nasal cannula reduces the demand for mechanical ventilation and improve outcome for patients with severe COVID-19 symptoms, and this clinical intervention reduces the need for intensive care unit (ICU) (119–121). In situation where shock is not indicated, fluid therapy after initial resuscitation may be necessary. Antibiotic treatment for secondary bacterial infections, and continuous oxygenation to prevent further oxygen shortage is also recommended (122).

Chloroquine and hydroxychloroquine received a lot of attention among researchers and clinicians who recommended their use for the management of acute COVID-19 infection, in combination with azithromycin (100,123). Antiviral drugs with broad spectrum of action such as remdesivir were used to manage COVID-19 cases. Drugs such as lopinavir and ritonavir were reported to improve COVID-19 outcomes (99,123). Additionally, drugs such as losartan, telmisartan, baricitinib, and darunavir were documented to have varying efficacies in the treatment of COVID-19 (123), and in other combined therapy approved for trial and emergency use (97) at various stages during the pandemic.

## 2.5. Prevention of COVID-19

### 2.5.1. Non-Pharmacological measures

Several preventive measures were initiated during the early stages of the pandemic and included the use of non-pharmaceutical interventions like self-isolation of suspected cases to prevent spread, hand hygiene (regular hand washing and use of hand sanitizers), and respiratory hygiene (covering of cough and sneeze). The use of personal protective equipment such as face masks/shields, and physical/social distancing to prevent individual and community transmission also became common

(118,124). Also considered as a preventive measure is adequate ventilation of indoor spaces (125). The use of these non-pharmaceutical approaches also served as control for other infectious respiratory diseases (126). The effectiveness of these non-pharmaceutical interventions have been demonstrated in Shanghai, China where implementation of the non-pharmaceutical interventions reduced the number of cases from 27 to 0 cases in 53 days (127). Another study by Girum et al. reported that social distancing, stay at home, travel ban and lockdown reduced the number of daily case count by at least 90% (128). Knowledge about COVID-19 plays a very good role in enhancing compliance with these preventive measures. As part of the ways to improve utilization of the non-pharmaceutical interventions, Zhang et al. (2020) reported the role of community engagement in the uptake of these non-pharmaceutical interventions in Shanghai. Studies in Ethiopia and Ghana identified that knowledge about the COVID-19 significantly influenced the utilization of these public health interventions that were instituted to prevent further spread of the disease (129,130).

#### 2.5.2. Pharmacological measures

Globally, several vaccine candidates have been rolled out to complement the non-pharmaceutical interventions and support in returning to normalcy. The approaches to implementing these vaccination campaigns differ across countries based on the nature of the pandemic, and the type of vaccines being utilized (131). With over 33 vaccine candidates and over 10 billion doses produced and distributed globally, the vaccines have reduced the number of cases, and severity of the COVID-19 pandemic, while helping to return life to normal (132). However, key issues have been noted around the introduction of vaccines. These issues include the emergence of the virus variants, and the need for multiple doses of the vaccines due to waning immunity conferred by the vaccines (133,134). The vaccines have been effective in reducing the number of new infections and in easing pressure on the use of non-pharmaceutical public health interventions.

### 2.6. Burden of the disease

#### 2.6.1. Global burden of COVID-19

Even with decreasing number of cases and deaths, COVID-19 remains a major global public health threat. A majority of cases occurred in Europe, North America and Asia with fewer confirmed cases reported in Africa and Australia (135). The number of daily cases reported, and mortality have dropped since the introduction of vaccine resulting in the easing of the stringent public health control measures. However, the SARS-CoV-2 virus remains a global threat due to periodic

emergence of variants for which vaccine candidates may not confer protection (136) and waning vaccine efficacy (137). Studies have shown that protection against re-infection is likely in COVID-19 (138), and this further explains the reason in the drop in number of new cases. Globally, the burden of COVID-19 has been reported to be underestimated as a result of asymptomatic cases that could be missed by the surveillance system, cases occurring with non-specific symptoms, and inadequate testing capacity especially in low resource settings (139,140). In Turkey, the policy of counting only PCR-confirmed cases—without consideration of suspected cases from hospitals or follow-up—was responsible for under-reported COVID case numbers in the country (141).

The burden of disease has been influenced by demographics, health care systems, and other factors that may not have been readily identified (142). A report on COVID-19 burden between Africa and other parts of the world states that the lower number of cases and deaths in Africa could be attributable to the younger population with median age of 18–30 years old compared to the Americas (with older population) where the median age was over 40 years old (143). Another study that involved 21 African countries underscored the role of medical comorbidities on the burden of COVID-19 in Africa (144). In Poland, it was reported that the impact of COVID-19 was greater among men than women, and that the impact of the pandemic increased with age for both men and women (145). An observational study to describe the burden of COVID-19 in 16 countries across Europe using disability-adjusted life years (DALYs) showed that Italy, Czech and Sweden had the highest DALYs per 100,000. The finding in Italy was attributable to the demographic characteristics of Italy, considering that the country was one of the worse hit in terms of number of cases and deaths (146).

In age-specific study among the Hispanics in the US, COVID-19 morbidity was significantly associated with workplace exposure with little evidence to support the role of pre-existing health condition, health inequalities and multigenerational household composition (147). A significant reduction number of COVID-19 cases was observed across the American continent; however, the Pan-American Health Organization (PAHO) on March 9, 2022 advised that countries should continue with surveillance (148). A study in the US reported that about one-third of the population had been infected with the SARS-CoV-2 (149). Hotez and colleagues reported that populations such as Indigenous populations may be at higher risk of severe COVID-19 with fatal outcomes because they could have little or no access to preventative vaccines and medicines (150). Another

study in the highlighted that US Blacks and Hispanics were the worst affected by the pandemic (151), further highlighting the role of demographic factors in the COVID-19 pandemic.

### 2.6.2. Burden of COVID-19 in Canada

In Canada, the burden of COVID-19 differed between the provinces but the age distribution of morbidity and mortality is similar across the provinces (152). The burden of infection has been highest among young people while the burden of mortality was higher in persons older than 80 (152). In Ontario, neighbourhoods with high proportion of migrants, Black populations, large household size, and low-income levels experienced the highest burdens of COVID-19 (153).

In the early stages of the pandemic, Quebec was the most severely affected province in terms of number of cases but other provinces had a sudden rise in the number of cases, with several other provinces reporting more daily number of new cases than Quebec (154). Responses to the pandemic differed between the provinces since they each have jurisdictional authority over the health of the people within the province (155); provinces were therefore impacted differently by the pandemic.

Differences were also reported across various groups. For instance, Indigenous and Black populations were identified to be more vulnerable, and more heavily impacted than White populations (156). This finding was confirmed by Choi and colleagues who reported that Black and low-income populations in Canada were more severely affected in terms of the number of cases and impact of the pandemic. They also reported that the impact by race was more difficult to measure since data on some of the determining variables were not collected by many provinces (157).

### 2.6.3. Waves of COVID-19 infection in Canada

The COVID-19 pandemic occurred through five documented waves across Canada between January 2020 (when the pandemic commenced) and December 2022. The pandemic started slowly in Canada but by the second and third waves, the disease produced higher number of cases in Canada than in many countries around the world (155). A seven-day moving average confirmed three waves of the pandemic as of May 2021 (152). The first waves of the pandemic started in January 2020 and lasted about five months (155). The second wave happened from September 2020 to March 2021 and was attributed to the Beta variant. This wave defied preventive measures that were introduced by the government despite strict adherence (158). Between March and April

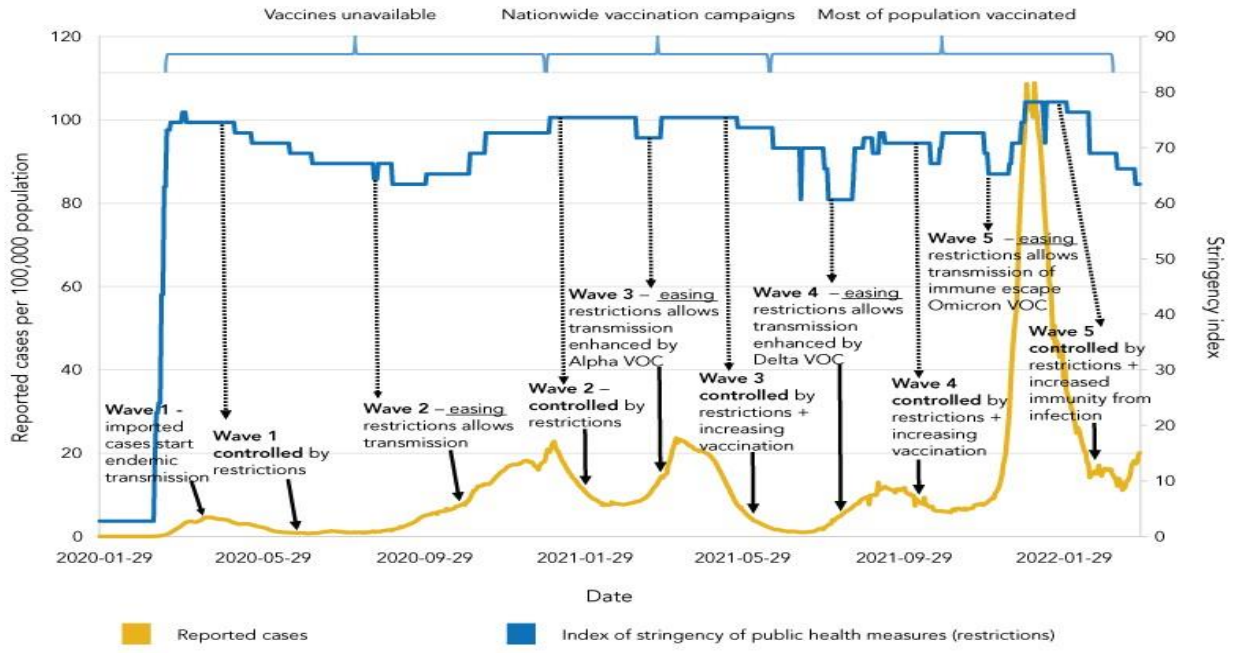
2021, the Canadian public health authorities declared the commencement of the third wave of the pandemic caused by Gamma variant. This wave had the most devastating effect on Alberta and Manitoba with infection rates that were higher than any state or province in North America (155). During this period, the number of cases in Saskatchewan also went exponentially high (155). This third wave of the pandemic lasted until September 2021 when the Delta variant-associated fourth wave of the pandemic began. This wave of the pandemic lasted until December 2021 when the Omicron variant started the fifth wave of the pandemic (159). By March 2022, due to policy changes associated with pandemic recovery, the surveillance approach to the pandemic changed in what was described as the "subsequent wave" with reduced adherence to strict tracking of COVID-19 cases. Figures 2.1 and 2.2 below provide a summary of the chronological order of the pandemic in Canada.

Figure 2- COVID-19 pandemic waves in Canada, March 2020 – May 2023 (160)

**COVID-19 infection waves in Canada**

| Waves (1,197 days) | Phases | Dates | Active cases | Deaths (52,231) | Fatality average (43.63 per day) |
|---|---|---|---|---|---|
| First (175 days) | Start | January 25, 2020 | 1 | 8,839 | 50.51 per day |
| | Peak (127 days after the start) | May 30, 2020 | 35,040 | | |
| | End (48 days after the peak) | July 17, 2020 | 4,143 | | |
| Second (230 days) | Start | July 18, 2020 | 4,455 | 13,312 | 57.88 per day |
| | Peak (177 days after the start) | January 10, 2021 | 85,595 | | |
| | End (53 days after the peak) | March 4, 2021 | 29,907 | | |
| Third (140 days) | Start | March 5, 2021 | 30,139 | 4,375 | 31.25 per day |
| | Peak (45 days after the start) | April 18, 2021 | 89,884 | | |
| | End (95 days after the peak) | July 22, 2021 | 4,513 | | |
| Fourth (104 days) | Start | July 23, 2021 | 4,550 | 2,569 | 24.70 per day |
| | Peak (66 days after the start) | September 26, 2021 | 51,747 | | |
| | End (38 days after the peak) | November 3, 2021 | 23,135 | | |
| Fifth (117 days) | Start | November 4, 2021 | 23,165 | 7,507 | 64.16 per day |
| | Peak (67 days after the start) | January 9, 2022 | 443,676 | | |
| | End (50 days after the peak) | February 28, 2022 | 110,504 | | |
| Subsequent (431 days) | Start | March 1, 2022 | 111,884 | 15,629 | 36.26 per day |
| | Current | May 5, 2023 | N/A | | |
| | There is no reliable tracking data on recoveries since March 1, 2022. | | | | |

Figure 3- Sequence of COVID-19 pandemic in Canada, March 2020 – January 2022 (161)




2.6.4. Burden of COVID-19 in Indigenous communities

The COVID-19 pandemic is intensified by health inequities that disproportionately affect Indigenous communities who live in under-resourced health care settings that may lack culturally appropriate care (162–164). In Australia, there was a reported decrease access to First Nations health assessments which impacted their risk of health outcomes (165). Studies among Indigenous communities in Brazil reported higher case fatality and mortality among Brazilian-Indians in the Central West region than the national figures for the general population (164). Another study in Brazil reported 34.8% increase in excess mortality due to COVID-19 among Indigenous population when compared to 18.1% in non-Indigenous communities (166). Similarly, the burden of COVID-19 in Columbia was reported to be highest in localities with Indigenous population and Black minorities (167).

In comparing the burden of COVID-19 between Indigenous and non-Indigenous populations, Alves et al. noticed no evidence that the Indigenous populations were more heavily impacted than non-Indigenous population, even though data was only available for March 2021 (168). On the contrary to the findings of Alves et al., a Canadian study among Indigenous population showed that the COVID-19 related hospitalization was higher, and incidence rate more than double than

the general population in two cities (169). In northern Saskatchewan where over 80% of residents identify as Indigenous (including First Nations and Métis), the COVID-19 infection rate was higher than the rest of the province during the first 8 months of the pandemic (170). Clusters of asymptomatic COVID-19 cases and deaths have also been reported in First Nations communities (171,172). Overall, Huyser et al. in 2022 reported that Indigenous populations across Canada were disproportionately affected by the COVID-19 pandemic, and this condition was attributed to the disparities in SDOH that is further complicated by transgenerational trauma and systemic racism (40,41).

### 2.7. Factors Affecting COVID-19 Severity and Outcome

Factors including demographics (including age, sex, and location of residence), occurrence of comorbidities, and vaccination status were critical in determining the severity and outcome of COVID-19 infection that would result to hospitalization and death respectively. This section describes the studies that have reported on these factors in determining the course of COVID-19 infection.

#### 2.7.1. Age

Age has been recognized as a key risk factor for COVID-19 (152). Studies have shown that age plays a critical role in determining hospitalization and mortality rates, and the length of hospital stay following COVID-19 infection. Hospitalization and death rates are known to be 23 times higher in people older than 65 years according Mueller et al. (2020); they stated that comorbidities alone without waning immunity (associated with age) would not produce the devastating effect currently seen in COVID-19 infection among older people. In 2020, a review of hospital records in Spain showed that hospitalization was significantly over 27% in adults ≥70 years old as compared to 5% among those who were younger (174). In the US, findings from hospitalized COVID-19 positive cases showed significantly higher mortality (20.9%) in persons older than 75 years old as compared to 0.2% among persons below the age of 18 (175). Machine learning model developed to predict the risk of severe COVID-19 infection among >6000 hospitalized adults revealed that the risks were higher in individuals ≥50 years old even for those with co-existing illnesses (176). In Bangladesh, a retrospective study conducted in 2021 reported a significant association between age and hospitalization (177).

A study in Canada that reviewed the infections from January 2021 to February 2022 reported that the probability of recovery was maximum (100%) among adults under 40 years old, and declined substantially with increasing age (178). In describing the characteristics of patients admitted during the first wave of the pandemic, Murthy et al. substantiated that age was a major predictor of the disease severity and outcome (28). Jantzen and colleagues reported a difference in the levels of infection between individuals <65 and those ≥65 years old (107). These findings were not in agreement with those of a seroprevalence study in Canada between November 2020 and April 2021 which showed higher seroprevalence of COVID19 among individuals <60 years old compared to those who were older than 60 years old (179).

### 2.7.2. Sex

From the available data, more men than women have suffered severe COVID-19 related illness and death globally (180). In a hospital-based study, Álvarez-Esteban et al. reported that hospitalization rate was about 15% for males and 8% for females (174). These findings were supported by Cunningham et al. who reported that the risk of death or need for mechanical ventilation were >1.5 times higher in male than female young adults in the US following the review of over 63,000 hospitalized cases (181). A study in Beijing stated that even though prevalence in males and females was similar, the risk of severe outcome and death was higher among males than in females (182). In Spain, a multi-centre study showed that in-hospital mortality for male adults was 19.1% compared to 16.0% in female adults (183). A hospital-based in Ethiopia found out that recovery rate in male adults was higher (36%) than in female adults (184). Though the role of sex is widely accepted to significantly affect COVID-19 recovery time, a study in India that reviewed cases over a two months period concluded that sex was not a statistically significant factor in the recovery time for the disease (185).

In Canada, similar reports of more severe infection and fatal outcomes have been reported in males than in females following COVID-19 infection. After controlling for occupation, O'Brien et al. observed that male patients aged 20-60 had higher rates of hospitalization, ICU admission, and case fatality rates than females within the same age group (108).

### 2.7.3. Race and ethnicity

A 2021 US study among over 63,000 young adults (aged 18–34) hospitalized for COVID-19 showed no significant variation in the risk of death or demand for mechanical ventilation between

racial/ethnic groups (181). On the contrary, another report in 2020 by Egede et al. in Wisconsin reported that Blacks and Hispanics were twice as likely as Whites to be hospitalized following COVID-19 infection, and the risk of dying was two times higher among the Hispanics than the Whites (186). These findings were supported by Nguyen et al. who observed elevated risk of hospitalization among Black non-Hispanics compared to Whites (187). A related study that adjusted for comorbidities and neighbourhood characteristics found out that Blacks were more likely to contract severe COVID-19 or die from the disease than Whites (188). After adjusting for demographic characteristics such as age, sex and regions, Navar et al. observed that Black adults were more likely to die from COVID-19 than their White counterparts due to higher incidence of comorbidity among the Black population in the US (189).

Buikema et al. (2021) reported that even though ethnic minorities (Blacks, Hispanics and Asians) in the US were more likely to be hospitalized than Whites, Blacks were less likely to die —a position that was attributable to health disparities among the racial groups (190). Also, Aburto et al. (2022) and Kopel et al. (2020) corroborated the finding that mortalities in minority populations were due to health disparities; they underscored the need to address health disparities in public health emergencies (191,192).

2.7.4. Location of residence

Residence plays a critical role in the determining the severity and outcome of COVID-19. In the US, concerns were raised about the increasing number of COVID-19 cases in the rural areas with fear of health facilities being possibly overwhelmed during the pandemic (193,194). Even the utilization of prevention protocol, including access to vaccination, was questioned in the US rural areas, with large population of Blacks, older and immunocompromised persons (14,195–197). Kaufman et al. projected that about 50% of rural Americans were at risk of severe COVID-19 infection and hospitalization (198). Comparing case fatality rates between rural and urban counties in the US, Iyanda et al. observed higher case fatality rate in rural counties compared to urban counties (199). Separate studies in Iran in 2021 and 2022 reported that even though the risk of COVID-19 hospitalization was higher among urban dwellers, the risk of fatal outcome was higher among semi-urban and rural dwellers (200,201).

2.7.5. Comorbidities

Occurrence of co-existing medical conditions has been widely reported to impact the severity and outcome of COVID-19. In a retrospective study in Bangladesh, Amin et al. (2021) reported significant association between hospitalization and presence of comorbidities among COVID-19 patients (177). In a related finding in Bangladesh, the occurrence of multiple comorbidities was reported to significantly increase the length of hospital stay, and chance of hospitalization by 20%–40%. According to this study, odds of severe COVID-19 were higher for persons with a combination of diabetes mellitus and cardiovascular diseases (OR = 5.14, 95%CI = 2.02–13.07), and further increasing to 6.82 times when these conditions occurred together with hypertension (202). In Saudi Arabia, patients with comorbidities such as hypertension had a longer period of stay in the hospital compared to those who had no comorbidities (203). In Kuwait, Al Saleh and colleagues (2022) also reported that patients with comorbidities such as hypertension and cardiovascular disease were at a higher risk of COVID-19 mortality when compared to people who were apparently healthy (204).

Elsewhere, a hospital-based study in Spain in 2021 reported that the rate of COVID-19 hospitalization was highest in persons with comorbid kidney disease (26.3%), followed by those previously diagnosed with diabetes (26.1%), and persons with cardiovascular disease (21.9%) (174). Obesity and hypertension were reported to present greater than 2 times the risk of death or need for mechanical ventilation among hospitalized young adults in the US (181). In Ethiopia, individuals without comorbidities were reported to recover from COVID-19 earlier than those who presented with pre-existing medical conditions (184). Studies have shown the with multiple comorbidities, the risk of severe infection leading to hospitalization and death increases as reported in the US, India and South Korea (205–207); these findings were corroborated by a systematic review (24).

In Canada, the effect of co-existing medical conditions on COVID-19 severity and outcome has been reported. Ge and colleagues (2021) reported that the risk of mortality in COVID-19 was about 3 times more likely among persons with comorbidities compared to those who did not report the presence of co-existing medical conditions. Diabetes, cardiovascular disease, hypertension, chronic obstructive pulmonary disease, among other diseases were significant risk factors of COVID-19 mortality (208). In children neurologic conditions, body mass index ≥3, and pulmonary

diseases were significant risk factors to severe SARS-CoV-2 infection with a high chance of mortality (209). Furthermore, in 2022 Downer and Sinha reported that Canada population is quickly ageing, and therefore the need to research of role of comorbidities which are common among older people should be encouraged by the government (210).

### 2.7.6. Vaccination status

As expected, the introduction of vaccines lowered the transmission rate, and reduced the incidence of severe COVID-19 that may result in hospitalization and/or death. A US study showed that the hospitalization rate was five times higher in unvaccinated patients than in patients who were vaccinated. The study also observed that vaccinated people who had severe infection that required hospitalization were much older (58–80 years) than unvaccinated persons with the age range of 46–70 years (58). This finding further emphasizes the role of vaccination in determining the severity and outcome of COVID-19. This assertion was confirmed by another US study that reported decreased risk of hospitalization among vaccinated persons compared to unvaccinated persons (211). Comparing the risk between two vaccine candidates, Tenforde et al. reported that the risk of hospitalization was lower with Moderna (mRNA-1273) when compared with Pfizer-BioNTech (BNT162b2) following three months of vaccination (211). Other studies in the US, Australia, and Bangladesh similarly reported significant association between vaccination and reduced severity of COVID-19 (212–215). Buchan et al. (2022) reported that two or more doses of COVID-19 vaccines conferred effective protection against SARS-CoV-2 infection (216).

# Chapter 3: Methods

Following a brief overview of the research design, this chapter provides greater detail regarding study participants and the relevant geographical context. The procedure for data abstraction is then described, followed by a description of the study variables, the statistical analyses conducted, and the ethics procedures followed.

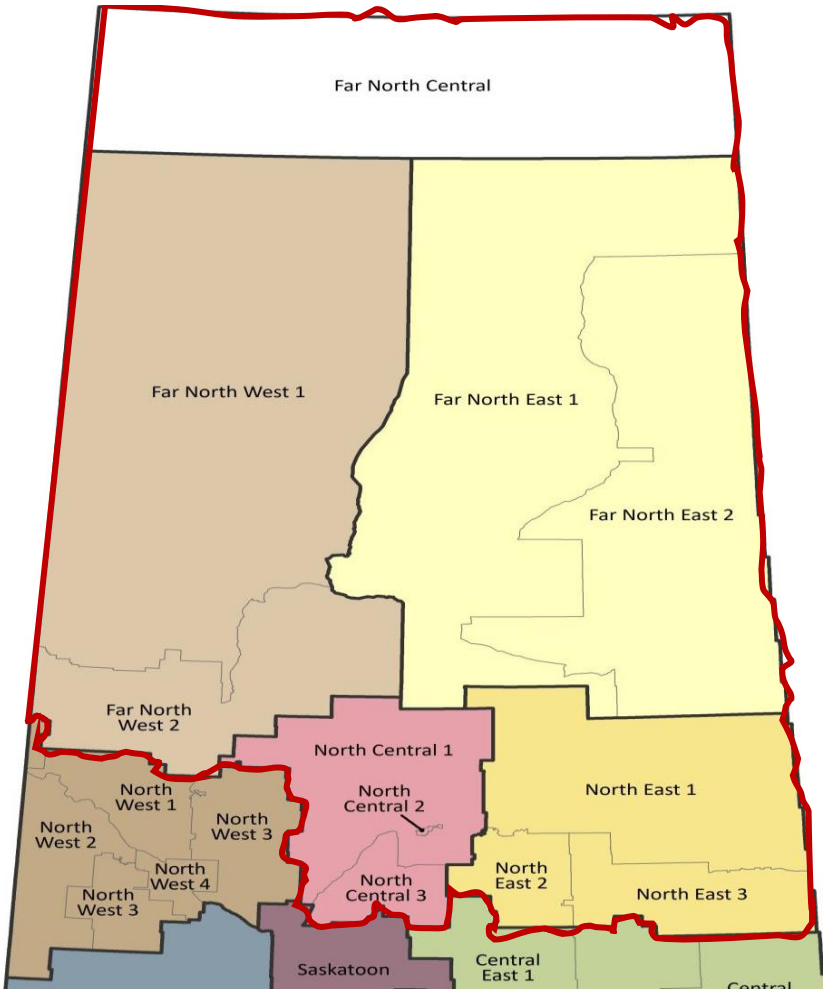
## 3.1. Research Design

This study adopted secondary analysis of quantitative data derived from a de-identified linelist of confirmed COVID-19 cases in on-reserve northern Saskatchewan First Nations communities (the study cohort). This linelist contains a total of 8,428 reported cases generated through laboratory and community reporting of confirmed COVID-19 cases in the northern Saskatchewan First Nation communities between March 2020 and December 2022.

## 3.2. Participants

The study participants were laboratory-confirmed COVID-19 cases in the Northern Saskatchewan First Nations Communities. The Northern Saskatchewan First Nations communities are made up of five distinguished groups and this includes the Cree, Dakota, Dene (Chipewyan), Nakota (Assiniboine), and Saulteaux (217). The median age of the Northern Saskatchewan Indigenous populations is 20 years, and they constitute about 50% of the total population living among the First Nations communities (218). This population's occupation revolves largely around subsistence agriculture, fishing, and hunting. In total, there are 31 on-reserve communities with a population of over 34,000 representing 23% of Saskatchewan First Nations (219). The communities are grouped under five zones that are administered by the Northern Inter-Tribal Health Authority (NITHA). The zones include Far North central (FNC), Far Northwest (FNW), Far Northeast (FNE), Northeast (NE), and North central (NC). These zones vary in the distribution of population and demographic characteristics. Figure 1 shows the map of the zones under the medical jurisdiction of NITHA.

Figure 4- Map of *n*orthern Saskatchewan *showing* the zones under NITHA's jurisdiction (240)




### 3.3. Inclusion and exclusion criteria

Data used for the study included:

i. De-identified individual records on the COVID-19 infection severity and outcome available on NITHA's linelist.

ii. Individual data for COVID-19 cases confirmed from March 1, 2020 to December 31, 2022.

Data excluded from being used for this study include:

i. Individuals with record of COVID-19 infection severity and outcome that is not available on NITHA's linelist.

ii. Individual record of COVID-19 cases confirmed outside the period from March 2020 to December 2022.

Study participants were drawn from the COVID-19 linelist available at NITHA for the period from March 1, 2020–December 31, 2022. This list contains information on all confirmed COVID-19 cases reported from all the communities under the jurisdiction of NITHA. This data is collected through community reporting and faxed notification from the provincial laboratories on the confirmation of COVID-19 cases. The details available on the linelist included Personal Health Number, name of patient, age, sex, co-existing medical conditions, residential address, presenting symptoms, vaccination status, data of admission at the treatment centre, date of discharge and outcome (recovered or dead); however, in the interest of patient confidentiality, Personal Health Number, name of patient, and residential address were not included in the abstracted data for this study.

At NITHA, the relevant information on the fax notes or community reports are transferred to the linelist of COVID-19 cases. This information is used to monitor course of COVID-19 infection in these infected individuals including management, disease progression and outcome (recovery or death). This de-identified data was obtained from the NITHA data repository and the relevant variables included in the analysis to answer the research questions for this study.

### 3.4. Data abstraction

Data abstraction was conducted in collaboration with a NITHA epidemiologist following operational approval. In total, 8,428 COVID-19 cases were abstracted to Microsoft Excel from the NITHA's internal linelist of COVID-19 cases. This linelist is generated by the public health nurse and epidemiologist at NITHA from the Panorama, Microstrategy, and Investigation Outbreak Module (IOM). The data abstracted contained: an internally assigned case identification number, zone of residence, sex, age, type of variant of concern isolated, type of accommodation, source of infection exposure, date of COVID-19 vaccine administration, date of onset, symptoms reported, co-existing medical conditions of the case, disease outcome, and history of hospitalization and ICU admission.

### 3.5. Study variables

#### 3.5.1. Dependent variables

COVID-19 severity/outcome was measured by three variables: hospitalization (yes/no), ICU admission among those hospitalized (yes/no), and death (yes/no) (90,90,92). As will be described in the statistical analysis section, these variables were used differently, depending on the research question; for the first question, they were primarily used to describe the COVID-19 experience of this population, whereas for the second research question, they were positioned as the dependent variables.

#### 3.5.2. Independent variables

The remaining variables used in this study are grouped into demographic, clinical, vaccine-related, and "other" categories and are described in more detail below. For the 1st research question, they were used to describe the COVID-19 experience of those affected; for the 2nd research question, these variables were positioned as potential independent variables.

*Demographic variables:* Three demographics characteristics were considered in this study: age, sex, and location of residence. Age was initially treated as continuous variable (to determine the mean age of individuals infected with SARS-CoV-2) and was eventually categorized into <65 and ≥65 years old as described by Jantzen and colleagues (107). Sex was measured dichotomously as male or female. The location of residence was taken to mean the zone from where the individual resides and was based on the five zones that are recognized by NITHA as "Far North Central", "Far North West", "North Central", "North East" or "Far North East" (220).

*Clinical factors*: Clinical factors referred to the presence of comorbidities and symptoms. Comorbidities were defined according the Saskatchewan Ministry of Health Communicable Disease Manual Section 2 and illustrated in Appendix C (221). There were two comorbidity variables, the first being a dichotomous one (yes/no) indicating the presence (one or more) or absence of a comorbidity. The second comorbidity variable, which was for infected individuals who reported the presence of comorbidities, had six categories: substance use issues (including smoking, alcoholism, and other substances), lung/respiratory diseases (CRD, chronic obstructive lung disease, asthma), diabetes mellitus, cardiovascular diseases (hypertension and other cardiovascular diseases), liver and kidney diseases, and other (solid organ transplant, cancers, debilitating diseases such as HIV and TB).

Presence of symptoms was assessed with three variables, the first being dichotomous (yes/no). Among those who reported symptoms, number of symptoms (one, two, three, four, five or more) formed the second categorical variable. In the third symptom variable, specific types of symptoms were identified in the following categories: fever, cough, breathing difficulties, loss of taste, loss of smell, chills, sore throat, runny nose/rhinitis, nasal congestion, body pain, fatigue, and gastrointestinal (GI) symptoms (diarrhoea, nausea, and vomiting).

*Vaccination related factors*: There were three vaccination variables. Vaccination status included whether an individual was vaccinated against COVID-19 or not, and this was dichotomized as vaccinated prior to COVID-19 infection and unvaccinated groups. For patients who were vaccinated prior to infection, the average duration between the administration of the last dose and onset of infection (in days) was considered and further grouped into 1–6 months, 6–12 months, and >12 months. Also considered was the number of vaccine doses received prior to disease onset, with responses categorized as either one dose or two or more doses (Appendix C).

3.5.4 Other epidemiological factors

The variables within this group included source of exposure, variant of concern (VoC), and wave of infection. Source of infection referred to the place or event where the infected persons reported to be the point where the SARS-CoV-2 virus was contracted. This variable was had six categories for individuals who identified the source of infection as follows: household contact, mass gathering/social event, travel, workplace contact, school, and unknown community contact/unspecified. Among the cases that were categorized, the VOC was determined and categorized, and the five categories included B.1.1.529 (Omicron), B.1.1.7 (Alpha), B.1.617.2 (Delta), P.1 (Gamma), and undetermined VOC lineage. The wave of infection was an epidemiological category, had six categories: waves 1–5 and subsequent wave (which corresponded to the period when the surveillance became passive and reporting mandates were relaxed).

### 3.6. Data analysis

The abstracted data was cleaned in Microsoft Excel® and exported to Stata v.12 for analysis. Univariate, bivariate, and multivariable analysis approaches were adopted to address the research questions.

### 3.6.1. Univariate analysis

Using the epidemiologic curve, the number of COVID-19 cases among the study cohort were described in comparison with the total number of cases reported in Saskatchewan, and Canada. Univariate frequency distribution and percentages were used to describe the demographic, clinical and vaccination-related characteristics of individuals with COVID-19 infection considering the overall cases and those with severe (i.e., hospitalized) COVID-19 infection. Measures of central tendency and dispersion (mean, median, and standard deviation) was explored for continuous variables such as age, number of vaccine doses received, and number of days between the last vaccine dose and infection. The overall individuals included the 8,428 cases reported across the Northern Saskatchewan on-reserve communities while the severe cases included the 223 cases that were hospitalized following infection with the SARS-CoV-2 virus.

### 3.6.2. Bivariate analysis

The bivariate analysis involved the use of cross-tabulation to determine associations between the categorical risk factors/independent variables (demographic factors, wave of infection, VOC, source of exposure, vaccination status, categorized number of vaccine doses received, categorized duration between the last COVID-19 vaccine dose administered and onset of infection, presence of symptoms, presence of co-existing medical conditions, and type of comorbidities), and the dichotomous categorical outcome/dependent variables (hospitalization, ICU admission, and disease outcome – death). Chi square was determined and values of $p<0.05$ were considered statistically significant.

### 3.6.2. Multivariable analysis

Logistic regression analysis was used to determine the strength of association between the risk factors and COVID-19 severity (hospitalization and ICU admission) and outcome (deaths). Independent variable (predictors) that were statistically significantly associated with the outcome variables were then included in the final multivariable logistic regression model, as were those considered biologically relevant (age and sex). Model building approach adopted the univariable selection method as described by Hafermann and colleagues (222). By this method, we selected variables that showed statistically significant association in the bivariate analysis with values of $p<0.05$. Furthermore, variables that showed multicollinearity upon inclusion in the multivariable logistic regression model were excluded from the final regression model.

In the end age sex, zone of residence, vaccination status prior to infection, categorized number of vaccine doses received prior to infection, presence of symptoms, presence of comorbidities and type of comorbidities presented at the time of reporting and diagnosis were the independent variables included in the final multivariable logistic regression model. Overall number of infected individuals (8,428) were considered for the association between hospitalization and disease outcome (death), and the independent factors. For the ICU admission, only the severe cases (223) were considered for this test of association in the final logistic regression model.

Model specification, goodness-of-fit, and other regression diagnostics such as deviance residuals, Pearson residuals, leverage (using _hat diagonal), difference of chi square, and influence (using Pregibon's dbeta) were deployed to detect the effect of the observations on the statistical findings. Statistical tests for the assumptions were applied at 95% CI, and p-values less than 0.05 were considered statistically significant.

### 3.7. Ethical approval

Research in Indigenous populations takes into account the principles of the ownership, control, access and possession (OCAP) principles (223). Therefore, ethical approval for this study was obtained from the Review Ethics Board of the University of Saskatchewan, and this study was conducted in accordance with the terms of the ethical approval (see appendix A). In addition, the study utilized de-identified that was obtained with approval from relevant NITHA authorities. This data excluded individual identifier information such as names, home address and other identifiers to ensure anonymity. The data were analyzed and presented in aggregates so that findings were not linked to individuals or their communities.

# Chapter 4. Results

This chapter begins with a descriptive overview of COVID-19 cases in Canada, Saskatchewan, and among Saskatchewan First Nations on-reserve, followed by the presentation of results according to research question.

## 4.1. Descriptive epidemiology for all COVID-19 cases in Saskatchewan and Canada

### 4.1.1. Pattern of all COVID-19 cases in Saskatchewan and Canada

The following describes the de-identified data that was abstracted from the NITHA COVID-19 case linelist. Aggregate data on the number of cases reported provincially and nationwide was obtained from the Government of Canada COVID-19 Epidemiology Update (224). This data was used to plot comparable epi-curves for the country, province, and northern Saskatchewan First Nations communities.

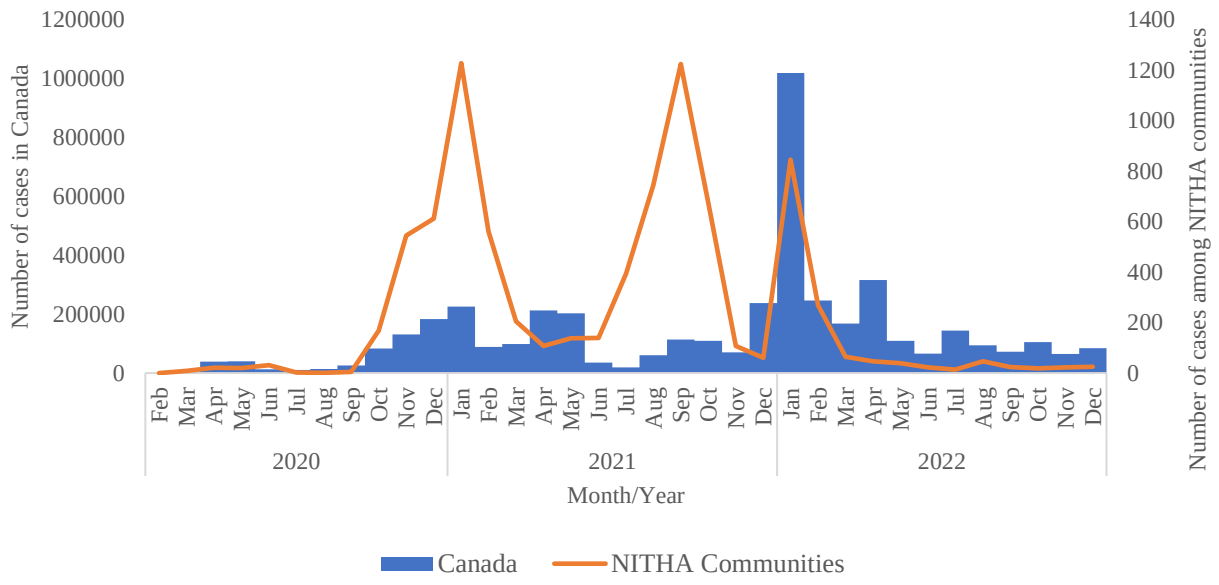
Across Canada, 4,507,307 cases of COVID-19 were confirmed during the period from February 1, 2020–December 2022. The provincial burden of COVID-19 cases from March 2020–December 2022 was 151,570 cases of which 8,428 (5.6%) were from northern Saskatchewan First Nations communities. The subsequent sections describe the results of that analysis of this data.

### 4.1.2. Pattern of COVID-19 infection in the study cohort from March 2020–December 2022

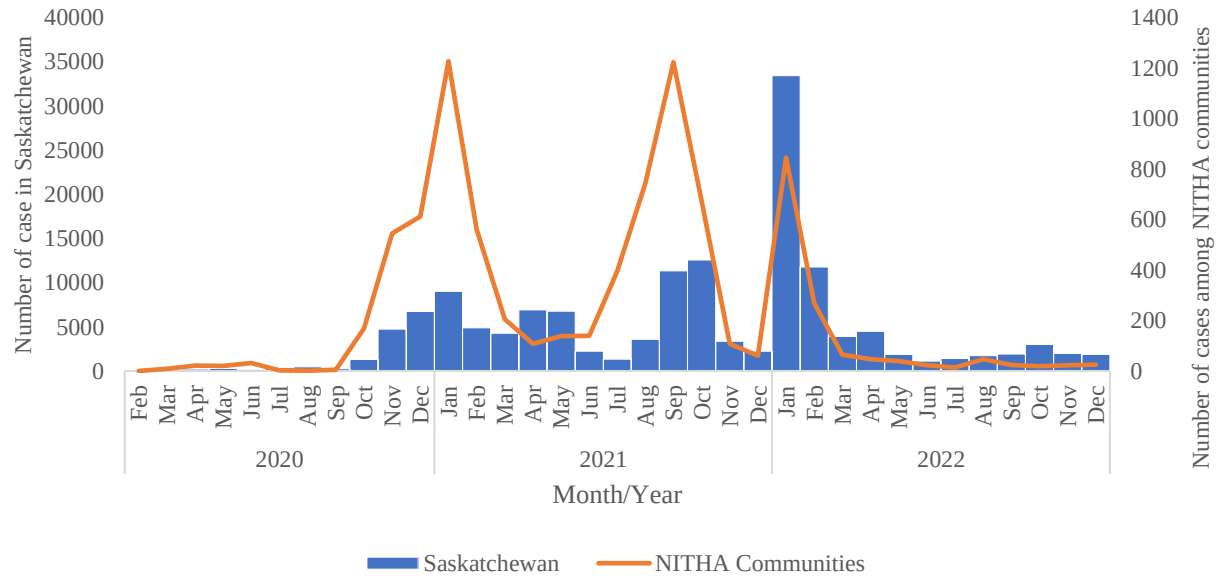
Between February 2020—when the first case was detected in Canada—to December 2022, the country had five waves of the pandemic which peaked in May 2020, January, April and September 2021, and January 2022 (Figure 5A). The province experienced four waves of the pandemic. The first three waves peaked in January, April, and October 2021 respectively, while the fourth wave peaked in January 2022 (Figures 5A and 5B). The Northern Saskatchewan First Nations communities also had four waves of the pandemic. The first wave peaked in June 2020 with 132 cases while the second and third waves peaked in January and September 2021 with 1,227 and 1,223 cases respectively. The fourth wave of the COVID-19 pandemic peaked in January 2022 with 845 cases (Figures 5A and 5B). This pattern of infection across the northern Saskatchewan First Nations on-reserve communities is similar to the pattern obtained across the country with the waves all aligning along their peak periods.

Figure 5- Pattern of COVID-19 in the study cohort, March 2020–December 2022

A. Pattern of COVID-19 pandemic across Canada, and Northern Saskatchewan First Nations on-reserve communities

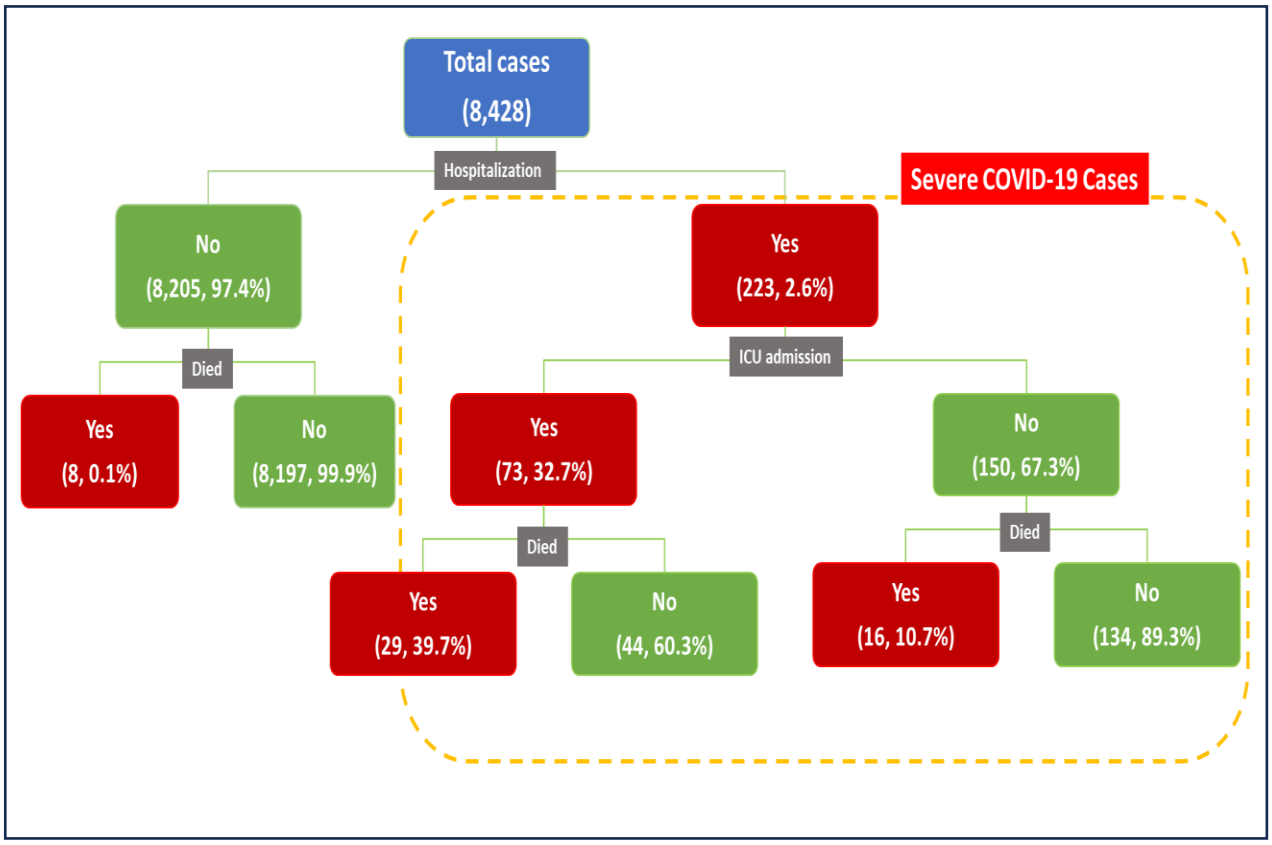



B. COVID-19 pandemic pattern across Saskatchewan and Northern Saskatchewan First Nations on-reserve communities



A total of 223 (2.7%) of COVID-19 cases among the Northern Saskatchewan First Nations on-reserve suffered severe infection that required hospital admission. The flow chart below shows the summary of COVID-19 cases (Figure 6).

Figure 6- Representation of all COVID-19 cases in the study cohort, March 2020–December 2022




4.1.3. Hospitalization, ICU admission, and death

A total of 8,205 (97.4%) of the 8,428 COVID-19 cases reported among on-reserve northern Saskatchewan First Nations communities over the study period did not require hospitalization; patients isolated or were managed at home. On the other hand, 2.6% (223) had severe infection that required admission to the hospital (inpatient and/or ICU) or treatment centre. Among those admitted to either the hospital or treatment centre, 73 (32.7%) required ICU admission, while 67.3% were did not require ICU admission (Table 4.5). A small proportion of confirmed COVID-19 cases in the study population died (53, 0.6%). Most cases recovered from the infection (8,375, 99.4%) (Table 4.1).

Table 4.1. Isolation, ICU admission, and disease outcome among the study cohort, March 2020–December 2022

| Isolation, ICU Admission and Disease Outcome | Frequency | Percent |
|---|---|---|
| **Isolation location (N=8,428)** | | |
| Home | 8,205 | 97.4% |
| Hospital | 223 | 2.7% |
| **ICU admission (N=223)** | | |
| No | 150 | 67.3% |
| Yes | 73 | 32.7% |
| **Disease outcome (N=8,428)** | | |
| Died | 53 | 0.6% |
| Recovered | 8,375 | 99.4% |

**Research Question 1:** What are the demographic, clinical, and vaccination-related characteristics of these individuals, both (a) overall and (b) among those with severe (i.e., hospitalized) COVID-19?

4.1.4. Demographic, clinical, and vaccination-related characteristics of COVID-19 cases

Research question 1a addresses demographic characteristics, source of infection, variant of concern, and wave of infection among all COVID-19 cases in the study cohort. A total of 8,428 COVID-19 cases occurred from March 1, 2020, to December 31, 2022, among NITHA communities. The mean age of individuals diagnosed with COVID-19 among Northern Saskatchewan First Nations on-reserve was 30.8years. Overall, more young people (<65 years old) were diagnosed with COVID-19 (7,877/8,428; 93.5%) compared to older individuals 65 years and above (551/8,428; 6.5%). COVID-19 infection among reported cases was about 50% (51.7% and 48.3% respectively) each for both females and males. Most cases occurred in the Far Northeast and Far Northwest communities which, together, accounted for over 69% (45.8% and 23.5% respectively) of the infections (Table 4.2). Of the 8,428 confirmed cases of COVID-19 among NITHA-administered communities, the source of exposure was identified for 1,949 (23.1%) individuals (Table 4.3). Overall, 15.8% (1,335) of the cases reported having contact with a confirmed infected person within the household, and 5.1% (429) identified mass/social gathering

(such as funeral) as a source of exposure. Those with unknown or unspecified contact community accounted for 0.8% (63) of the cases (Table 4.3). A total of 970 (11.5%) cases were due to B.1.617.2 (Delta) variant, 1.6% (138) and 1.5% (130) of the cases were due to the Omicron and Alpha variants respectively. The variant of concern (VOC) lineage was undetermined for 6.5% (550) of the cases that were characterized. Overall, the 78.4% (6,606) of the cases were not characterized to determine the variant of concern (Table 4.3). The finding showed that over one-third of cases (3,196, 37.9%) occurred during the second wave of the pandemic. This was followed by Wave 4 during which 2,788 (33.1%) cases were confirmed. The least number of cases (49; 9.6%) was recorded during the first wave of the pandemic (Table 4.3).

Table 4.2. Demographic characteristics of all COVID-19 cases in study cohort, March 2020 – December 2022 (n = 8,428)

| **Demographic characteristics** | **Frequency** | **Percent** |
|---|---|---|
| **Age group** | | |
| <65 | 7,877 | 93.5% |
| 65+ | 551 | 6.5% |
| **Sex** | | |
| Female | 4,354 | 51.7% |
| Male | 4,074 | 48.3% |
| **Zone of Residence** | | |
| Far North central | 593 | 7.0% |
| Far Northeast | 3,860 | 45.8% |
| Far Northwest | 1,982 | 23.5% |
| North central | 983 | 11.7% |
| Northeast | 1,010 | 12.0% |

Table 4.3. Source of exposure, VoC, and wave of infection for all COVID-19 cases in the study cohort, March 2020 – December 2022 (n = 8,428)

| Exposure characteristics | Frequency | Percent |
|---|---|---|
| **Source of Exposure** | | |
| Household contact | 1,335 | 15.8% |
| Mass gathering/Social event | 429 | 5.1% |
| Travel | 41 | 2.1% |
| Workplace contact | 44 | 0.5% |
| School | 37 | 0.5% |
| Unknown contact in community/unspecified | 63 | 0.8% |
| Information not available | 6,479 | 76.9% |
| **Variant of Concern (VoC) Isolated** | | |
| B.1.1.529 (Omicron) | 138 | 1.6% |
| B.1.1.7 (Alpha) | 130 | 1.5% |
| B.1.617.2 (Delta) | 970 | 11.5% |
| P.1 (Gamma) | 35 | 0.4% |
| Undetermined VoC lineage | 550 | 6.5% |
| Information not available | 6,606 | 78.4% |
| **Cases by Wave of Infection** | | |
| Wave 1 | 49 | 0.6% |
| Wave 2 | 3,196 | 37.9% |
| Wave 3 | 831 | 9.9% |
| Wave 4 | 2,788 | 33.1% |
| Wave 5 | 1,241 | 14.7% |
| Subsequent | 323 | 3.8% |

4.1.5. Vaccination status

As shown in Table 4.4, the majority (53.4%) of individuals were unvaccinated at the time of COVID-19 infection diagnosis, while 46.6% had received at least one dose of the COVID-19 vaccine prior to being infected. Most of the vaccinated cases (3,422, 40.6%) had received at least two doses of COVID-19 vaccine while 503 (12.8%) had one dose of COVID-19 vaccine prior to infection.

The mean time from the last vaccine dose and report of SARS-CoV-2 infection was 76±104 days. Over one-third (38.7%) of the infected persons contracted COVID-19 within six months after their last dose (Table 4.4).

Table 4.4. Vaccination status of all COVID-19 cases at the time of infection in the study cohort, March 2020 – December 2022 (n=8,428)

| **Vaccination status** | **Frequency** | **Percent** |
|---|---|---|
| **Vaccination status at the time of infection** | | |
| Unvaccinated | 4,503 | 53.4% |
| Vaccinated | 3,925 | 46.6% |
| **Doses received at the time of infection** | | |
| One dose | 503 | 6.0% |
| Two or more doses | 3,422 | 40.6% |
| Unvaccinated | 4,503 | 53.4% |
| **Interval between the last vaccine dose and COVID-19 infection** | | |
| 1 – 6 months | 3,262 | 38.7% |
| 7 – 12 months | 612 | 7.3% |
| >12 months | 51 | 0.6% |
| Unvaccinated | 4,503 | 53.4% |

**Mean number of days between date of last dose of vaccine and date of infection onset 76.2±104.4*

4.1.6. Presenting symptoms and co-existing medical conditions

Among the COVID-19 cases reported across the nothern on-reserve Saskatchewan First Nations communities, 4,456 (52.9%) did not report the occurrence of symptoms, while approximately 3,044 (36.1%) showed documented symptoms at the time of infection diagnosis. The symptoms for 928 (11.0%) of the cases were unknown at the time of reporting (Figure 7). A total of 904

(10.7%) of those persons infected with SARS-CoV-2 across communities presented with one symptom while the remaining 70% had two or more clinical symptoms at the time of diagnosis (Figure 8). Out of the 3,011 (46.8%) cases whose clinical symptoms were documented at the time of presentation, 49.9% reported cough. This was followed by fever (29.7%), headache (29.5%), and loss of taste and loss of smell (27.3% and 26.7% respectively). Gastrointestinal symptoms such as diarrhea, nausea and vomiting were reported by 6.1% of the patients while non-specific signs (such as dizziness, fainting, conjuctivitis) reported were reported in 2.8% of the confirmed COVID-19 cases among northern Saskatchewan First Nations (Figure 9).

Figure 7- Presence of symptoms among all confirmed COVID-19 cases in the study cohort, March 2020 – December 2022 (n = 8,428)

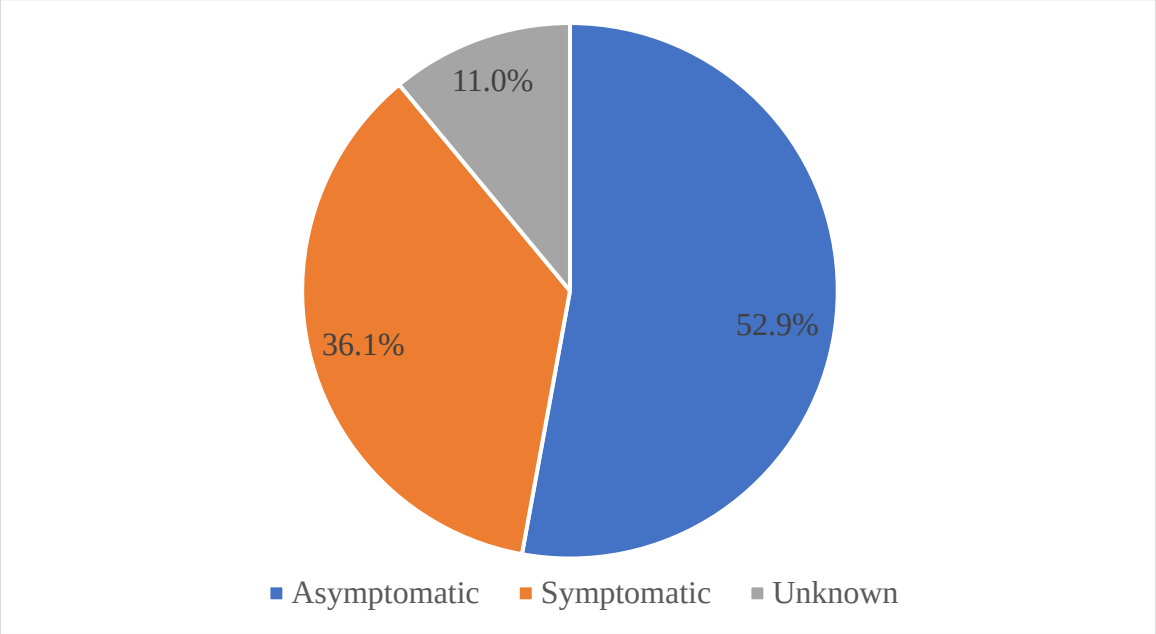


Figure 8- Number of clinical symptoms at presentation among all individuals infected with COVID-19 in the study cohort, March 2020 – December 2022 (n=8,428)

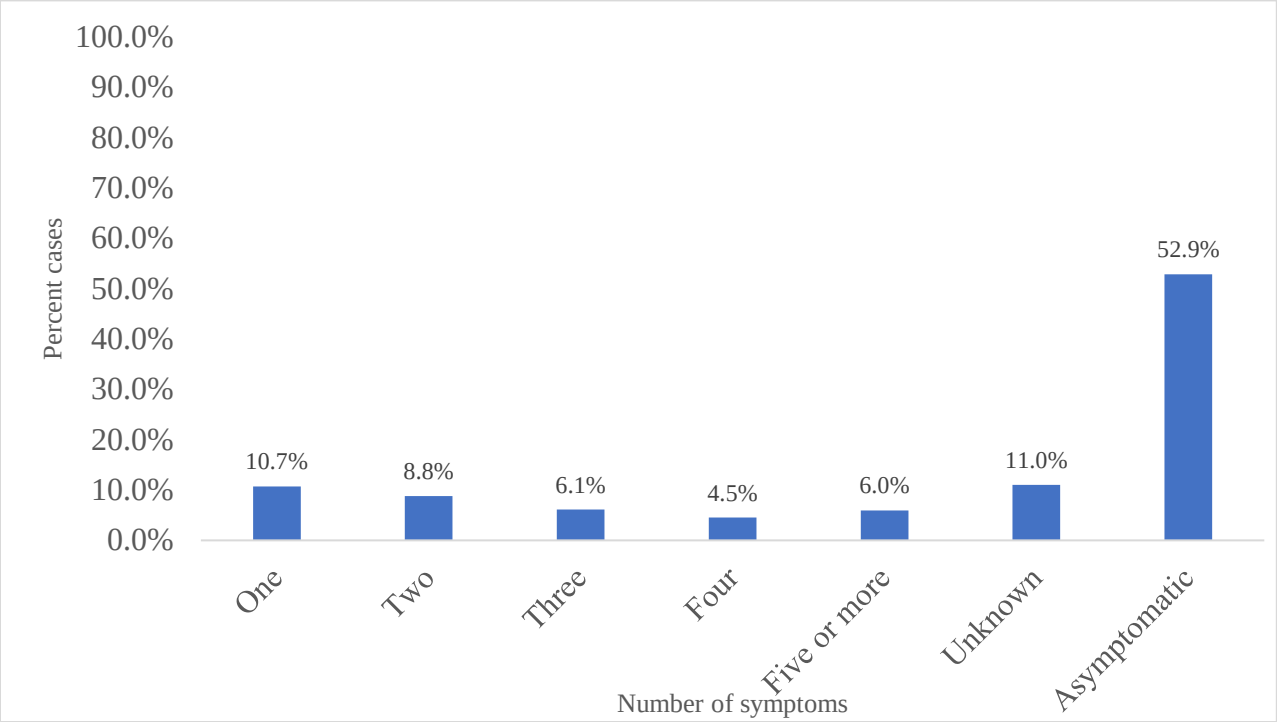
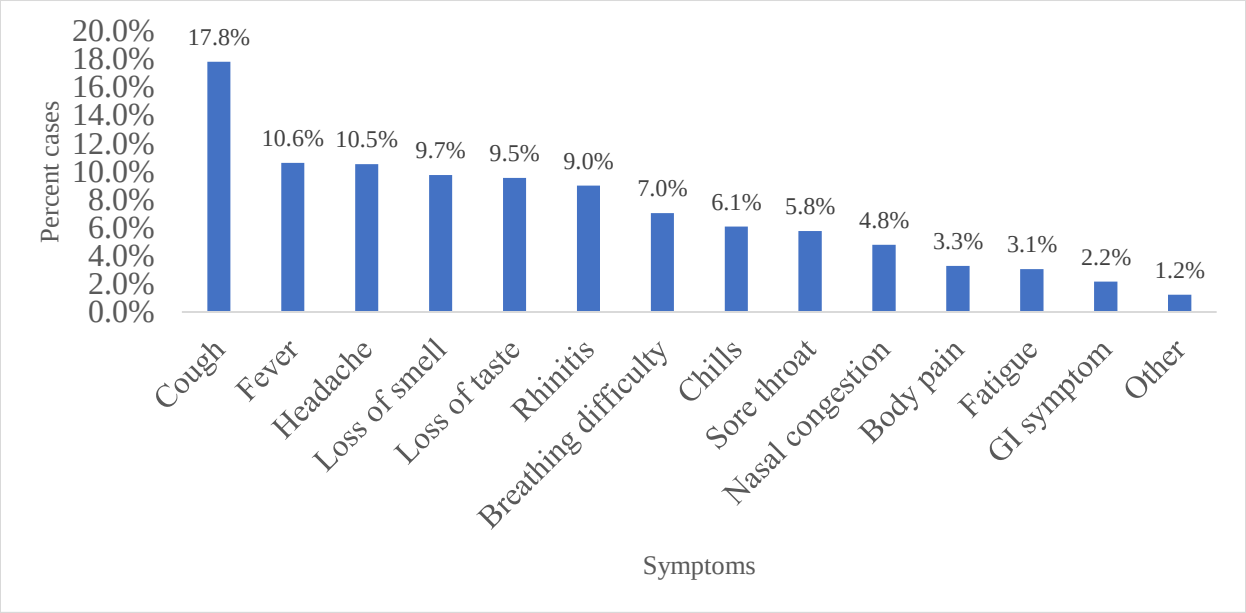



Figure 9- Figure 4.5. Type of clinical symptoms presented by all COVID-19 Cases in the study cohort, March 2020 – December 2022 (n=8,428)



Out of the 8,428 individuals confirmed with COVID-19 from March 2020–December 2022, 1,709 (20.3%) presented with co-existing medical conditions. The predominant co-existing medical condition among COVID-19 patients was substance use disorder (which included alcoholism and smoking), reported among 1,114 (13.2%) of the diagnosed cases (Table 4.5). Diabetes mellitus was reported among 308 (3.6%) of the COVID-19 cases, while cardiovascular diseases such as hypertension and lung disease were reported for 128 (1.5%) and 79 (0.9%) of the COVID-19 cases respectively (Table 4.5).

Table 4.5. Type of co-existing medical conditions in the study cohort, March 2020 – December 2022 (n=8,428)

| Types of co-existing medical condition | Frequency | Percent |
|---|---|---|
| **Presence of Comorbidities** | | |
| No | 6,719 | 79.7% |
| Yes | 1,709 | 20.3% |
| **Types of co-existing medical condition** | | |
| Substance use | 1,114 | 13.2% |
| Diabetes Mellitus | 306 | 3.6% |
| Cardiovascular disease | 128 | 1.5% |
| Lung disease | 79 | 0.9% |
| Liver and Kidney diseases | 28 | 0.3% |
| Other (HIV, Obesity, Cancers, Unspecified) | 54 | 0.6% |
| No documented comorbidities | 6,719 | 79.7% |

## 4.2. Descriptive epidemiology of severe COVID-19 cases

### 4.2.1. Demographic characteristics, source of infection, variant of concern, and wave of infection

Of the 223 severe COVID-19 cases reported, 51.1% occurred among males while about 48.9% occurred among females. Those aged less than 65 years old accounted for 59.6% of the cases compared to 40.4% of those who were 65 years and older. The finding further showed that one-third (35.0%) of the severe COVID-19 cases that required hospitalization occurred among residents of the Far Northeast zone, and this was followed by Far Northwest (30.5%), while the least number of severe cases (9.4%) were seen among the residents of North Central zone. (Table 4.6).

Of the 223 of the severe COVID-19 cases that occurred among the Northern Saskatchewan First Nations on-reserve, the source infection was identified for 22% of the cases while 78% (174) of the severe COVID-19 cases had no known source of infection documented. About 13.0% of the severe cases contracted the infection from members of their households and this was followed by mass gathering (5.4%). The most common variant of concern lineage identified among the Northern Saskatchewan severe cases was the B.1.617.2 (Delta variant) which was identified from 15.7% of the COVID-19 cases, while the Omicron (B.1.1.529) and P1 (Gamma) lineages were isolated from 0.9% of the severe COVID-19 cases (Table 4.7). Based on the Wave of infection, 84 (37.7%) of the severe cases occurred during the second wave of the pandemic while 73 (32.7%) occurred during the fourth wave. The fewest severe cases (3, 1.4%) were reported during the first wave of COVID-19 outbreak among the Northern Saskatchewan First Nations (Table 4.7).

Table 4.6. Demographic characteristics of severe COVID-19 cases in study cohort, March 2020 – December 2022 (n=223)

| **Characteristics** | Frequency | Percent |
|---|---|---|
| **Sex** | | |
| Female | 109 | 48.9% |
| Male | 114 | 51.1% |
| **Age group** | | |
| <65 | 133 | 59.6% |
| 65+ | 90 | 40.4% |
| **Zone of Residence** | | |
| Far North central | 25 | 11.2% |
| Far Northeast | 78 | 35.0% |
| Far Northwest | 68 | 30.5% |
| North central | 21 | 9.4% |
| Northeast | 31 | 13.9% |

Table 4.7. Source of exposure, VOC, and wave of infection in study cohort, March 2020 – December 2022 (n = 223)

| Exposure characteristics | Frequency | Percent |
|---|---|---|
| **Source of Exposure** | | |
| Household contact | 29 | 13.0% |
| Mass gathering/Social event | 12 | 5.4% |
| Workplace contact | 3 | 1.3% |
| Travel | 2 | 0.9% |
| School | 0 | 0.0% |
| Unknown contact in community/unspecified | 3 | 1.3% |
| Missing | 174 | 78.0% |
| **Variant of Concern (VOC) Isolated** | | |
| B.1.617.2 (Delta) | 35 | 15.7% |
| Undetermined VOC lineage | 14 | 6.3% |
| B1.1.7 (Alpha) | 4 | 1.8% |
| B.1.1.529 (Omicron) | 2 | 0.9% |
| P.1 (Gamma) | 2 | 0.9% |
| Unknown (Uncharacterized) | 166 | 74.4% |
| **Cases by Wave of Infection** | | |
| Wave 1 | 3 | 1.4% |
| Wave 2 | 84 | 37.7% |
| Wave 3 | 32 | 14.4% |
| Wave 4 | 73 | 32.7% |
| Wave 5 | 15 | 6.7% |
| Subsequent | 16 | 7.2% |

4.2.2. Vaccination status of severe COVID-19 cases in study cohort

Assessment of the vaccination status of the severe COVID-19 cases among the Northern Saskatchewan First Nations on-reserve showed that 125 (56.1%) of the cases were unvaccinated at the time of infection while 98 (48.8%) had received at least one dose of COVID-19 vaccine at

the time of infection diagnosis. Eleven (4.9%) of the severe cases and 87 (39.0%) of the severe cases among the NITHA communities received one and two or more vaccine doses respectively.

The average time interval between the last dose of COVID-19 vaccine, and onset of disease was 68 days among the severe COVID-19 cases. Over 30% of the cases (81, 36.3%) of the severe cases happened within the 6 months following vaccination, while 3 (1.3%) of the cases were reported after one year between the last dose of vaccine received and infection diagnosis (Table 4.8).

Table 4.8. Vaccination status of severe COVID-19 cases at the time of infection in study cohort, March 2020 – December 2022 (n=223)

| Vaccination status | Frequency | Percent |
|---|---|---|
| **Vaccination status at the time of infection** | | |
| Unvaccinated | 125 | 56.1% |
| Vaccinated | 98 | 43.9% |
| **Doses received at the time of infection** | | |
| One dose | 11 | 4.9% |
| Two or more doses | 87 | 39.0% |
| Unvaccinated | 125 | 56.1% |
| **Interval between the last vaccine dose and COVID-19 Infection** | | |
| 1 – 6 months | 81 | 36.3% |
| 7 – 12 months | 14 | 6.3% |
| >12 months | 3 | 1.3% |
| Unvaccinated | 125 | 56.1% |

**Mean number of days between date of last dose of vaccine and date of infection onset 68 days*

4.2.3. Clinical symptoms and co-existing medical conditions

The summary of the clinical symptoms associated with severe COVID-19 across NITHA communities from March 2020 to December 2022 shows that 158 (70.0%) of the severe cases reported symptoms at the time of diagnosis while 53 (23.8%) of the cases were asymptomatic, and 12 (5.4%) were of unknown symptoms status (Figure 11). The finding further showed that 45 (20.2%) of the severe cases presented with one symptom while 40 (17.9%) of the cases should two symptoms at the time of infection diagnosis. Individuals who presented with three, four, and five or more symptoms were reported by 31 (13.9%), 15 (6.7%) and 27 (12.1%) of the severe cases

respectively (Figure 12). Among the severe COVID-19 cases reported across Northern Saskatchewan First Nations communities under NITHA's administration, breathing difficulty was the most reported symptom (130; 58.3%). Occurrence of cough and fever was observed in 85 (38.1%) and 63 (28.3%) respectively of the severe COVID-19 cases. Nasal congestion and other unspecific symptoms (such as feeling unwell, and sweating, amongst others) were reported by 8 (3.6%) among severe COVID-19 cases across NITHA-administered communities (Figure 13).

Exploring the occurrence of comorbidities among confirmed severe COVID-19 cases among northern Saskatchewan First Nations showed that 116 (52.0%) of the cases presented with no known co-existing medical condition while 107 (48.0%) presented with other medical conditions occurring with severe COVID-19 infection. Diabetes Mellitus was the most common (47, 21.1%) co-existing medical condition reported among those with severe SARS-CoV-2 infection, and followed by CVD (24, 10.8%), substance use issues (12, 5.4%), and other medical conditions (including HIV, obesity, cancers) (10, 4.5%). Liver and kidney diseases were the least reported comorbidities observed among 6 (2.7%) of the confirmed severe COVID-19 cases (Table 4.9).

Figure 10- Occurrence of symptoms among confirmed severe COVID-19 cases in study cohort, March 2020 – December 2022 (n = 223)

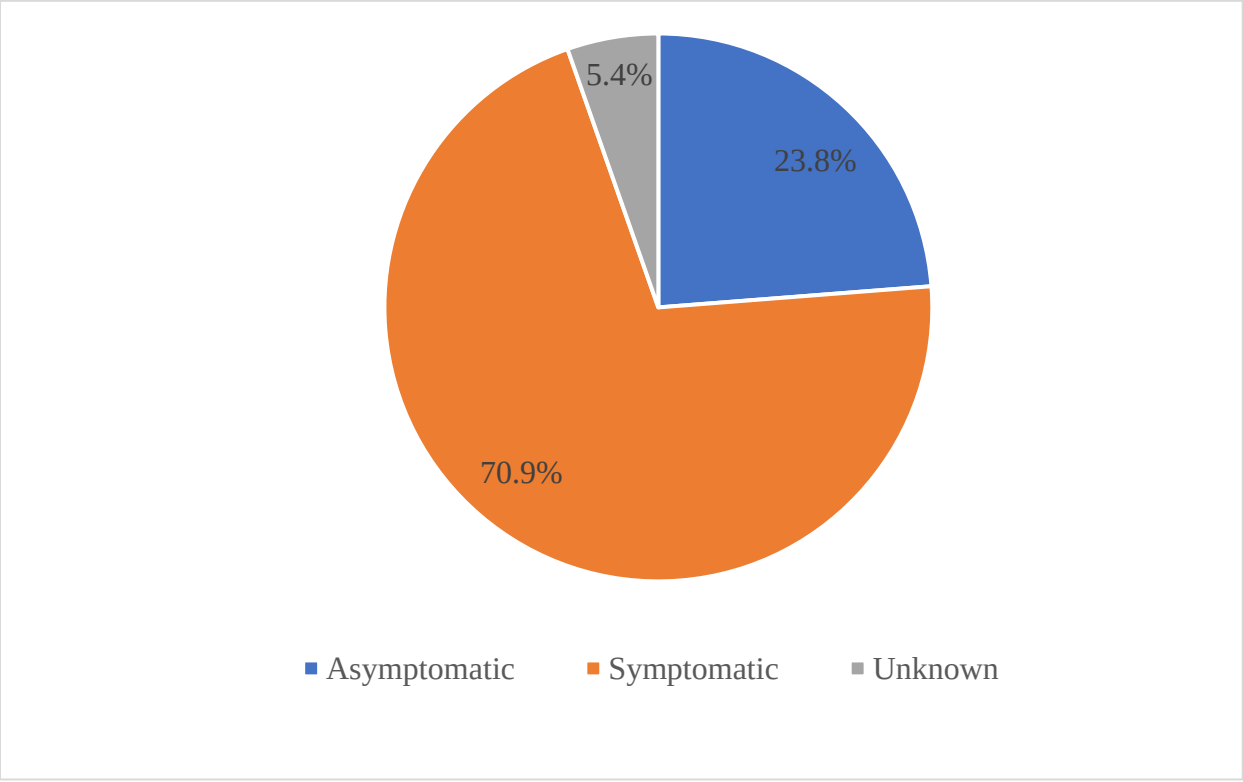


Figure 11- Number of symptoms shown by severe COVID-19 cases across NITHA communities from March 2020–December 2022 (n=223)

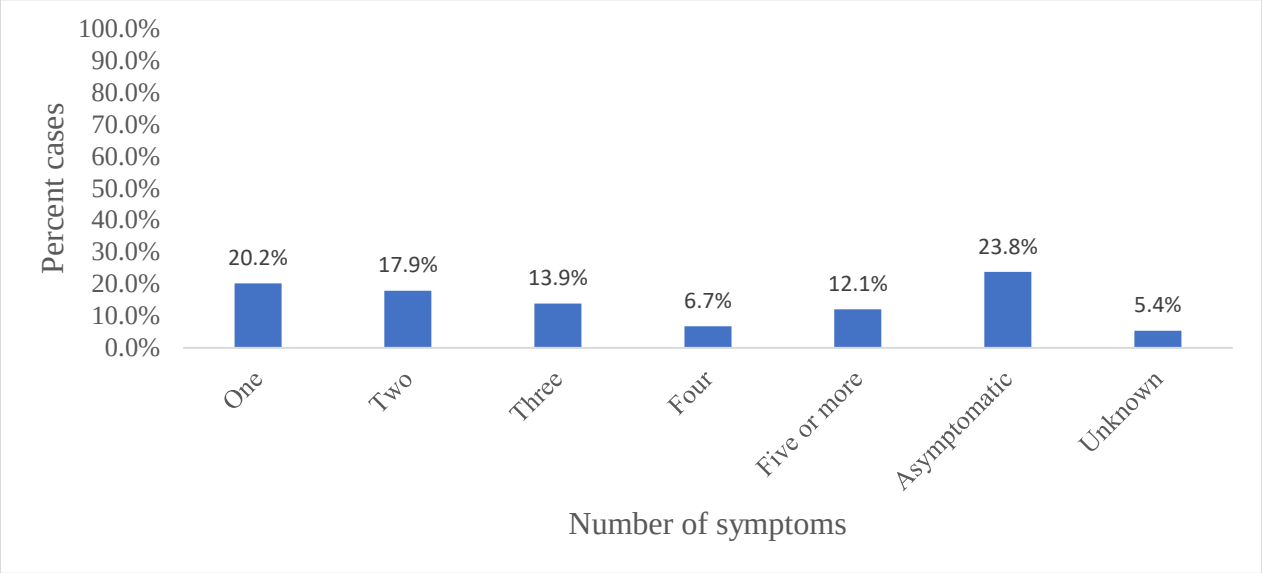



Figure 12- Types of symptoms observed at presentation in severe COVID-19 cases among Northern Saskatchewan First Nations (n=223)

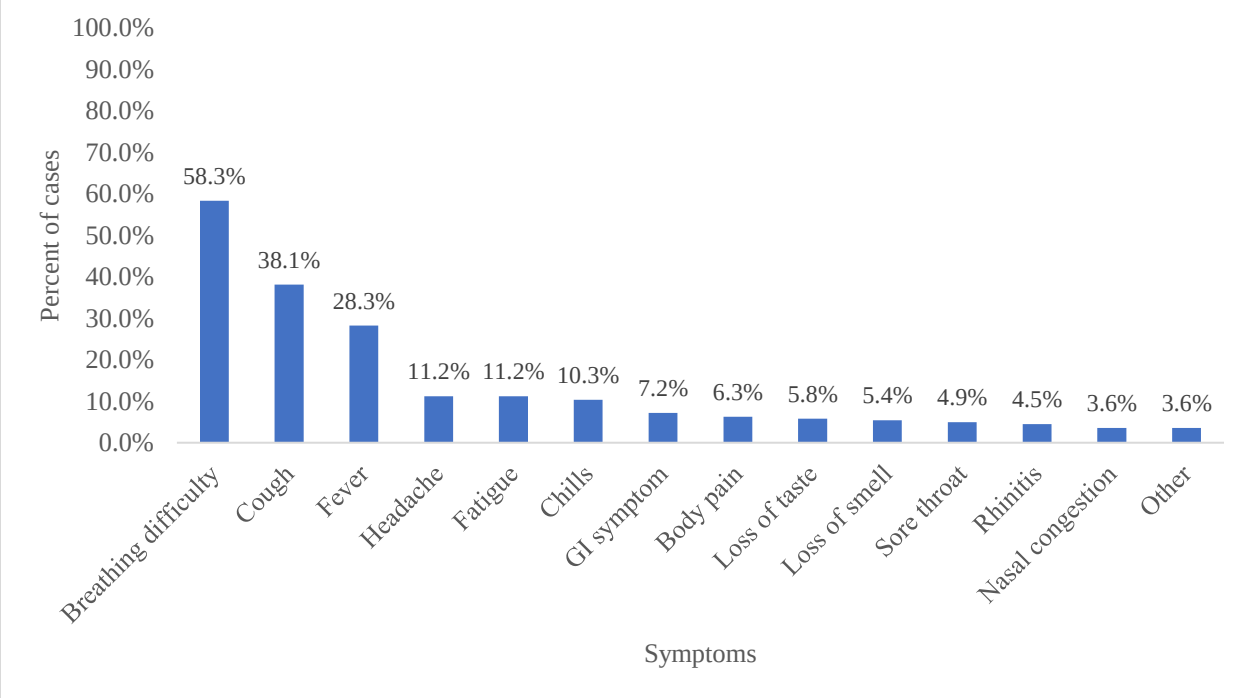


Table 4.9. Type of co-existing medical conditions with severe COVID-19, March 2020 – December 2022 (n=223)

| Types of co-existing medical condition | Frequency | Percent |
|---|---|---|
| **Presence of Comorbidities** | | |
| No | 116 | 52.0% |
| Yes | 107 | 48.0% |
| **Types of co-existing medical condition** | | |
| Diabetes Mellitus | 47 | 21.1% |
| Cardiovascular diseases | 24 | 10.8% |
| Substance use | 12 | 5.4% |
| Lung disease | 8 | 3.6% |
| Liver and Kidney diseases | 6 | 2.7% |
| Other (HIV, Obesity, Cancers, Unspecified) | 10 | 4.5% |
| No documented comorbidities | 116 | 52.0% |

**Research Question 2:** What demographic, clinical, and vaccination-related characteristics are associated with COVID-19 severity as indicated by hospitalization, ICU admission, and death?

### 4.3. Analytical Epidemiology of COVID-19 cases

4.3.1. Univariate association: COVID-19 hospitalization, ICU admission, death, and demographic factors

There was a statistically significant association between zone of residence, age group and living condition. There was a higher hospitalization rate reported among patients in Far Northcentral (4.2%; $\chi^2$=18.83, p<0.05), and 65 years and older (16.2%; $\chi^2$=417.51, p<0.05) compared to the other groups within their respective categories (Table 4.6). Even though there was no statistically significant association, hospitalization was marginally higher in male (2.8%) than female (2.5%) patients (Table 4.10).

There was no statistically significant association between demographic factors and ICU admission (p>0.05). Nevertheless, ICU admission was higher among male (34.2%) than female (31.2%). Also, more patients in the North Central zone (47.6%) than the other zones required ICU admission, and more patients <65 years old (34.3%) were treated in the ICU compared to the other age groups (65 years old and above) (Table 4.11).

More deaths were associated with males (0.9%) than females (0.4%), and patients who were 65 years and older (6.7%) compared to the younger age group (<65 years). This association between sex and age groups, and disease outcome was statistically significant at 95% confidence level with $p<0.05$ (Table 4.8). There was no statistically significant association between zone of residence and living condition, and disease outcome ($p>0.05$). However, mortality was higher among patients in the Far North Central (1.2%) than the other zones of residence. The least number of deaths (0.5%) was recorded in the Far Northeast (Table 4.12).

Table 4.10. Chi square, demographic characteristics, and hospitalization in all COVID-19 cases among study cohort (n=8,428)

| **Risk factors** | **Hospitalization** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Sex** | | | |
| Female | 4,246 (97.5%) | 108 (2.5%) | $\chi^2$=0.95 |
| Male | 3,959 (97.2%) | 115 (2.8%) | p=0.33 |
| **Zone of residence** | | | |
| Far North Central | 568 (95.8%) | 25 (4.2%) | $\chi^2$=18.83 |
| Far Northeast | 3,783 (98.0%) | 77 (2.0%) | **p<0.01*** |
| Far Northwest | 1,914 (96.6%) | 68 (3.4%) | |
| North Central | 962 (97.9%) | 21 (2.1%) | |
| Northeast | 978 (96.8%) | 32 (3.2%) | |
| **Age groups** | | | |
| <65 | 7,743 (98.3%) | 134 (1.7%) | $\chi^2$=417.51 |
| 65+ | 462 (83.9%) | 89 (16.2%) | **p<0.01*** |

Table 4.11. Chi square, demographic factors, and ICU admission in severe COVID-19 cases among study cohort (n=223)

| **Risk factors** | **ICU Admission** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Sex** | | | |
| Female | 75 (68.8%) | 34 (31.2%) | $\chi^2$=0.23 |
| Male | 75 (65.8%) | 39 (34.2%) | p=0. 63 |
| **Zone of residence** | | | |
| Far North Central | 16 (64.0%) | 9 (36.0%) | $\chi^2$=5.26 |
| Far Northeast | 59 (66.2%) | 19 (24.4%) | p=0.26 |
| Far Northwest | 45 (96.6%) | 23 (33.8%) | |
| North Central | 11 (52.4%) | 10 (47.6%) | |
| Northeast | 19 (61.3%) | 12 (38.7%) | |
| **Age groups** | | | |
| <65 | 88 (65.7%) | 46 (34.3%) | $\chi^2$=0.39 |
| 65+ | 62 (69.7%) | 27 (30.3%) | p=0.53 |

Table 4.12. Chi square, demographic characteristics of all COVID-19 deaths among study cohort (n=8,428)

| **Risk factors** | **Death** | | **Statistics** |
|---|---|---|---|
| | **Yes (%)** | **No (%)** | |
| **Sex** | | | |
| Female | 18 (0.4%) | 4,336 (99.6%) | $\chi^2$=6.69 |
| Male | 35 (0.9%) | 4,039 (99.1%) | **p=0.01*** |
| **Zone of residence** | | | |
| Far North Central | 7 (1.2%) | 586 (98.8%) | $\chi^2$=6.65 |
| Far Northeast | 18 (0.5%) | 3,842 (99.5%) | p=0.16 |
| Far Northwest | 12 (0.6%) | 1,970 (99.4%) | |
| North Central | 6 (0.6%) | 977 (99.4%) | |
| Northeast | 10 (1.0%) | 1,000 (99.0%) | |
| **Age groups** | | | |
| <65 | 16 (0.2%) | 7,861 (99.8%) | $\chi^2$=349.46 |
| 65+ | 37 (6.7%) | 514 (93.3%) | **p<0.01*** |

4.3.2. Univariable associations: COVID-19 hospitalization, ICU admission, death, and immunization status

Hospital admission was higher among the unvaccinated (2.7%) compared to those who were vaccinated (2.5%); however, this difference was not statistically significant. Among those who were vaccinated, hospitalization was higher for individuals who had received two or more doses of COVID-19 vaccine (2.5%), followed by those who had received one dose of COVID-19 vaccine (2.4%). More hospitalizations (5.8%) were reported among those who had received the vaccine after one year, compared those who received a dose within twelve months (Table 4.13).

As shown in Table 4.14, there was a statistically significant association between vaccination status and ICU admission ($\chi^2$=5.44, p=0.02). More (39.2%) of the unvaccinated hospitalized patients required ICU admission compared to vaccinated patients (p<0.05). The number of vaccine doses received and the duration between the last dose received showed no statistically significant association with ICU admission. However, ICU admission occurred more often among individuals

who had received two vaccine doses (25.3%), and those vaccinated within the first six months (25.9%) prior to infection compared with the other groups within their categories (Table 4.14). There was a statistically significant association between vaccination and mortality ($p<0.05$). Mortality rate due to the pandemic among Northern Saskatchewan First Nations on-reserve communities was about three times higher (0.9%) among unvaccinated persons when compared to 0.3% those who had received at least one dose of COVID-19 vaccine at the time of diagnosis ($\chi^2=12.27$, $p=0.01$). Consequently, more (1.0%) individuals who received one dose of the vaccine died from SARS-CoV-2 infection compared to those who received two or more doses of the vaccine (0.2%), and the finding was statistically significant ($\chi^2=9.20$, $p=0.01$) as shown in Table 4.15.

Table 4.13. Chi square, Vaccination, and hospitalization for all COVID-19 cases in study cohort, March 2020 – December 2022

| **Risk factors** | **Hospitalization** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Vaccination status at the time of infection (N=8,428)** | | | |
| Unvaccinated | 4,379 (97.3%) | 124 (2.7%) | $\chi^2= 0.44$ |
| Vaccinated | 3,826 (97.5%) | 99 (2.5%) | p= 0.51 |
| **Number of vaccines doses received at infection (N=3,925)** | | | |
| One | 491 (97.6%) | 12 (2.4%) | $\chi^2= 0.04$ |
| Two or more | 3,335 (97.5%) | 87 (2.5%) | p= 0.83 |
| **Interval between the last dose of COVID-19 vaccination and Infection (N=3,925)** | | | |
| 1 – 6 months | 3,181 (97.5%) | 81 (2.5%) | $\chi^2= 2.37$ |
| 7 – 12 months | 597 (97.6%) | 15 (2.4%) | p= 0.31 |
| >12 months | 48 (94.1%) | 3 (5.9%) | |

Table 4.14. Chi square, vaccination, and ICU admission in severe COVID-19 cases among the study cohort, March 2020 – December 2022

| **Risk factors** | **ICU Admission** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Vaccination status at the time of infection (N=223)** | | | |
| Unvaccinated | 76 (60.8%) | 49 (39.2%) | $\chi^2$=5.44 |
| Vaccinated | 74 (75.5%) | 24 (24.5%) | **p=0.02*** |
| **Number of vaccines doses received at infection (N=98)** | | | |
| One | 10 (83.3%) | 2 (16.3%) | $\chi^2$=0.43 |
| Two or more | 65 (74.7%) | 22 (25.3%) | p=0.51 |
| **Interval between the last dose of COVID-19 vaccination and Infection (N=98)** | | | |
| 1 – 6 months | 60 (74.1%) | 21 (25.9%) | $\chi^2$=1.13 |
| 7 – 12 months | 11 (78.6%) | 3 (21.4%) | p= 0.57 |
| >12 months | 3 (100.0%) | 0 (0.0%) | |

Table 4.15. Chi square vaccination status and death among Northern Saskatchewan First Nations on-reserve communities, March 2020 – December 2022

| **Risk factors** | **Death** | | **Statistics** |
|---|---|---|---|
| | **Yes (%)** | **No (%)** | |
| **Vaccination status at the time of infection (N=8,428)** | | | |
| Unvaccinated | 41 (0.9%) | 4,462 (99.1%) | $\chi^2$=12.27 |
| Vaccinated | 12 (0.3%) | 3,913 (99.7%) | **p<0.01*** |
| **Number of vaccines doses received at infection (N=3,925)** | | | |
| One | 5 (1.0%) | 498 (99.0%) | $\chi^2$=9.20 |
| Two | 7 (0.2%) | 3,415 (99.8%) | **p=0.01*** |
| **Interval between the last dose of COVID-19 vaccination and Infection (N=3,925)** | | | |
| 1–6 months | 8 (0.3%) | 3,254 (99.7%) | $\chi^2$=2.98 |
| 7–12 months | 4 (0.7%) | 608 (99.3%) | p= 0.23 |
| >12 months | 0 (0.0%) | 51 (100.0%) | |

4.3.3. Chi square association: COVID-19 hospitalization, ICU admission, death, and variant of concern, wave of infection and source of exposure

Tables 4.16–4.18 show the association between variant of concern, vaccination, sources of exposure and disease outcome. From Table 4.19, hospitalization was higher among individuals infected with the P.1 (Gamma) variant (5.7%) compared to the other VoC ($p>0.05$). Based on the wave of infection, more (6.1%) admissions were recorded during the first wave of the pandemic as compared to the subsequent waves. The finding shows statistically significant association between the wave of infection and hospitalization ($p<0.05$). There was no significant association between the source of infection and hospitalization. However, more hospital admission was seen among patients with workplace exposure (6.8%) in relation to those who were exposed from mass gathering, household contact, travel, school, or unknown sources from the community ($p>0.05$) as shown in Table 4.16.

Similarly, there was a significant association between wave of infection and ICU admission. Consequently, more ICU admission (60.0%) were recorded during the fifth wave of the pandemic among Northern Saskatchewan First Nations on-reserve compared with the other waves of the pandemic ($p<0.05$). Intensive Care Unit (ICU) admission rate was higher among those infected with B.1.1.7 (Alpha), and P.1 (Gamma) with 50.0%. However, there was no statistically significant association between the identified variant of concern and ICU admission ($p>0.05$). Patients who acquired the infection from unknown community sources (66.7%) had higher ICU demand than other subgroup within their respective categories ($p>0.05$) as shown in Table 4.17.

Although there were more deaths associated with the Gamma COVID-19 variant (0.9%) compared to the other variants, the finding was not statistically significant ($p>0.05$). Also, the wave of infection was significantly associated with disease outcome but more (0.8%) deaths were recorded during the second wave of the pandemic compared to the other waves. Similarly, there was no significant association (statistically) between variant of concern and source of COVID-19 exposure with outcome among infected persons among Northern Saskatchewan First Nations on-reserve ($p>0.05$), but more (1.6%) deaths were seen in those with unknown source of infection (Table 4.18).

Table 4.16. Chi square, variant of concern, wave, source of exposure, and hospitalization all COVID cases among the study cohort, March 2020 – December 2022

| **Risk factors** | **Hospitalization** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Variant of Concern (VOC) Isolated (N=1,823)** | | | |
| B.1.1.529 (Omicron) | 135 (97.8%) | 3 (2.2%) | $\chi^2$=2.26 |
| B.1.1.7 (Alpha) | 126 (96.9%) | 4 (3.1%) | p=0.69 |
| B.1.617.2 (Delta) | 936 (96.4%) | 34 (3.6%) | |
| P.1 (Gamma) | 33 (94.3%) | 2 (5.7%) | |
| Undetermined VOC lineage | 536 (97.5%) | 14 (2.5%) | |
| **Wave of Infection (N=8,428)** | | | |
| Wave 1 | 46 (93.2%) | 3 (6.8%) | $\chi^2$=25.57 |
| Wave 2 | 3,112 (97.4%) | 84 (2.6%) | **p<0.01*** |
| Wave 3 | 799 (96.2%) | 32 (3.8%) | |
| Wave 4 | 2,716 (97.4%) | 32 (3.6%) | |
| Wave 5 | 1,226 (98.8%) | 15 (1.2%) | |
| Subsequent | 306 (94.7%) | 17 (5.3%) | |
| **Source of Exposure (N=1,949)** | | | |
| Mass gathering/social event | 417 (97.2%) | 12 (2.8%) | $\chi^2$=7.29 |
| Travel | 39 (95.1%) | 2 (4.9%) | p=0.20 |
| Household contact | 1306 (97.8%) | 29 (2.3%) | |
| Workplace contact | 41 (93.2%) | 3 (6.8%) | |
| School | 37 (100.0%) | 0 (0.0%) | |
| Unknown contact in community | 60 (95.2%) | 3 (4.8%) | |

Table 4.17. Chi square variant of concern, wave, source of exposure and ICU admission in severe COVID-19 cases among the study cohort, March 2020 – December 2022

| **Risk factors** | **ICU Admission** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Variant of Concern (VOC) Isolated (N=57)** | | | |
| B.1.1.529 (Omicron) | 2 (100.0%) | 0 (0.0%) | $\chi^2$=2.65 |
| B1.1.7 (Alpha) | 2 (50.0%) | 2 (50.0%) | p=0.62 |
| B.1.617.2 (Delta) | 23 (65.7%) | 12 (34.3%) | |
| P.1 (Gamma) | 1 (50.0%) | 1 (50.0%) | |
| Undetermined VOC lineage | 11 (78.6%) | 3 (21.4%) | |
| **Wave of Infection (N=223)** | | | |
| Wave 1 | 2 (66.7%) | 1 (33.3%) | $\chi^2$=11.36 |
| Wave 2 | 53 (63.1%) | 31 (36.9%) | **p=0.045*** |
| Wave 3 | 23 (71.9%) | 9 (28.1%) | |
| Wave 4 | 51 (69.9%) | 22 (30.1%) | |
| Wave 5 | 6 (40.0%) | 9 (60.0%) | |
| Subsequent | 15 (93.8%) | 1 (6.2%) | |
| **Source of Exposure (N=49)** | | | |
| Mass gathering/Social event | 8 (66.7%) | 4 (33.3%) | $\chi^2$=1.45 |
| Travel | 1 (50.0%) | 1 (50.0%) | p=0.84 |
| Workplace contact | 2 (66.7%) | 1 (33.3%) | |
| Unknown contact in community | 1 (33.3%) | 2 (66.7%) | |
| Other | 4 (50.0%) | 4 (50.0%) | |

Table 4.18. Chi square, variant of concern, wave, source of exposure and deaths in all COVID-19 cases among the study cohort, March 2020 – December 2022

| Risk factors | Death | | Statistics |
|---|---|---|---|
| | Yes (%) | No (%) | |
| **Variant of Concern (VOC) Isolated (N=1,823)** | | | |
| B.1.1.529 (Omicron) | 0 (0.0%) | 138 (100.0%) | $\chi^2$=3.19 |
| B1.1.7 (Alpha) | 0 (0.0%) | 130 (100.0%) | p=0.53 |
| B.1.617.2 (Delta) | 9 (0.9%) | 961 (99.1%) | |
| P.1 (Gamma) | 0 (0.0%) | 35 (100.0%) | |
| Undetermined VOC lineage | 3 (0.6%) | 547 (99.4%) | |
| **Wave of Infection (N=8,428)** | | | |
| Wave 1 | 0 (0.0%) | 49 (100.0%) | $\chi^2$=5.23 |
| Wave 2 | 27 (0.8%) | 3,169 (99.2%) | p=0.39 |
| Wave 3 | 5 (0.6%) | 826 (99.4%) | |
| Wave 4 | 16 (0.6%) | 2,772 (99.4%) | |
| Wave 5 | 4 (0.3%) | 1,237 (99.7%) | |
| Subsequent | 1 (0.3%) | 322 (99.7%) | |
| **Source of Exposure (N=1,936)** | | | |
| Mass gathering/Social event | 3 (0.7%) | 426 (99.3%) | $\chi^2$=1.60 |
| Travel | 0 (0.0%) | 41 (100.0%) | p=0.90 |
| Household contact | 9 (0.7%) | 1,326 (99.3%) | |
| Workplace contact | 0 (0.0%) | 44 (100.0%) | |
| School | 0 (0.0%) | 37 (100.0%) | |
| Unknown contact in community | 1 (1.6%) | 62 (98.4%) | |

4.3.4. Univariable association: COVID-19 hospitalization, ICU admission and death, and between symptoms and comorbidities

Our findings show a statistically significant association between occurrence of symptoms at presentation and place of isolation. More patients (5.2%) who presented with symptoms (symptomatic patients) required hospitalization compared to those who were asymptomatic (1.2%) or unknown symptoms status (1.3%) respectively with p-value <0.05 (Table 4.19). There was no

statistically significant association ($p>0.05$) between the number of symptoms at presentation and the need for hospitalization, although more (6.0%) of patients with three symptoms were hospitalized than those with one (5.0%), two (5.4%), four (3.9%), and five or more (5.4%) symptoms (Table 4.15). Also, there was a statistically significant association between the presence of comorbidities and the need for hospitalization ($p<0.05$). More (6.3%) of patients who presented with comorbidities required hospitalization as compared to those without comorbidities (1.7%) ($\chi^2=108.76$, $p<0.01$). Consequently, higher proportion of patients with liver and kidney disease (21.4%) disease required hospitalization as compared to those with other co-existing medical conditions ($\chi^2=155.00$, $p<0.05$) as shown in Table 4.19.

There was no statistically significant association between the presence of symptoms at the time of diagnosis and ICU admission. A total of 34.2% of patients who presented with symptoms required ICU admission when compared to patients who were asymptomatic (28.3%) and whose symptom status was unknown (33.3%), and $p>0.05$ (Table 4.20). Although there was no statistically significant association between the number of symptoms the patients presented with or the type comorbidities and ICU admission ($p>0.05$), more people with four symptoms (46.7%), and those with liver and kidney diseases (50.0%) required ICU admission than those presenting with once, two, three or five or more symptoms, and those with other co-existing medical conditions respectively (Table 4.20).

For deaths, there was a statistically significant association between the presence of symptoms at COVID-19 diagnosis and disease outcome ($p<0.05$). More patients who presented with symptoms (1.2%) died, compared to those who were asymptomatic (0.3%) and those with unknown symptoms (0.6%) (Table 4.21). Conversely, there was no statistically significant association between the number of symptoms at the time of diagnosis and COVID-19 outcome ($p>0.05$).

The presence of comorbidities showed significant association with COVID-19 outcome as 2.1% of cases that presented with co-existing medical conditions died compared to 0.3% who had no co-existing medical conditions ($\chi^2=69.09$, $p<0.05$). Also, there was statistically significant association between the type of co-existing medical condition and disease outcome ($p<0.05$). More people with cardiovascular disease such as hypertension (13.3%) died from COVID-19 than those with other comorbidities ($\chi^2=111.04$, $p<0.01$) as shown in Table 4.21.

Table 4.19. Chi square, symptoms and comorbidities, and hospitalization among all COVID-19 cases among the study cohort, March 2020 – December 2022

| **Risk factors** | **Hospitalization** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Occurrence of symptoms at presentation (N=8,428)** | | | |
| Asymptomatic | 4,403 (98.8%) | 53 (1.2%) | $\chi^2$=119.81 |
| Symptomatic | 2,886 (94.8%) | 158 (5.2%) | **p<0.01*** |
| Unknown | 916 (98.7%) | 12 (1.3%) | |
| **Number of symptoms observed at presentation (N=3,044)** | | | |
| One | 859 (95.0%) | 25 (5.0%) | $\chi^2$=2.10 |
| Two | 700 (94.6%) | 40 (5.4%) | p=0.72 |
| Three | 485 (94.0%) | 31 (6.0%) | |
| Four | 366 (96.1%) | 15 (3.9%) | |
| Five or more symptoms | 476 (94.6%) | 27 (5.4%) | |
| **Presence of comorbidities (N=8,248)** | | | |
| No | 6,603 (98.3%) | 116 (1.7%) | $\chi^2$=108.76 |
| Yes | 1,602 (93.7%) | 107 (6.3%) | **p<0.01*** |
| **Types of co-existing medical condition (N=1,709)** | | | |
| Substance use | 1,102 (98.9%) | 12 (1.1%) | $\chi^2$=155.00 |
| Diabetes Mellitus | 259 (84.6%) | 47 (15.4%) | **p<0.01*** |
| Cardiovascular disease | 104 (81.3%) | 24 (18.8%) | |
| Liver and Kidney disease | 22 (78.6%) | 6 (21.4%) | |
| Lung disease | 71 (89.9%) | 8 (10.1%) | |
| Other (HIV, Obesity, Cancers, Unspecified) | 44 (81.5%) | 10 (18.5%) | |

Table 4.20. Chi square, symptoms, comorbidities, and severe COVID-19 ICU admission among the study cohort, March 2020 – December 2022

| **Risk factors** | **ICU Admission** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Occurrence of symptoms at presentation (N=223)** | | | |
| Asymptomatic | 38 (71.7%) | 15 (28.3%) | $\chi^2$=0.62 |
| Symptomatic | 104 (65.8%) | 54 (34.2%) | p=0.73 |
| Unknown | 8 (66.7%) | 4 (33.3%) | |
| **Number of symptoms observed at presentation (N=158)** | | | |
| One | 29 (64.4%) | 16 (35.6%) | $\chi^2$=3.14 |
| Two | 30 (75.0%) | 10 (25.0%) | p=0. 53 |
| Three | 21 (67.7%) | 10 (32.3%) | |
| Four | 8 (53.3%) | 7 (46.7%) | |
| Five or more symptoms | 16 (59.3%) | 11 (40.7%) | |
| **Presence of Comorbidities (N=223)** | | | |
| No | 81 (69.8%) | 35 (30.2%) | $\chi^2$=0.72 |
| Yes | 69 (64.5%) | 38 (35.5%) | p=0.40 |
| **Types of co-existing medical condition (N=107)** | | | |
| Substance use | 8 (66.7%) | 4 (33.3%) | $\chi^2$=2.56 |
| Diabetes Mellitus | 30 (63.8%) | 17 (36.2%) | p=0.77 |
| Cardiovascular disease | 15 (62.5%) | 9 (37.5%) | |
| Liver and Kidney disease | 3 (50.0%) | 3 (50.0%) | |
| Lung disease | 7 (87.5%) | 1 (12.5%) | |
| Other (HIV, Obesity, Cancers, Unspecified) | 6 (60.0%) | 4 (40.0%) | |

Table 4.21. Chi square, symptoms, comorbidities, and outcome for all COVID-19 cases among the study cohort, March 2020 – December 2022

| **Risk factors** | **Death** | | **Statistics** |
|---|---|---|---|
| | **No (%)** | **Yes (%)** | |
| **Occurrence of symptoms at presentation (N=8,428)** | | | |
| Asymptomatic | 4,445 (99.7%) | 11 (0.3%) | $\chi^2$=25.35 |
| Symptomatic | 3,008 (98.8%) | 36 (1.2%) | **p<0.01*** |
| Unknown | 922 (99.4%) | 6 (0.6%) | |
| **Number of symptoms observed at presentation (N=3,044)** | | | |
| One | 892 (98.7%) | 12 (1.3%) | $\chi^2$= 3.00 |
| Two | 730 (98.7%) | 10 (1.3%) | p=0.56 |
| Three | 508 (98.4%) | 8 (1.6%) | |
| Four | 379 (99.5%) | 2 (0.5%) | |
| Five or more symptoms | 499 (99.2%) | 4 (0.8%) | |
| **Presence of Comorbidities (N=8,428)** | | | |
| No | 6,701 (99.7%) | 18 (0.3%) | $\chi^2$=69.09 |
| Yes | 1,674 (97.9%) | 35 (2.1%) | **p<0.01*** |
| **Types of co-existing medical condition (N=1709)** | | | |
| Substance use | 1113 (99.9%) | 1 (0.1%) | $\chi^2$=111.04 |
| Diabetes Mellitus | 294 (96.1%) | 12 (3.9%) | **p<0.01*** |
| Cardiovascular disease | 111 (86.7%) | 17 (13.3%) | |
| Liver and kidney disease | 27 (96.4%) | 1 (3.6%) | |
| Lung disease | 78 (98.73%) | 1 (1.3%) | |
| Other | 51 (94.4%) | 3 (5.6%) | |

4.3.5. Multivariable association: Demographic factors, vaccination, symptoms, comorbidities and COVID-19 hospitalization

Findings from the multivariable logistic regression showed that the odds of hospitalization increase with age, and patients aged 65 years and older were >6 times more likely to be hospitalized compared those less than 65 years old (OR=6.90 95%CI=4.96 – 9.61; p<0.01). Male patients had over 1.24 times chances of being hospitalized compared to female patients (OR=1.74 95%CI=0.93

– 1.65; p=0.15). However, this finding was not statistically significant (p>0.05). Also, the odds of hospitalization were significantly lower among COVID-19 patients across the FNE zone (OR=0.4, 95%CI=0.27 – 0.72; p<0.01) and FNW (OR=0.55, 95%CI=0.33 – 0.92; p=0.02) compared to patients across the FNC zone (Table 4.22). Receiving two or more doses of COVID-19 vaccine was protective as individuals who had received at least two doses of COVID-19 vaccines had significantly lesser odds of hospitalization than unvaccinated patients at the time COVID-19 diagnosis (OR=0.68, 96%CI=0.50 – 0.92; p=0.01). In addition, patients who presented with symptoms were significantly 3 times more likely to be hospitalized compared to asymptomatic patients (OR=3.30, 95%CI=2.36 – 4.62; p<0.01). Among patients with comorbidities, individuals with diabetes (OR=7.84, 95%CI=3.96 – 15.52; p=<0.01), cardiovascular disease (OR=7.93 95%CI=3.65 – 17.19, p<0.01), liver and kidney diseases (OR=22.69, 95%CI=7.42 – 69.39, p<0.01), lung disease (OR=6.82, 95%CI=2.59 – 18.00; p<0.01), and other diseases (OR=11.26, 95%CI=4.37 – 29.05; p<0.01) respectively had higher odds of hospitalization than patients with smoking and other substance use issues (Table 4.22).

Table 4.22. Multivariable logistics regression, between demographic factors, vaccination, symptoms, comorbidities, and hospitalization among the study cohort; March 2020 – December 2022

| Variable | OR | SE | 95%CI | p-value |
|---|---|---|---|---|
| **Age groups** | | | | |
| <65 | Ref | | | |
| 65+ | 6.90 | 1.16 | 4.96 – 9.61 | <**0.01*** |
| **Sex** | | | | |
| Female | Ref | | | |
| Male | 1.24 | 0.18 | 0.93 – 1.65 | 0.15 |
| **Zone** | | | | |
| Far North Central | Ref | | | |
| Far Northeast | 0.44 | 0.11 | 0.27 – 0.72 | <**0.01*** |
| Far Northwest | 0.55 | 0.14 | 0.33 – 0.92 | **0.02*** |
| North Central | 0.55 | 0.18 | 0.29 – 1.03 | 0.06 |
| Northeast | 0.59 | 0.17 | 0.33 – 1.05 | 0.07 |
| **Vaccination status** | | | | |
| Unvaccinated | Ref | | | |
| One dose | 0.95 | 0.31 | 0.49 – 1.83 | 0.88 |
| Two or more doses | 0.68 | 0.11 | 0.50 – 0.92 | **0.01*** |
| **Presence of symptoms** | | | | |
| Asymptomatic | Ref | | | |
| Symptomatic | 3.30 | 0.57 | 2.36 – 4.62 | <**0.01*** |
| Unknown | 0.68 | 0.11 | 0.58 – 2.14 | 0.74 |
| **Type of co-existing medical condition** | | | | |
| Substance use | Ref | | | |
| Diabetes | 7.84 | 2.73 | 3.96 – 15.52 | <**0.01*** |
| Cardiovascular disease | 7.93 | 3.13 | 3.65 – 17.19 | <**0.01*** |
| Liver and kidney diseases | 22.69 | 12.94 | 7.42 – 69.39 | <**0.01*** |
| Lung disease | 6.82 | 5.45 | 2.59 – 18.00 | <**0.01*** |
| Other | 11.26 | 5.45 | 4.37 – 29.05 | <**0.01*** |
| Undocumented comorbidities | 1.77 | 0.55 | 0.97 – 3.26 | 0.07 |

*Ref = Reference category*
***** *Statistical test of Significance*

Log likelihood = -815.04; LR $chi^2$ = 429.91 Prob > $chi^2$ < 0.01
Number of observations = 8,428 Pseudo $R^2$ = 0.21

4.3.6. Model specification and logistic regression diagnostics for hospitalized COVID-19 cases

*4.3.6.1. Model specification and goodness of fit*

To assess for model specification errors, we performed linktest. The finding showed statistically significant _hatsq ($p<0.05$) which indicates that even though there was model specification error, the variables with appropriate for the model (Table 4.23). We also assessed the goodness of fit using Hosmer and Lemeshow's goodness-of-fit test to assess if the data fits the model, we obtained a $chi^2$ $p<0.05$ which indicated that the model did not fit data well (Table 2.24). This error, however, was correct by including interaction terms in the model (Appendix E, Table 1b).

Table 4.23. Model Specification for Multivariable logistic regression, predictors of COVID-19 hospitalization

| **Hospitalization** | **Coefficient** | **Standard error** | **95%CI** | **p-value** |
|---|---|---|---|---|
| _hat | 0.50 | 0.17 | 0.16 – 0.83 | <0.01 |
| _hatsq | -0.10 | 0.03 | -0.16 – -0.03 | <0.01 |

Log likelihood = -810.29

LR $chi^2$=439.40; Prob>F<0.01

Number of observations=8,428; Pseudo $R^2$=0.21

Table 4.24. Hosmer-Lemeshow goodness-of-fit test for multivariable model on predictors of hospitalization among COVID-19 cases

| **Group** | **Prob** | **Obs_1** | **Exp_1** | **Obs_0** | **Exp_0** | **Total** |
|---|---|---|---|---|---|---|
| 1 | <0.01 | 8 | 4.9 | 1092 | 1095.1 | 1100 |
| 2 | <0.01 | 5 | 6.6 | 1039 | 1037.4 | 1044 |
| 3 | <0.01 | 4 | 3.2 | 443 | 443.8 | 447 |
| 4 | <0.01 | 2 | 6.5 | 785 | 780.5 | 787 |
| 5 | 0.01 | 2 | 8.3 | 901 | 894.7 | 903 |
| 6 | 0.01 | 1 | 9.0 | 790 | 782.0 | 791 |
| 7 | 0.02 | 12 | 14.5 | 829 | 826.5 | 841 |
| 8 | 0.02 | 27 | 20.5 | 827 | 833.5 | 854 |
| 9 | 0.04 | 33 | 26.7 | 796 | 802.3 | 829 |
| 10 | 0.66 | 129 | 122.8 | 703 | 709.2 | 832 |

Number of observations =8,428; number of groups=10

Hosmer-Lemeshow chi2=22.02; Prob>chi2=0.005

*4.3.6.2. Regression diagnostics for hospitalized COVID-19 cases*

Figure 13- Deviance residual for COVID-19 hospitalization among the study cohort, March 2020 – December 2022

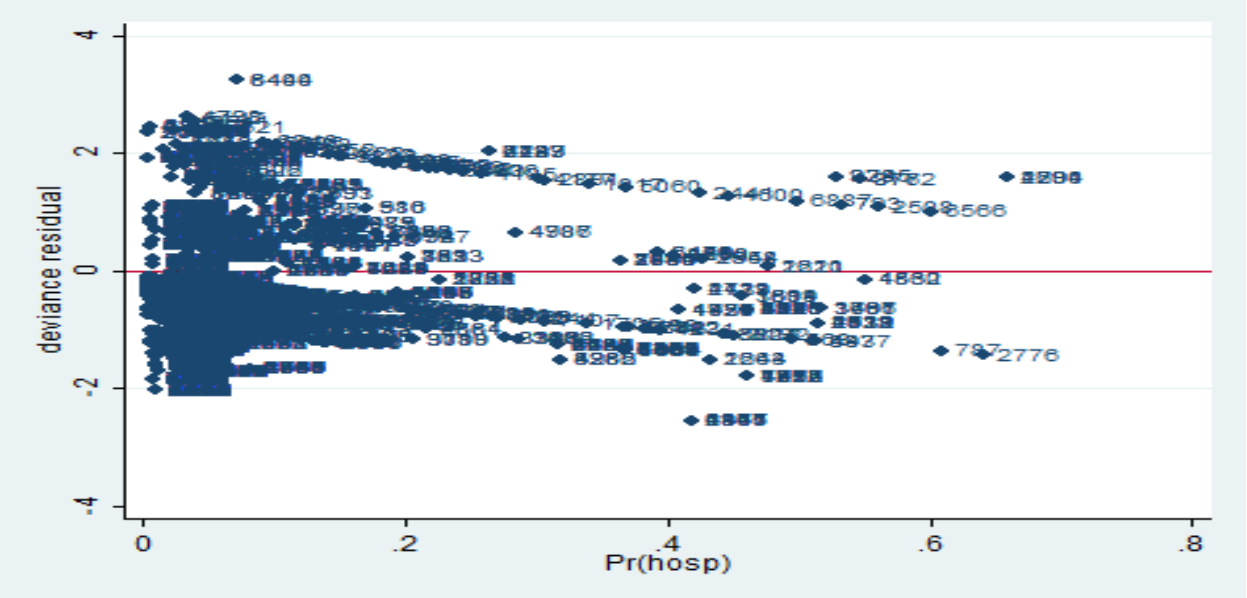



Figure 14- Standardized Pearson residual for COVID-19 hospitalization among the study cohort, March 2020 – December 2022

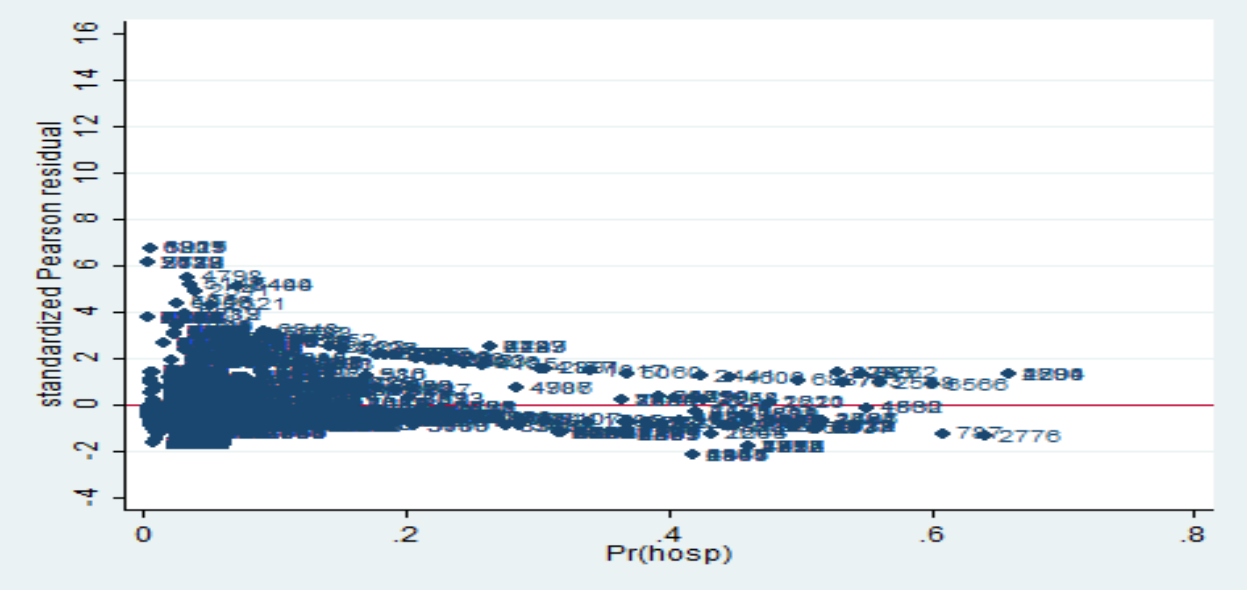


Figure 15- Leverage (_hat diagonal) for hospitalized COVID-19 cases among the study cohort, March 2020 – December 2022

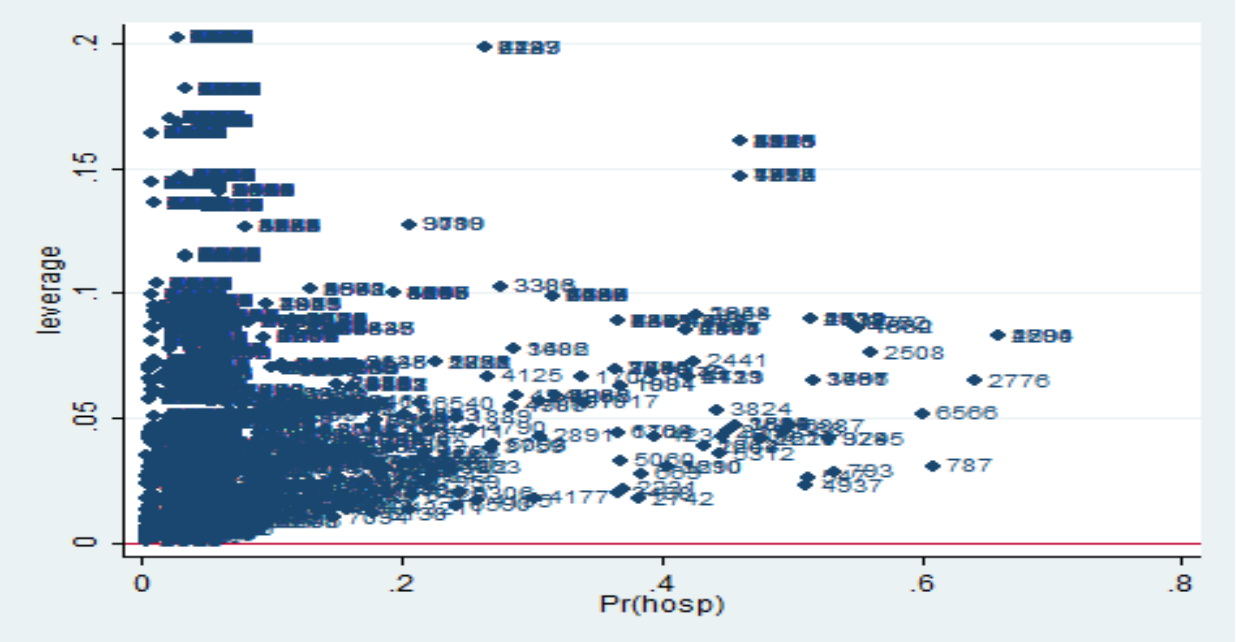



Figure 16- Difference of chi square (dx2) for hospitalized COVID-19 cases the study cohort, March 2020 – December 2022

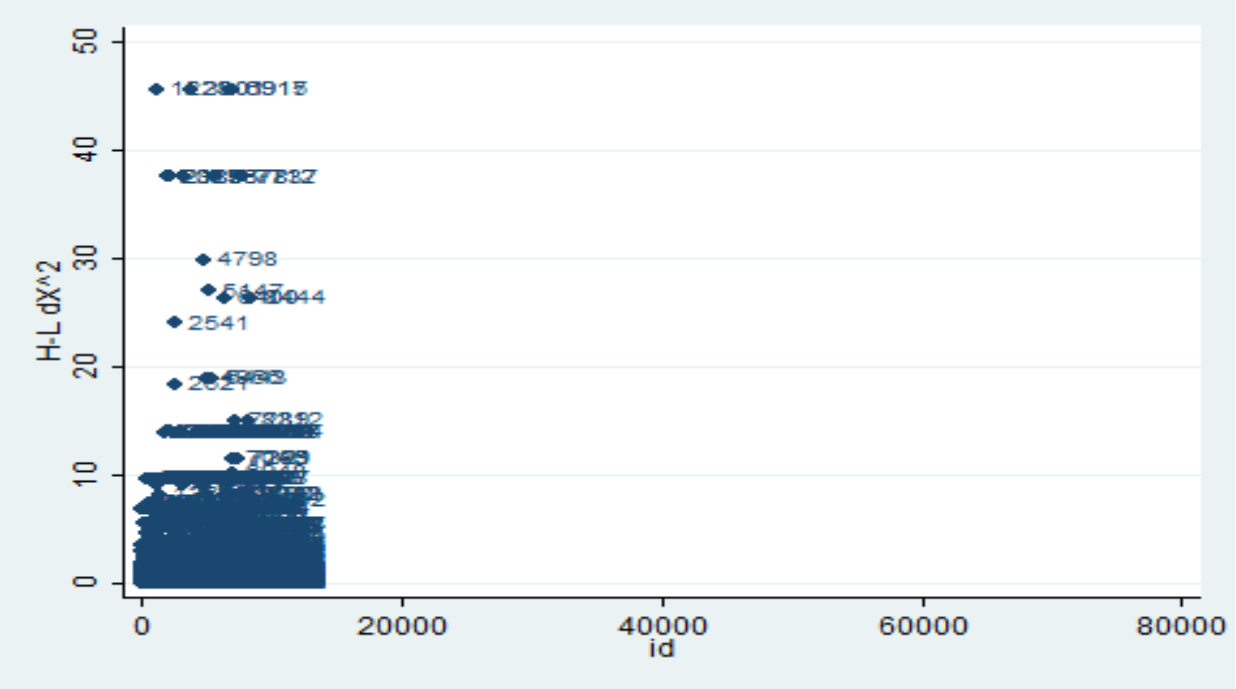
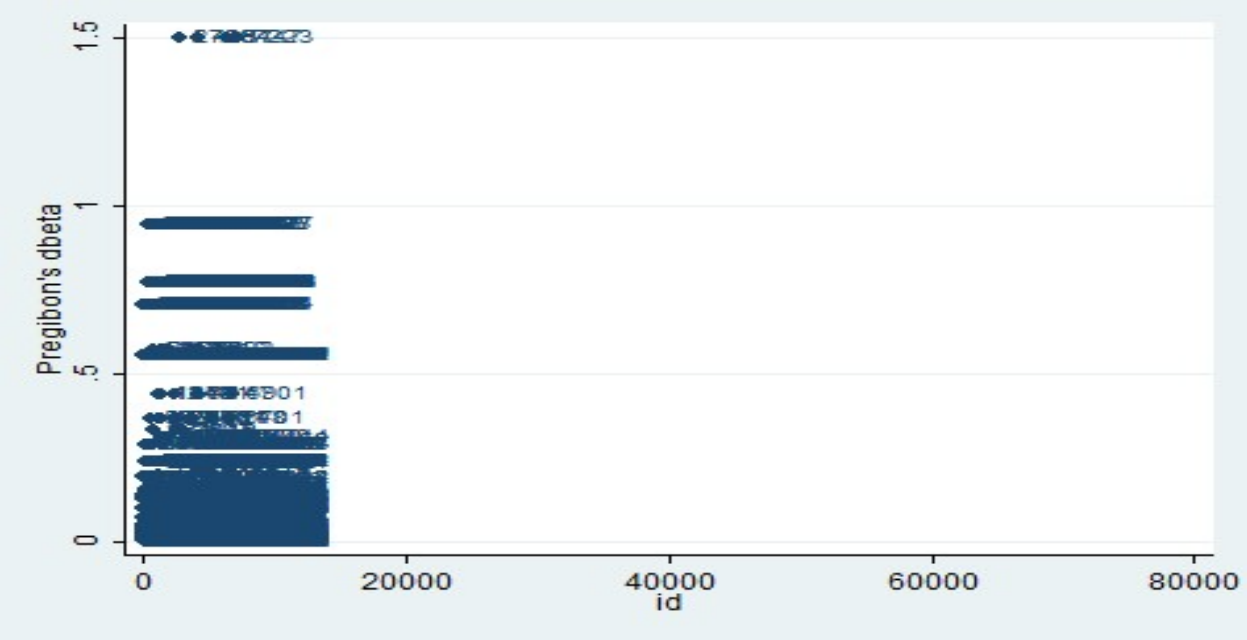


Figure 17- Figure 4.13. Influence (Pregibon's dbeta) for hospitalized COVID-19 cases among the study cohort, March 2020 – December 2022




4.3.7. Determinants of COVID-19 ICU admission

In the final model (Table 4.25), the findings show no statistically significant association between the demographic factors, presence of symptoms, and comorbidities as determinants of ICU admission. However, the odds of ICU admission were significantly about 51% lower among patients who received two or more doses of COVID-19 vaccines compared to those who were unvaccinated at the time of infection diagnosis (OR=0.49, 95%CI=0.26 – 0.94; p=0.03).

Even though not statistically significant, Male patients had slightly higher odds of ICU admission than females (OR=1.09, 95%CI=0.58 – 2.03; p=0.79). Patients who showed clinical symptoms were more likely to require ICU admission compared to patients who had reported not having symptoms (OR=1.43, 95%CI=0.67 – 3.06; p=0.36 for symptomatic patients, and OR=1.40, 95%CI=0.33 – 5.94; p=0.64). Also, patients who had diabetes (OR=1.06 95%CI=0.25 – 4.43; p=0.94), cardiovascular disease (OR=1.02, 95%CI=0.22 – 4.70; p=0.98), liver and kidney diseases (OR=1.82, 95%CI=0.21 – 4.34; p=0.41) respectively had higher odds of ICU admission than those with smoking and other substance use issues (Table 4.25).

The odds of ICU admission were lower among the Far Northeast (OR=0.48, 95%CI=0.17 – 1.34; p=0.16), Far Northwest (OR=0.71, 95%CI=0.25 – 2.00; p=0.52) and Northeast (OR=0.81,

95%CI=0.26 – 2.57; p=0.72) respectively when compared to patients from the Far North Central zone; finding that was not statistically significant. The odd was also lower among patients 65 years and older compared to <65 years old (OR=0.82, 95%CI=0.43 – 1.54; p=0.54). These findings were, however, not statistically significant (p>0.05) as shown in Table 4.25.

Table 4.25. Multivariable association; demographic factors, vaccination, symptoms, comorbidities, and ICU admission among the study cohort, March 2020 – December 2022

| Variable | Odds Ratio | Standard Error | 95%CI | p-value |
|---|---|---|---|---|
| **Age groups** | | | | |
| <65 | Ref | | | |
| 65+ | 0.82 | 0.26 | 0.43 – 1.54 | 0.54 |
| **Sex** | | | | |
| Female | Ref | | | |
| Male | 1.09 | 0.27 | 0.58 – 2.03 | 0.79 |
| **Zone** | | | | |
| Far North Central | Ref | | | |
| Far Northeast | 0.48 | 0.25 | 0.17 – 1.34 | 0.16 |
| Far Northwest | 0.71 | 0.38 | 0.25 – 2.00 | 0.52 |
| North Central | 1.94 | 1.28 | 0.53 – 7.10 | 0.32 |
| Northeast | 0.81 | 0.48 | 0.26 – 2.57 | 0.72 |
| **Vaccination status at the time of infection** | | | | |
| Unvaccinated | Ref | | | |
| One dose | 0.22 | 0.20 | 0.04 – 1.23 | 0.09 |
| Two or more doses | 0.49 | 0.16 | 0.26 – 0.94 | **0.03*** |
| **Presence of symptoms** | | | | |
| Asymptomatic | Ref | | | |
| Symptomatic | 1.43 | 0.55 | 0.67 – 3.06 | 0.36 |
| Unknown | 1.40 | 1.03 | 0.33 – 5.94 | 0.64 |
| **Presence of comorbidities** | | | | |
| Substance use | Ref | | | |
| DM | 1.06 | 0.77 | 0.25 – 4.43 | 0.94 |
| CVD | 1.02 | 0.79 | 0.22 – 4.70 | 0.98 |
| Liver & Kidney disease | 1.82 | 2.01 | 0.21 – 4.34 | 0.41 |
| Lung disease | 0.34 | 0.44 | 0.03 – 4.34 | 0.41 |

| | | | | |
|---|---|---|---|---|
| Other | 0.71 | 0.69 | 0.11 – 4.81 | 0.73 |
| Undocumented comorbidities | 0.75 | 0.51 | 0.20 – 2.85 | 0.67 |

*Ref = Reference category*
***** Statistical test of Significance*

Log likelihood = -132.49 LR chi$^2$ = 17.03 Prob > chi$^2$ = 0.38
Number of observations = 223 Pseudo $R^2$ = 0.06

4.3.8. Model specification and model diagnostics for COVID-19 ICU admission

*4.3.8.1. Model specification and goodness-of-fit for COVID-19 ICU admission*

Using the linktest to assess the model specification errors, the model showed a p-value of 0.28 (not statistically significant at 95%CI) for _hatsq indicating that there was no model specification error with the variable that were in the model (Table 4.27). The Hosmer-Lemeshow test for goodness-of-fit showed p=0.66 which indicated that the model was a good fit for the predictors of ICU admission among Northern Saskatchewan COVID-19 cases (Table 4.27).

Table 4.26. Model Specification for Multivariable logistic regression, predictors of COVID-19 ICU admission among the study cohort, March 2020 – December 2022

| **Hospitalization** | **Coefficient** | **Standard error** | **95%CI** | **p-value** |
|---|---|---|---|---|
| _hat | 1.28 | 0.50 | 0.29 – 2.26 | 0.01 |
| _hatsq | 0.18 | 0.28 | -0.36 – 0.72 | 0.51 |

Log likelihood = -132.28
LR chi$^2$=17.45; Prob>F<0.01
Number of observations=223; Pseudo $R^2$=0.06

Table 4.27. Hosmer-Lemeshow goodness-of-fit test for multivariable model on predictors of ICU admission among COVID-19 cases among the study cohort, March 2020 – December 2022

| **Group** | **Prob** | **Obs_1** | **Exp_1** | **Obs_0** | **Exp_0** | **Total** |
|---|---|---|---|---|---|---|
| 1 | 0.17 | 3 | 2.9 | 20 | 20.1 | 23 |
| 2 | 0.21 | 6 | 4.2 | 16 | 17.8 | 22 |
| 3 | 0.25 | 4 | 5.2 | 18 | 16.8 | 22 |
| 4 | 0.28 | 8 | 6.2 | 15 | 16.8 | 23 |
| 5 | 0.32 | 5 | 8.0 | 21 | 18.0 | 26 |
| 6 | 0.35 | 7 | 6.1 | 11 | 11.9 | 18 |
| 7 | 0.40 | 10 | 9.1 | 14 | 14.9 | 24 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 8 | 0.43 | 6 | 8.8 | 15 | 12.2 | 21 |
| 9 | 0.48 | 10 | 10.1 | 12 | 11.9 | 22 |
| 10 | 0.66 | 14 | 12.5 | 8 | 9.5 | 22 |

Number of observations =223; number of groups=10
Hosmer-Lemeshow chi2=5.92; Prob>chi2=0.66

*4.3.8.1. Logistic regression diagnostics COVID-19 ICU admission*

Figure 18- Deviance residual for COVID-19 ICU admission among study cohort, March 2020 – December 2022

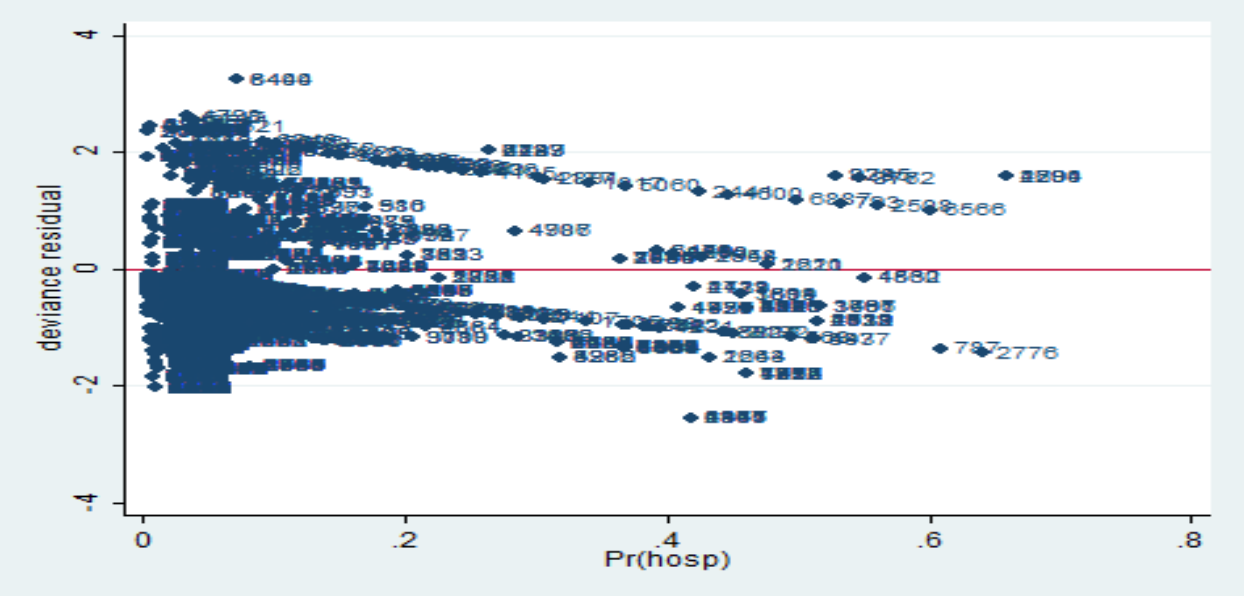


Figure 19- Pearson residual for COVID-19 ICU admission among the study, March 2020 – December 2022

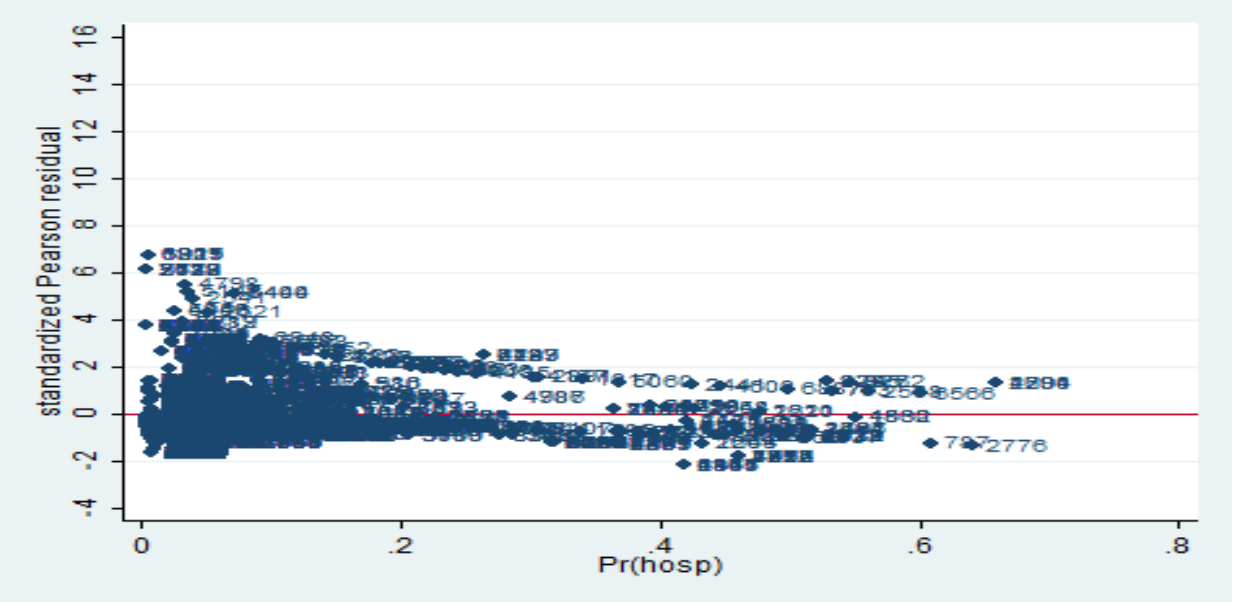



Figure 20- Leverage (_hat diagonal) for COVID-19 ICU admission among the study cohort, March 2020 – December 2022

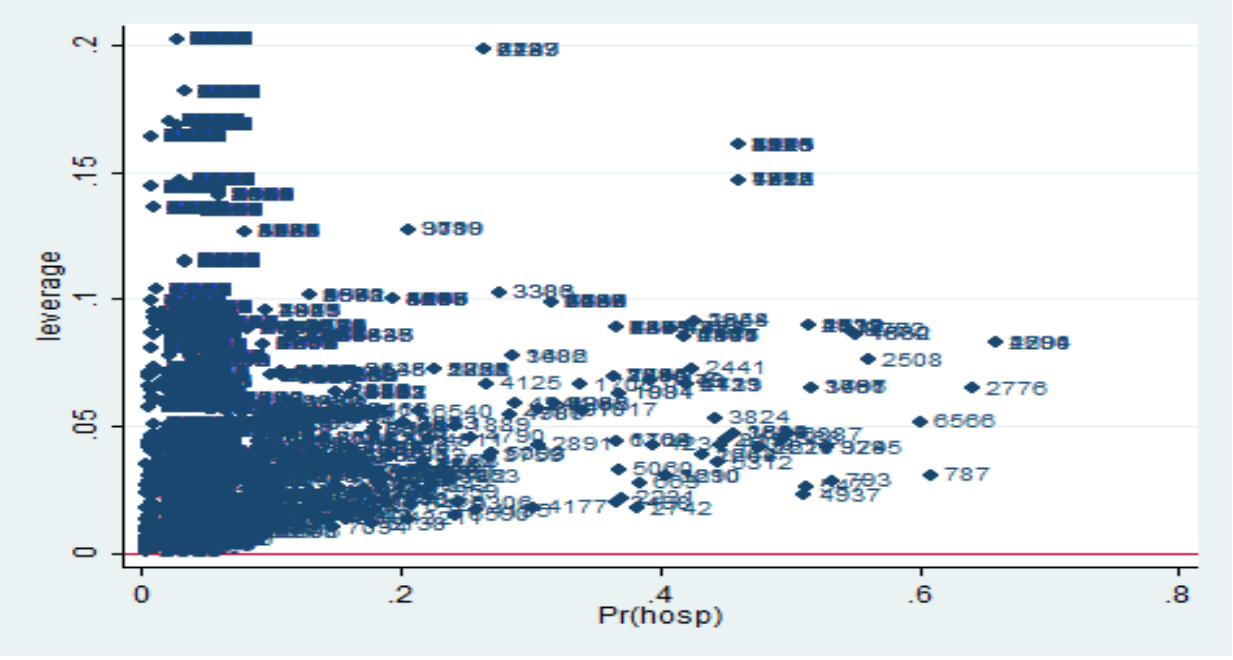


Figure 21- Figure 4.17. Difference of chi square (dx2) for COVID-19 ICU admission among the study cohort, March 2020 – December 2022

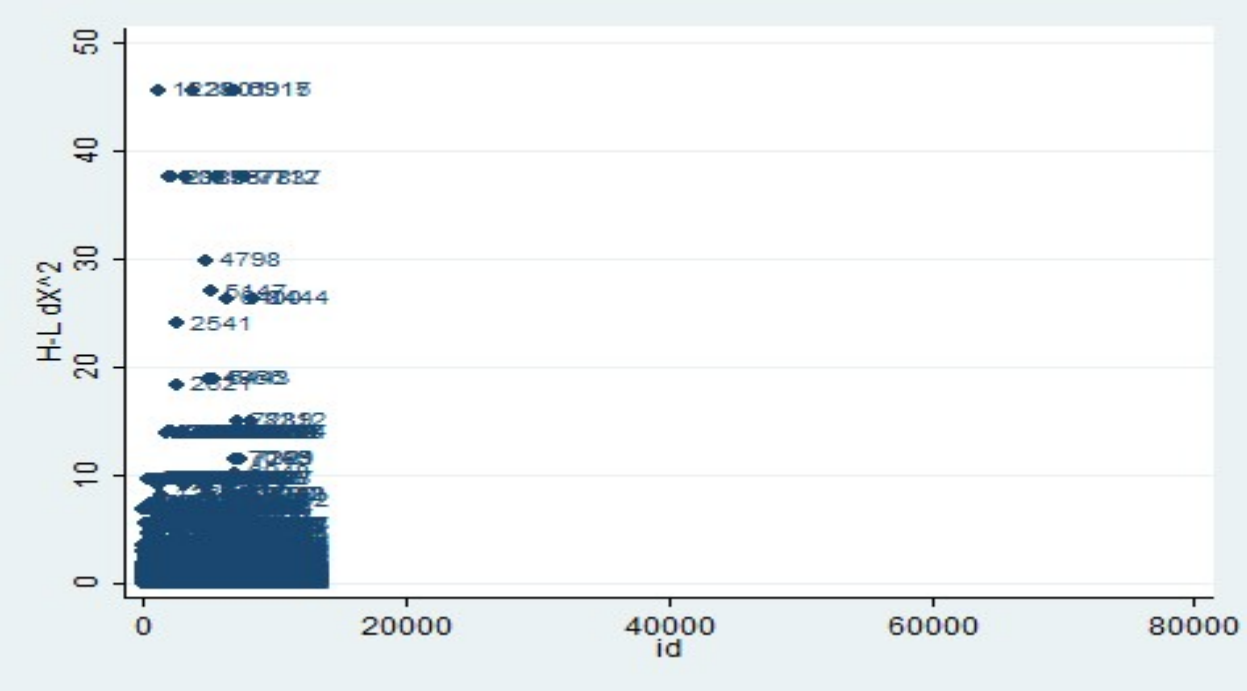
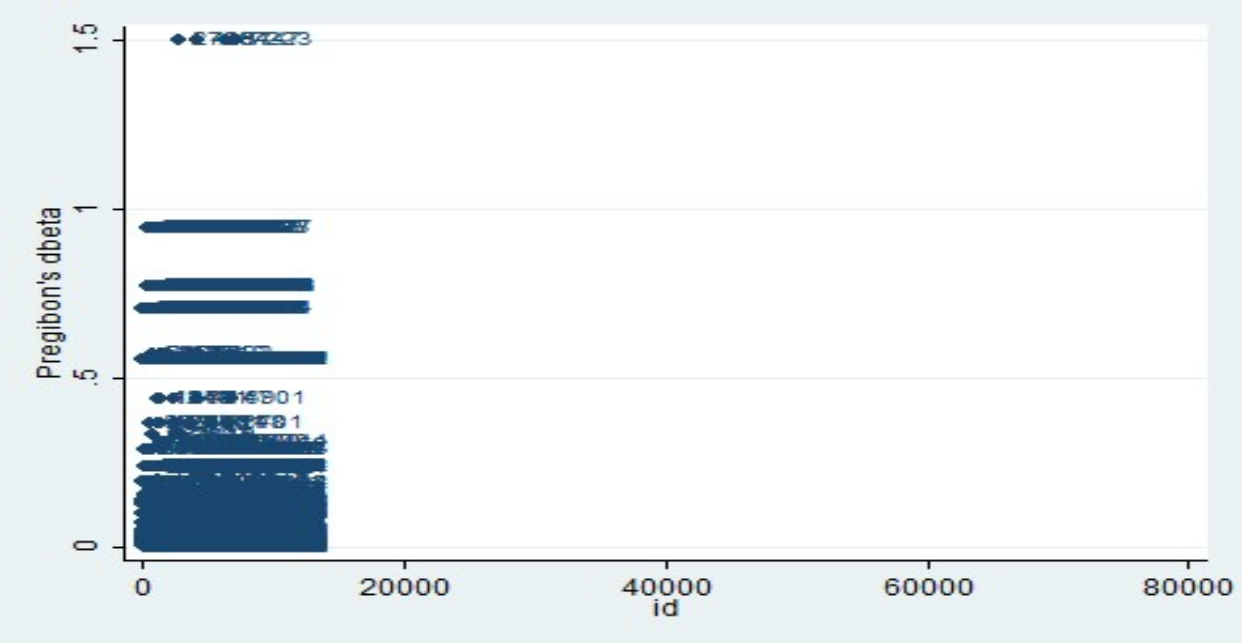



Figure 4.22. Influence (Pregibon's dbeta) for COVID-19 ICU admission among Northern Saskatchewan First Nations on-reserve, March 2020 – December 2022



### 4.3.9. Relationship between demographic factors, vaccination, symptoms, comorbidities and COVID-19 outcome

In the multivariable model, the odds of dying from COVID-19 were significantly 23 times higher among infected elderly patients aged 65+ years old than in those below 65 years old (OR=23.35, 95%CI=11.32 – 48.20; p<0.01). Male patients were about twice more likely to have a fatal outcome from the infection than female patients (OR=1.84, 95%CI=0.96 – 3.50; p=0.07), although this finding was statistically not significant (Table 4.28).

The odds of dying from COVID-19 were higher among symptomatic patients than those who were asymptomatic (OR=2.11, 95%CI=0.98 – 4.57; p=0.76). This finding was statistically not significant with p-value>0.05. Among patients who had medical comorbidities, the odds of having COVID-19-related fatalities were significantly 12 times for patients with diabetes mellitus (OR=12.22, 95%CI=1.48 – 101.09; p=0.02), 35 times higher for patients with pre-existing cardiovascular disease (OR=35.07, 95%CI=4.27 – 287.82; p<0.01), about 30 times higher for patients with liver and kidney disease (OR=29.55, 95%CI=1.62 – 539.10; p=0.02), and about 13 times higher for patients with other comorbidities (OR=12.97, 95%CI=1.12 – 150.71; p=0.04) compared to those with substance use issues (such as smoking and alcohol consumption) at the time of infection (Table 4.28).

Receiving two or more doses of COVID-19 vaccine was found to be protective against COVID-19-related death as the odds of dying were significantly lower among those who had received two or more doses of COVID-19 vaccine (OR=0.12, 95%CI=0.05 – 0.28; p<0.01) compared to those who had received no COVID-19 vaccine at the time of infection diagnosis (Table 4.28).

Table 4.28. Multivariable logistic regression, demographic factors, vaccination, symptoms, comorbidities, and death among the study cohort, March 2020 – December 2022

| Variable | Odds Ratio | SE | 95%CI | p-value |
|---|---|---|---|---|
| **Age groups (years)** | | | | |
| <65 | Ref | | | |
| 65+ | 23.35 | 8.63 | 11.32 – 48.20 | **<0.01*** |
| **Sex** | | | | |
| Female | Ref | | | |
| Male | 1.84 | 0.60 | 0.96 – 3.50 | 0.07 |
| **Zone** | | | | |
| Far North Central | Ref | | | |
| Far Northeast | 0.37 | 0.21 | 0.12 – 1.10 | 0.07 |
| Far Northwest | 0.33 | 0.20 | 0.10 – 1.05 | 0.06 |
| North Central | 0.86 | 0.59 | 0.23 – 3.29 | 0.83 |
| Northeast | 1.09 | 0.67 | 0.32 – 3.65 | 0.89 |
| **Doses of vaccine received** | | | | |
| Unvaccinated | Ref | | | |
| One dose | 1.19 | 0.66 | 0.40 – 3.51 | 0.76 |
| Two or more doses | 0.12 | 0.05 | 0.05 – 0.28 | **<0.01*** |
| **Presence of symptoms** | | | | |
| Asymptomatic | Ref | | | |
| Symptomatic | 2.11 | 0.83 | 0.98 – 4.57 | 0.06 |
| Unknown | 2.72 | 1.53 | 0.91 – 9.17 | 0.07 |
| **Presence of co-existing medical condition** | | | | |
| Substance use | Ref | | | |
| DM | 12.22 | 13.17 | 1.48 – 101.09 | **0.02*** |
| CVD | 35.07 | 37.66 | 4.27 – 287.82 | **<0.01*** |
| Liver & Kidney disease | 29.55 | 43.78 | 1.62 – 539.10 | **0.02*** |
| Lung disease | 5.29 | 7.83 | 0.29 – 96.02 | 0.26 |
| Other | 12.97 | 16.23 | 1.12 – 150.71 | **0.04*** |
| Undocumented comorbidities | 2.27 | 2.36 | 0.30 – 17.44 | **0.43** |

*Ref = Reference category*
***** *Statistical test of Significance*

Log likelihood = -190.77 LR $chi^2$ = 261.45 Prob > $chi^2$ < 0.01
Number of observations = 8428 Pseudo $R^2$ = 0.41

4.3.10. Model specification and regression diagnostics for COVID-19 deaths

*4.3.10.1. Model Specification and goodness-of-fit for COVID-19 deaths*

Model specification was assessed using linktest to identify possible specification errors. Findings revealed the p-value for the linktest to be 0.32 (not statistically significant), and this indicates the absence of visible model specification errors (Table 4.29).

The Hosmer-Lemeshow goodness-of-fit test was used to determine the model's goodness of fit with the table collapsed on quantiles of estimated probabilities. According to the finding, the Hosmer-Lemeshow's statistic measured by Pearson chi-square gave a p-value <0.04 (Table 4.30).

Table 4.29. Table 4.29. Model Specification for multivariable logistic regression, predictors of COVID-19 outcome among the study cohort, March 2020 – December 2022

| **Hospitalization** | **Coefficient** | **Standard error** | **95%CI** | **p-value** |
|---|---|---|---|---|
| _hat | 0.74 | 0.21 | 0.32 – 1.16 | 0.01 |
| _hatsq | -0.04 | 0.32 | -0.10 – 0.22 | 0.20 |

Log likelihood = -198.92
LR $chi^2$=263.13; Prob>F<0.01
Number of observations=8,428; Pseudo $R^2$=0.41

Table 4.30. Hosmer-Lemeshow goodness-of-fit test for multivariable model on predictors of COVID-19 deaths the study cohort, March 2020 – December 2022

| **Group** | **Prob** | **Obs_1** | **Exp_1** | **Obs_0** | **Exp_0** | **Total** |
|---|---|---|---|---|---|---|
| 1 | <0.01 | 0 | 0.1 | 936 | 935.9 | 936 |
| 2 | <0.01 | 1 | 0.1 | 785 | 785.9 | 786 |
| 3 | <0.01 | 1 | 0.3 | 810 | 810.7 | 811 |
| 4 | <0.01 | 0 | 0.8 | 1162 | 1161.2 | 1162 |
| 5 | <0.01 | 0 | 0.6 | 581 | 580.4 | 581 |
| 6 | <0.01 | 2 | 1.1 | 781 | 781.9 | 783 |
| 7 | <0.01 | 1 | 1.5 | 856 | 855.5 | 857 |
| 8 | <0.01 | 0 | 2.5 | 890 | 887.5 | 890 |
| 9 | <0.01 | 0 | 3.2 | 786 | 782.8 | 786 |
| 10 | 0.76 | 48 | 42.8 | 788 | 793.2 | 836 |

Number of observations =8,428; number of groups=10
Hosmer-Lemeshow chi2=16.10; Prob>chi2=0.04

*4.3.10.2. Regression diagnostics for COVID-19 deaths*

Figure 23- Deviance residual for COVID-19 deaths among the study cohort, March 2020 – December 2022

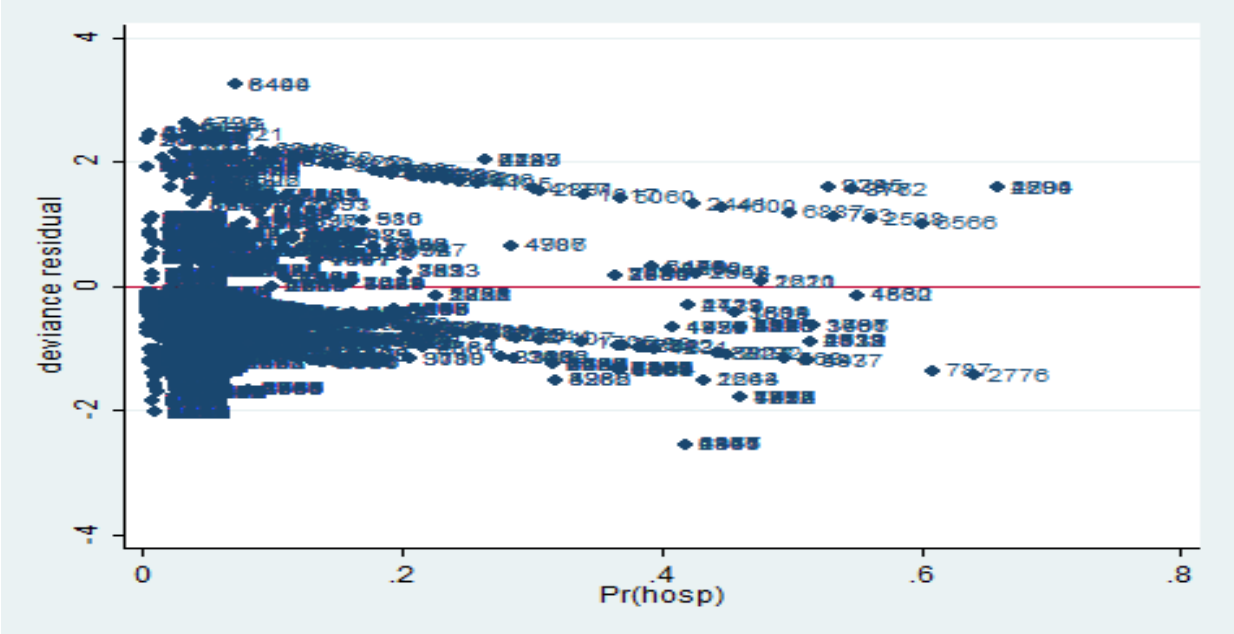



Figure 24- Pearson residual for COVID-19 deaths among the study cohort, March 2020 – December 2022

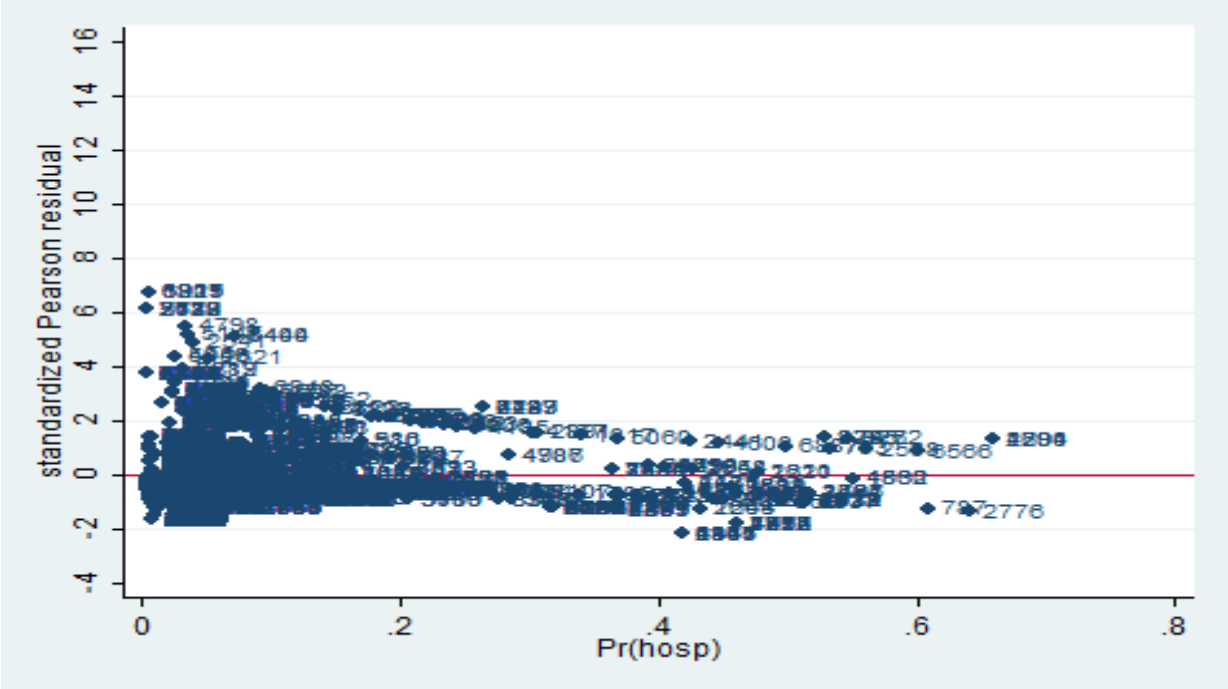


Figure 25- Leverage (_hat diagonal) for COVID-19 deaths among the study cohort, March 2020 – December 2022

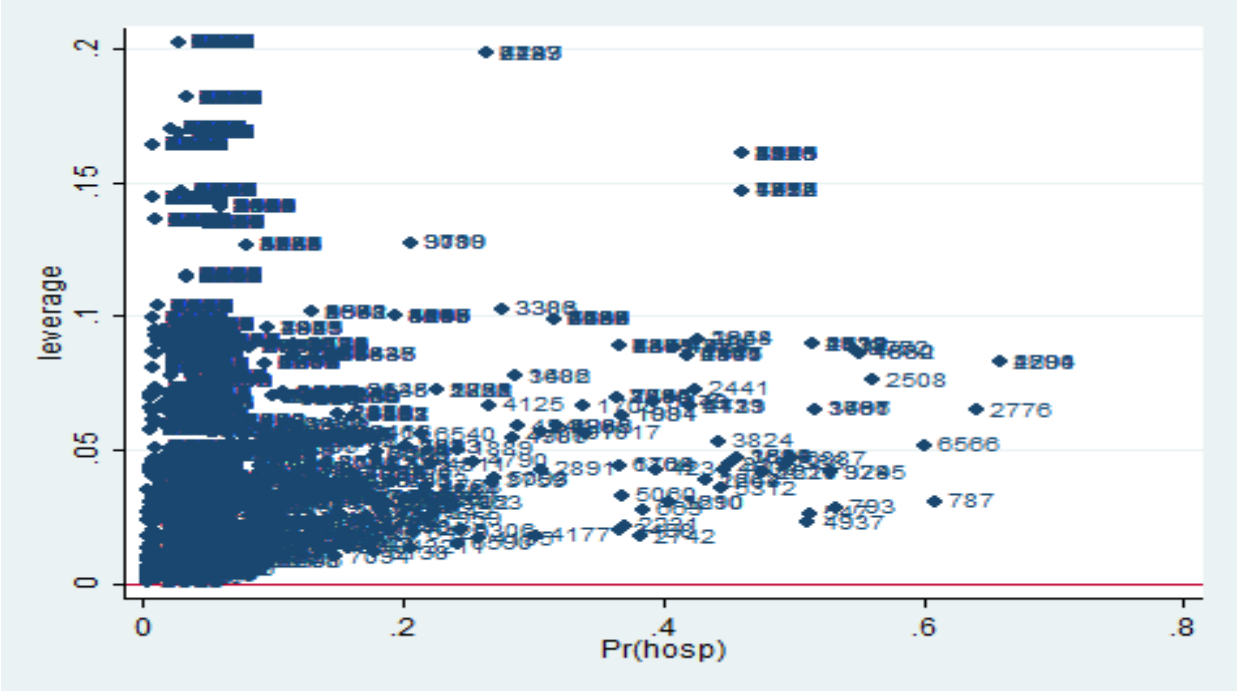



Figure 26- Difference of chi square (dx2) for COVID-19 among the study cohort, March 2020 – December 2022

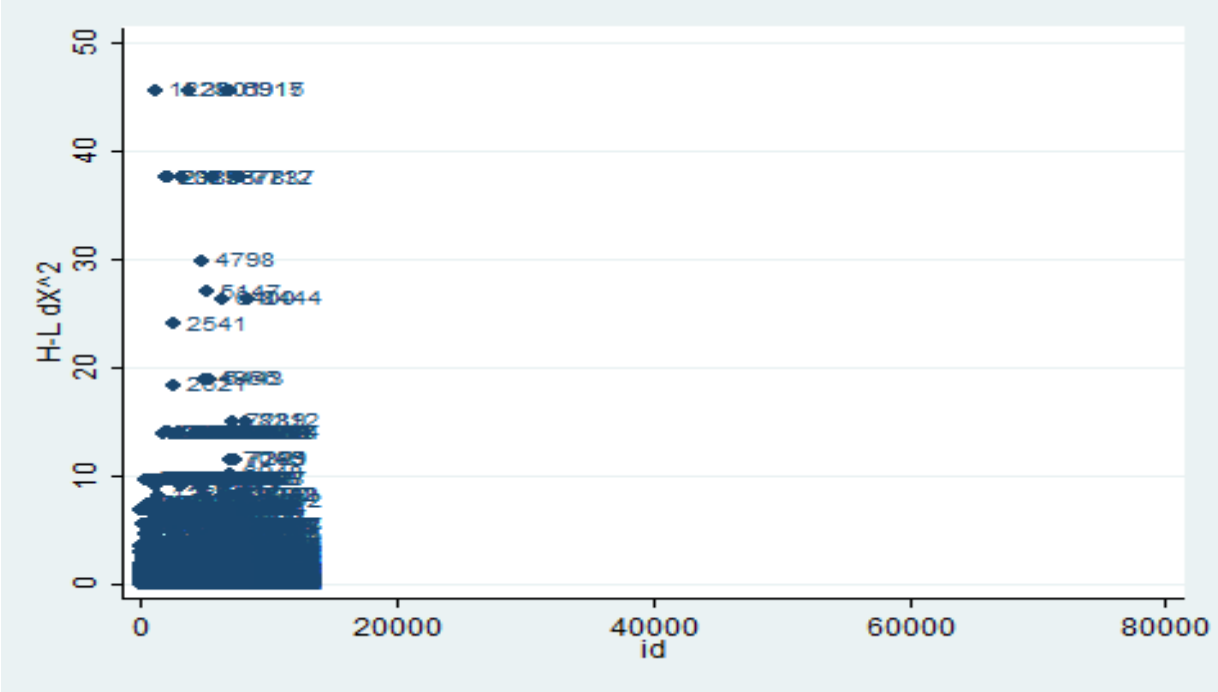
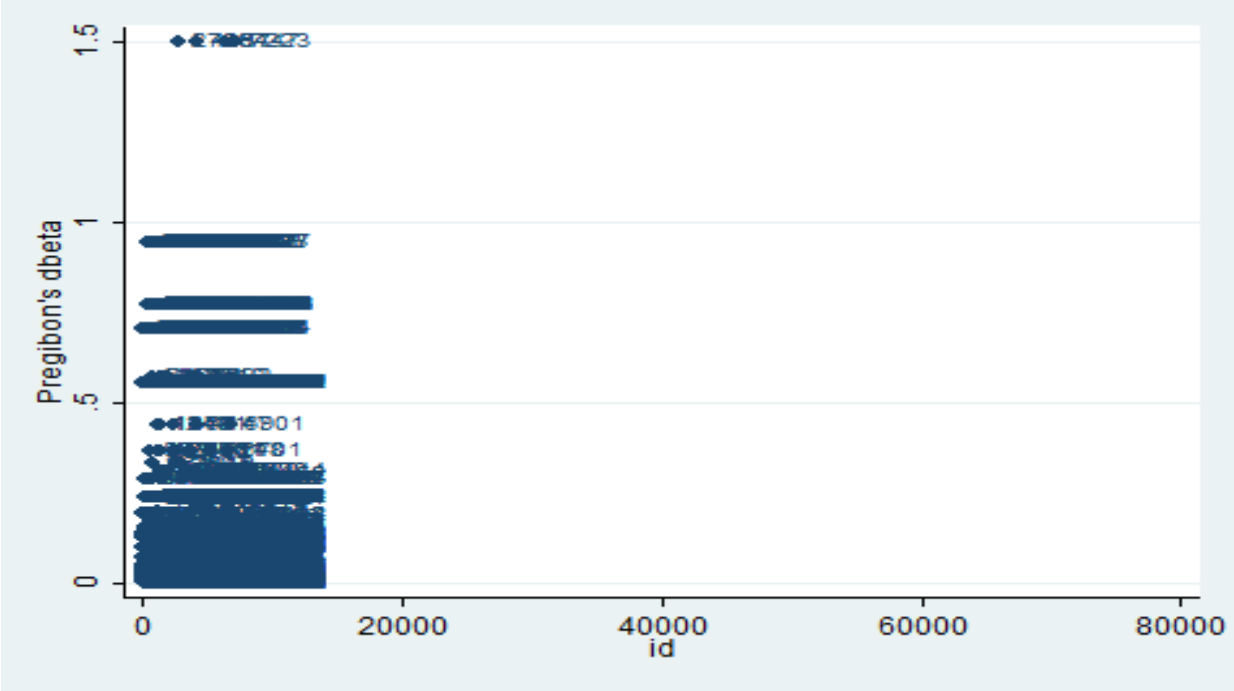


Figure 27- Influence (Pregibon's dbeta) for COVID-19 deaths among the study cohort, March 2020 – December 2022



## Chapter 5. Discussion, Conclusions, and Recommendations

This chapter summarizes the findings based on the research questions and presents the discussions which compare this study's findings with others. Finally, the chapter highlights the strengths and limitations of this study.

### *Research Question 1: What are the demographic, clinical, and vaccination-related characteristics of these individuals, both (a) overall and (b) among those with severe (i.e., hospitalized) COVID?*

A majority (93.5%) of the COVID-19 cases in northern Saskatchewan First Nations on-reserve were among those younger than 65 years, while 6.5% of the cases were among those 65 years and older. However, for severe COVID-19 cases, 59.6% were below 65 years and 40.4% were 65 years and older. About 51% each for the overall and severe COVID-19 cases respectively were among males while about 49% were female (Tables 4.2 and 4.6). The pattern of occurrence in all the cases and severe cases was similar for zone of residence: the highest number of cases were reported in the FNE (45.8% for all cases and 35.0% for severe cases) as shown in Tables 3 and 7. While 53.4% of all the cases in the study cohort were unvaccinated, 56.1% of severe cases did not have previous COVID-19 vaccination history prior to infection. Among the vaccinated individuals, 40.6% of those infected with SARS-CoV-2 had two or more doses of COVID-19 vaccine while among those with severe infection, receiving two or more doses prior to infection was reported among 39.0% (Table 4 and 8). While cough was identified as the main symptom that occurred in 17.8% of all the cases, breathing difficulty was the major symptom reported by about 58% of the severe COVID-19 cases (Figures 5 and 8). Similar finding was obtained for presence of comorbidities which was reported by 20.3% and 48.0% of all and severe COVID-19 cases respectively. Substance use issues were more common (occurred in 13.2%) in all the COVID-19 cases. On the contrary, DM was the most common co-existing medical condition reported by severe COVID-19 cases and occurred in 21.1% of individuals with severe COVID (Tables 5 and 9).

### *Research Question 2: What factors are associated with severe COVID-19 among Northern Saskatchewan First Nations on-reserve?*

There was a significant association between demographic factors (age, and zone of residence) with hospitalization rate among COVID-19 patients in northern Saskatchewan First Nations on-reserve

communities. However, sex was found not to be a significant determinant of hospitalization in the multivariable model in the study cohort (Table 4.22). Similarly, vaccination status at the time of infection, presence of symptoms, and presence of comorbidities were significant determinants of COVID-19 hospitalization among COVID-19 cases from March 2020–December 2022. Although these demographic factors, vaccination, presence of symptoms, and presence and type of comorbidities were significant determinants of hospitalization, they were not significantly associated with ICU admissions within the study cohort except for number of doses received prior to onset of infection (Table 4.22 and Table 4.25).

The study findings showed significant relationships between age, vaccination status indicated by the number of vaccine doses received prior to infection onset, the presence of comorbidities, and the risk of COVID-19 deaths among northern Saskatchewan First Nations on-reserve communities between March 2020 and December 2022. The significant predictors of fatality were age (65+ years compared to being younger than 65 years). Also, being vaccinated with two or more doses of COVID-19 vaccine and having co-existing medical conditions showed significant relationship with COVID-19 mortality. Furthermore, receiving two doses of COVID-19 vaccine was significantly protective against COVID-19 deaths compared to not being vaccinated (Table 4.28).

## 5.1 Interpretation of Results

### 5.1.1. Pattern of all COVID-19 among northern Saskatchewan First Nations on-reserve communities

The pattern of all COVID-19 cases across Northern Saskatchewan First Nations on-reserve communities was similar to that reported across Canada. The second wave of the pandemic, which started in September 2020, had a high number of cases and was at the time of school opening across the country (152). The third wave of the pandemic in the Northern Saskatchewan First Nations on-reserve did not align with the country-wide pattern. Bignami et al. attributed the difference in the pattern experienced during this wave to different schedules for vaccine rollout across the country following province-specific implementation strategic guidelines, the timing and pace of interventions which impacted the rate COVID-19 spread in the provinces (152). The distribution of COVID-19 cases across the waves was also influenced by the testing policy which promoted mandatory laboratory testing during the first and second waves. Policy reviews resulted in higher attention given to self-testing/screening during the waves that occurred later in the

pandemic (waves 4, 5, and subsequent wave when surveillance activities were relaxed). A higher proportion of infection was recorded among individuals younger than 65 years old compared to those who were 65 years and older. This finding corroborated the report by Bushnik et al. which finds higher seropositive cases among younger population in a study across Canada from November 2020–April 2021 (179). The age distribution of infected individuals could be attributed to the lifestyle of the younger population (219) who have been reported to be more engaged in risky behaviour, increasing their chance of exposure to the disease. The occurrence of most cases in the FNE and FNW zones could be attributed to high population in these zones. Therefore, the chances of having high number of cases may increase in a way similar to urban areas with high population density as identified by studies in Iran (200,201).

The Delta variant accounted for 11.5% of the cases reported among the study cohort. This variant was reported to be prevalent during ease of movement restrictions, and this enhanced transmission. Based on the research findings, the highest number of cases were associated with Waves 2 and 4. The high number of cases in Wave 2 (37.9%) corresponded with the period that preceded introduction of vaccines, with increased testing, and active community transmission. The rise in the number of cases in Wave 4 (33.1%) could be attributed to the easing of restrictions which allowed transmission to fester (152,161).

About 53% (4,503) of the cases were among unvaccinated persons as compared to 46.6% of vaccinated persons. Overall, 40.6% of infection occurred among individuals who had received two or more doses of COVID-19 vaccine at the time of infection, and about 38.7% had received the vaccine within 1–6 months prior to the time of infection. The reasons that could explain higher rate of infection among those with two or more doses of vaccine could be due to non-cross immunity of the vaccine candidates available for COVID-19. For this reason, persons vaccinated with one antigen may not have been conferred immunity against another antigen. Also, majority of the persons had their infection within the first six months after the last dose. One possibility could be that the infections could have happened prior to seroconversion of the vaccine. Alternatively, the vaccinated persons could have garnered confidence post-vaccination and possibly abandoned the use protective/safety instructions leading to exposure and subsequent infections.

COVID-19 symptoms were manifested by 36.1% of the cases among northern Saskatchewan First Nations on-reserve communities (Figure 7). Studies in Bangladesh showed similar trend in the occurrence of symptoms with about 50% of the cases reporting a variety of symptoms among non-Indigenous populations (177). Similarly, a prospective cohort study in Ethiopia observed a similar pattern of clinical manifestation with cough and headache being prominent clinical symptoms observed at presentation (184).

About 80% of reported SARS-CoV-2 infections were among individuals who had no comorbidities. Consequently, over 65% of the cases were among those with substance use issues that included alcohol use and smoking, among others. Smoking and alcohol consumption have been reported to significantly increase the risk of respiratory diseases and metabolic disorders (such as obesity, diabetes mellitus and cardiovascular diseases) respectively which further increase the risk of severe COVID-19 infection (225,226). Understanding that COVID-19 hugely affected individuals with comorbidities (177) means that persons with co-existing medical conditions may tend to be more careful in obeying the public health measures when compared to those without comorbidities who felt that they were more resilient to COVID-19, and may experience COVID-19 fatigue earlier with resultant disregard for public health regulations.

### 5.1.2 COVID-19 hospitalization and death

In the multivariable regression model (Table 4.22), the odds of hospitalization were significantly higher among patients 65 years or older (elderly patients) compared to patients who were younger than 65 years old. Similarly, the odds of dying were higher among patients who were 65 years and older (Table 4.28). This finding was similar to that of Liu et al. who reported that patients older than 60 years had more severe disease with longer course with respiratory complications, and increased chance of dying compared to those who were younger than 60 years old (227). In Canada, similar reports about the impact of age on severe COVID-19 have been reported among the general population. An Ontario study indicated that the highest rates of COVID-19 hospitalization were seen in individuals older than 60 years (108). Papst et al. in 2021, in another study that involved over 270,000 COVID-19 patients across Ontario, reported similar findings that COVID-19 hospitalization was higher among older patients from age 60-90 years (178). Elsewhere in the United States, after controlling for other covariates, and age was noted to be a significant factor for poor prognosis in COVID-19 infection (228). Another US study reported similar finding

with the highest proportion of hospitalized COVID-19 cases being older than 65 years (175). In Spain, hospitalization/death rate was a significant risk factor for severe COVID-19 as the hospitalization rate was about 20% in individuals older than 69 years and compared to those who were 69 years and below (174). The occurrence of severe COVID-19 in elderly individuals has been attributed to changes in the immune system that affect immune response to comorbidities that further alter the course of SARS-CoV-2 infection among affected individuals (173) resulting to more severe infection that may require hospitalization with increased likelihood of death among the elderly patients.

The odds of hospitalization were 1.2 times higher among males than females (Table 4.22). Males also were about 2 times more likely to die from COVID-19 compared to females. These findings were, however, not statistically significant. The findings were also contrary to those of other researchers who documented that more males than females were impacted by severe COVID-19, and had higher death rate across different countries including Canada (108,174,180–185). A cross-Canada study that extracted data from the national database observed, similarly, higher risk of hospitalization in males than in females (108). Lavoie and colleagues in a population-based online survey reported that males were more likely to not adhere to the use of preventive measure, and this put them at higher risk of COVID-19 infection than the females (229). On the contrary, in describing the epidemiology of COVID-19 in the spring of 2020 in Quebec, Jantzen et al. reported that males were less likely to test positive to COVID-19 compared to females (107). The increased COVID-19 infectivity, severity and mortality associated with COVID-19 in males as compared to females can be attributed to biological, psychological and behavioural factors (180). Biologically, immune responses, enzymatic reactions and genetic factors have been reported to increase the infectivity and severity of COVID-19 in males compared to females. Females, generally, are known to have stronger innate immunity as a result of immunogenic factors in relation to the genes that are contained in the X-chromosomes making them better protected against bacterial, fungal, viral and parasitic infections (230,231) than the males. Also, the SARS-CoV-2 is reported to have high affinity for angiotensin-converting enzyme II (ACE-2) which is reported to be higher in males than in females, thereby increasing males' susceptibility to severe COVID-19 (180,230). Additionally, men are reported to be predisposed to psychological and behavioural patterns that further expose them to COVID-19 with severe outcomes. Baker et al. reported that men were more likely to trivialize the impact of COVID-19, and are involved more in risky habits such as drinking

and smoking which predispose them to comorbidities that could worsen the course and outcome of COVID-19 (232). In addition to feeling that they were more resilient than women, more men could be driven by a sense of over-confidence which reduces their adherence to preventative public health measures in times of emergency compare to women thereby becoming more predisposed to the infection risk than females (180,232).

The risk of COVID-19 hospitalization was lower in NITHA communities across all other zones than communities in the FNC zone. These findings were significant for Far Northeast and Far Northwest zones which also had the least odds of hospitalization compared to FNC zone. This finding could be attributed to the interventions and other health care support that may be available in the communities within the FNE and FNW zones with higher population, higher number of cases, and in proximity to urban centers. These interventions could be critical in preventing severe infection that could require hospitalization in relation to more rural communities. The population in the FNC zone may be further rural and geographically isolated. This makes them more difficult to access when compared to the communities in the FNE and FNW zone which has more urban settlements, with relatively easier accessibility. Studies in the US and Bangladesh among non-Indigenous populations observed that rural communities with inadequate preventative interventions such as vaccination services and other health disparities may have higher risk of COVID-19 that require hospitalization (193–199,215); finding that is similar to the findings from our study. The odds of COVID-19 hospitalization were significantly less in individuals who had received at least two doses of COVID-19 vaccine compared to those who were unvaccinated at the time of infection. Similarly, the odds of death were significantly lower in individuals who received two or more doses of COVID-19 vaccine than unvaccinated patients. The finding in this study is similar to the finding of a population-based case-control study in Quebec, Canada which reported that receiving two or more doses of COVID-19 vaccine conferred about 90% protection against COVID-19 Omicron BA variants (233). According to the findings from two Ontario studies, receiving two doses of COVID-19 vaccine was reported to be highly protective against COVID-19 (134,234). These findings also conform with result obtained by Havers and colleagues in the US where hospitalization was about 2.5 times higher in single-dosed vaccinated patients without an additional dose compared to those who had more than one dose of the vaccine (58). Also, in the US, Tenforde et al. reported that vaccines were about 87% effective in preventing severe

COVID-19 (211). Furthermore, there was a disproportionately higher number of individuals who had received two or more doses of the vaccine, and this may have significantly impacted the result.

Findings from this study observed that comorbidities were significantly associated with hospitalization and death (Table 4.22 and Table 4.28). The odds of hospitalization were significantly over 7 times for diabetic patients, about 8 times for patients who and CVD, 22 times for patients with liver and kidney diseases, >6 times for patients with lung diseases respectively more when compared to those with co-existing substance use issues (such as smoking and alcoholism) as shown in Tables 4.22 and 28 respectively. These findings from this study agrees with those of a population-based cohort in Ontario showed that diabetes, CVD, kidney disease, and cancers were significant predictors of severe COVID-19 infection (208). A study in Bangladesh also found out that DM, CVD, and chronic kidney disease were significant risk factors of COVID-19 severity and hospitalization (202). Similar findings were obtained by Al Saleh and colleagues in Kuwait where diabetes mellitus, CVD, and lung disease linked with shortness of breath were significant risk factors for in-hospital COVID-19 mortality (204). In the US, obesity, DM, and hypertension were the co-existing medical conditions that presented the greatest need for severe COVID-19 infection that required mechanical ventilation and increased risk of death among hospitalized COVID-19 patients (181). Generally, patients with comorbidities are known to experience waning immune response that could impact the ability of their bodies to effectively respond to infectious agents (180) resulting in more severe disease conditions and increased chance of fatality.

### 5.1.3 ICU admission

The findings in this study showed no statistically significant association between demographic factors, comorbidities, vaccination, and ICU admission. In the multivariable model, the odds of ICU admission were >2 times higher among patients in the NC zone than those in the FNC zone (Table 4.25). Also, males, were more likely to be admitted in ICU compared to females. Admission into the ICU was higher among patients with co-existing diabetes mellitus, CVD, and liver and kidney diseases compared to those with substance use disorders (Table 4.25). The elderly patients (65+ years) had lower odds of ICU admission compared to the younger group (<65 years old). However, those who had been vaccinated prior to being infected with SARS-CoV-2 were less likely to be in ICU compared to unvaccinated patients (Table 4.25). These findings correspond to

those of other studies that demonstrate the role of vaccination in reducing the occurrence and severity of COVID-19 infection (58,133,134,211,233,234).

Other research findings have reported on the factors associated with ICU admission in COVID-19 among non-Indigenous populations. A study on ICU admission in Ontario during the first wave of the pandemic observed that ICU admission was significantly higher in patients older than 50 years, which differs from the findings in our study (30). Murthy et al. reported in a national cohort study that comorbidities such as diabetes, hypertension and cardiac, kidney, and respiratory disease were common among COVID-19 patients who required hospitalization (28). Results obtained from patients in Germany showed that COVID-19 ICU admission was significantly higher among younger age group compared to the elderly, similar to the findings in our study, although our finding was not statistically significant. Individuals with comorbidities were reported to have significantly higher ICU admission rates compared to those without comorbidities (235). Contrary to our finding, a study in Turkey observed that beside other factors, higher ICU admission was significantly associated with older individuals compared to younger people (236). Studies in China and Sweden revealed that comorbidities such as CVD, kidney diseases, and diabetes were significant risk factors of increased COVID-19 ICU admission (237,238). A study in the US found out that more individuals with at least one comorbid condition had higher odds of ICU admission (239), similar to the findings in this study.

Admission into ICU could be influenced by several factors. The factors that could determine hospitalization and possibly ICU admission include but not limited to the presence of comorbidities, and waning immunity which could increase with age (178,227,228). Males have been reported to be more vulnerable to co-existing medical conditions that may exacerbate the course of COVID-19 (239), and result to hospitalization with a possible need for ICU admission. The NC zone could have higher capacity to take more COVID-19 patients in the ICU since the zone is more urbanized and may have more medical resources. Also, being more urbanized means that the population, and psychosocial behavioural factors that predispose individuals to severe COVID-19 which could result in increased number of cases that may require the use of the ICU management. However, most of these findings were not statistically significant association between the risk factors in this study and ICU admission.

## 5.2 Conclusion and Recommendations

- Being 65 years and older, presenting with symptoms, and presenting of medical comorbidities were significant determinants of COVID-19 hospitalization among northern Saskatchewan First Nations on-reserve. However, vaccination, especially with at least two doses of COVID-19 vaccine, was found to be significantly protective against COVID-19 hospitalization and ICU admission. Therefore, the provincial government, in collaboration with northern Saskatchewan First Nations jurisdiction should develop appropriate preventative measures to protect the vulnerable Indigenous populations and other minority groups from the impact of the pandemic. This could include intensifying vaccination in the communities among the vulnerable groups. Subsequently, Indigenous elderly population including those with comorbidities, and those at risk of developing severe clinical disease with complications should be prioritized with interventions that would protect them against impact of COVID-19, and other public health emergencies to reduce the burden that their infection would add to the health care system.
- COVID-19 deaths were significantly higher among the elderly (65+ years), those who had one dose of COVID-19 vaccine, patients with symptoms, and those who presented medical comorbidities. The provincial government and other relevant health authorities should put in place adequate measures to protect these group of people against the COVID-19 pandemic, and in future public health emergencies to prevent casualties. Measures should be instituted to improve healthy living among males to address the psychosocial attributes that increase their vulnerability to disease outbreaks. However, receiving two or more doses of COVID-19 vaccine was found to be protective with over 88% risk reduction. Vaccination should be intensified, and partially vaccinated individuals among northern Saskatchewan First Nations on-reserve should be encouraged to received additional doses to maintain level of immunity against COVID-19. Additional studies should be conducted to further understand the role of vaccination in preventing communicable diseases and the results should be used to improve planning.

## 5.3. Strengths and Limitations

### 5.3.1. Strengths of the study

This study utilized the administrative data that contain information elicited at the point of care. Therefore, the bias associated with primary data collection were, largely, eliminated in this study. The data was collected and entered by highly trained and skilled staff of NITHA which reduces events of data quality issues.

The study adopted a large sample size which gave room for more representative inference to further understand the determinants of COVID-19 in the northern Saskatchewan First Nations on-reserve communities. Since all the COVID-19 cases within period were included in the study, findings generated from this study would be more confidently applied to the population within these communities.

### 5.3.2. Study limitations

Despite the large sample size and skills of the staff in data capturing, few data quality issues were identified, and addressed during data cleaning. For instance, almost all the cases in this data had only one comorbidity recorded at presentation. Understanding that in the general population, some individuals could have more than one co-existing medical conditions, it is possible that some comorbidities could be missing from the available dataset which will affect the inference made on the role of comorbidities as determinants of COVID-19 hospitalization and outcome.

Demographic information collected was limited to age, sex, and zone of residence. Other important demographic information such as education, and occupation which could be valuable determinants of the disease course and outcome were not captured in this study. The data obtained for this study was limited to cases reported in the Northern Saskatchewan First Nations under the jurisdiction of NITHA. Therefore, findings from the study might only be interpreted in the context of NITHA's operating guidelines when applying the results to communities outside of NITHA's coverage area.

The number of cases in this study could be underreported since the linelist captured only confirmed individuals who presented for confirmatory diagnosis of infection. This implies that asymptomatic cases who missed out on testing or those who tested privately without reporting to treatment centres were not captures in the linelist and therefore omitted from the study resulting to sampling bias. However, severe outcomes (hospitalization and death) are less likely to be underreported as

individual who were severely affected presented at the treatment centre/hospital, and all deaths were investigated with cause of death ascertained and documented.

Confirmatory PCR testing, and vaccine availability and rollout procedures were not universally available throughout the pandemic. Based on the policy for diagnosis of COVID-19, more testing was widely available during Delta wave, but testing was restricted during Omicron wave in order not to overwhelm laboratory capacity. Similarly, vaccines were not available during the initial waves of the pandemic. As a result, more cases were reported during the first three waves that was associated with the Delta variant than the other waves of the pandemic.

Multi-level modeling was not conducted in this study to account for potential clustering by geographic area. There might be differences in the factors associated with severity if homogeneity is accounted for within geographical clusters.

Also, information bias due to under-reporting and incomplete reporting by patients or challenges with documentation by the health officials due to high volume of cases, self-reporting influenced by social norms, guilt and legal standpoint may be responsible for some missing data on some variables that would be useful in further understanding the COVID-19 situation among this population.

Despite the few limitations that exist with this data, findings from the study identified significant determinants of COVID-19 hospitalization and outcomes (recovery or death). The findings from this study present valuable addition to the existing knowledge on severe COVID-19 among Indigenous population in Saskatchewan, Canada, and globally. These findings can be useful in planning for the post-active phase of the COVID-19 pandemic, and for future public health emergencies. Implementing the recommendations from this study would be an important step towards repositioning the health care system in NITHA communities for more efficient service delivery, especially in the events of future outbreaks as the region exits the active phase of the COVID-19 pandemic. In addition, follow-up studies on the COVID-19 situation on Indigenous communities that are not based on administrative case reporting and management data is recommended to further understand the COVID-19 situation in Northern Saskatchewan First Nations.

# Appendices

## Appendix A: Ethics Approval Certificate

UNIVERSITY OF SASKATCHEWAN

Biomedical Research Ethics Board (Bio-REB) 27-Mar-2023

**Certificate of Approval**

| | |
|---|---|
| Application ID: | 4044 |
| Principal Investigator: | Nnamdi Ndubuka Department: Northern Inter-Tribal Health Authority |
| Locations Where Research Activities are Conducted: | This research will be conducted in the province of Saskatchewan. The de-identified data (COVID-19 linelist) is available at NITHAs data repository in Prince Albert. The de-identified data will be obtained from the data management team with due authorization inspection by the relevant NITHA leaderships permission., Canada |
| Student(s): | Isaac Ieren |
| Funder(s): | |
| Sponsor: | University of Saskatchewan |
| Title: | Determinants of Covid-19 Severity and Outcome Among Northern Saskatchewan First Nations |
| Protocol Number: | |
| Approved On: | 26-Mar-2023 |
| Expiry Date: | 26-Mar-2024 |
| Approval Of: | * Bio 4044 NER_IsaacMarch20_2023 - (Response)<br>* ERB_Application_Igbaver_03282023<br>* Data collection tool_Isaac, rec'd 21-Mar-2023<br>* Master List for Data Abstraction, rec'd 22-Mar-2023 |
| Acknowledgment Of: | * McMaster Chart Review Tutorial Certificate of Completion for Igbaver Isaac Ieren<br>* TCPS 2: CORE Tutorial Certificate of Completion for Isaac Ieren-Agbadu<br>* NNdubuka - Community Health and Epi - CV - Jan 2023 |
| Review Type: | Delegated Review |
| IRB Registration Number: | Not Applicable |

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**CERTIFICATION**

The University of Saskatchewan Biomedical Research Ethics Board (Bio-REB) has reviewed the above-named project. The project was found to be acceptable on scientific and ethical grounds. The principal investigator is responsible for obtaining any other administrative or regulatory approvals that may pertain to this project, and for ensuring that the authorized project is carried out according to governing law. This approval is valid for the specified period, provided there is no change to the approved project.

**FIRST TIME REVIEW AND CONTINUING APPROVAL**

The University of Saskatchewan Research Ethics Boards review above minimal risk projects at full-board meetings. If a project is reviewed at a full board meeting, any subsequent projects being added with the same protocol may be reviewed through the delegated review process. Research classified as minimal risk is reviewed through the delegated review process. The initial Certificate of Approval indicates the approval period the REB has assigned to a study.

To remain in compliance, the REB must receive a status report form (renewal or closure) prior to the assigned expiry date each year. Any specific requirements of the sponsoring organizations deemed necessary for continuing ethics review (e.g., requirement for full-board review and approval) should be indicated by the researcher to the REB. Any change to the approved project must be reported to the Chair of the Bio-REB for consideration in advance of its implementation through the amendment process.

**REB ATTESTATION**

In respect to clinical trials, the University of Saskatchewan Bio-REB complies with the membership requirements for Research Ethics Boards defined in Part 4 of the Natural Health Products Regulations and Part C Division 5 of the Food and Drug Regulations, and carries out its functions in a manner consistent with Good Clinical Practices. The University of Saskatchewan is constituted and operates in accordance with the current version of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans - TCPS 2 (2022). If a member of the REB is named as an investigator on a project under review, the member is absent from REB deliberations and decisions regarding the project. This approval and the views of the Bio-REB have been documented in writing.

***Digitally Approved by Dr. Ildiko Badea, Ph.D.***
***Chair, Biomedical Research Ethics Board***
***University of Saskatchewan***

**Appendix B: Definition of variables shared on the dataset**

**Serial Number:** Chronological figure assigned to the cases in the database; ranges from 1–8478.

***Participant ID:*** Unique identifiers that are assigned to the cases and will be used to by the NITHA epidemiologists to trace issues on the data base in event of call-back.

***Sex:*** This is assigned Female and Male as collected by NITHA's record staff

***Zone:*** Geographical area under which the subzones and communities of residence are located as categorized by NITHA.

***Age:*** Collected as discrete numerical figures, the number of years that an individual has lived from birth to the time of infection.

***Case status:*** Outcome of COVID-19 infection and was classified as deceased/dead or recovered.

***Variant of concern (VOC) positive:*** Result of Sars-CoV-2 characterization classified as positive or negative.

***Date of vaccination (Dose 1 – 5):*** Date of vaccination against COVID-19; includes date for all the vaccine doses that have been received by the case.

***Episode date:*** Date of presentation of the case or the date that the public health authority was notified about the case.

***Occupation:*** Profession or job of the case at the time of infection. This included carpenters, health care workers, cooks, daycare workers amongst others. Data on this variable was available for just over 2% of the cases.

***Exposure setting:*** Source of infection as identified by the cases at the time of reporting. Information on this variable was available for 27.5% of the respondents. Source of exposure identified by the cases include Travel within and outside the community; Household exposure; Contact with a known case; Community transmission; Unknown; School; and Social, etc.

***Risk factors:*** Risk factors such as chronic medication condition, travel withing and outside Canada, occupation – health care worker, underlining medical condition, etc.

***Presentation of symptoms:*** This included the nature of symptoms at the time of presentation. Cases were classified as either symptomatic or asymptomatic. For cases that were symptomatic, information was collected on symptoms such as fever, cough, sore throat, shortness of breath, had ache, loss of taste, loss of smell, runny nose, arthralgia, fatigue, diarrhoea or other GI symptoms, other.

***Isolation:*** Place where the cases stayed (were isolated) in accordance with the management guideline during treatment to prevent further transmission during the infectious period: home or hospital. For patients who isolated in the hospital, date of admission, date of discharge, name of hospital, admission into ICU (yes/no) where collected.

***End of monitoring period/recovered:*** Date that the case was closed either because the patient recovered (for those treated/isolated at home) and/was discharged. For deceased cases, it is the date that the patient died.

**Appendix C: List of variables extracted from the original dataset**

Table 1. List of variables from the original line list

| Serial # | Variable Code | Variable definition |
|---|---|---|
| 1 | NITHA ID | NITHA ID |
| 2 | Sex (M,F,O,U) | serial |
| 3 | Age | Zone |
| 4 | Age Group | Subzone |
| 5 | Type | Sex |
| 6 | Case Status | Age |
| 7 | Case Active | Age Group |
| 8 | SNP Positive | Case Status |
| 9 | VOC Positive | VOC Positive |
| 10 | VOC Variant Type | VOC Variant Type |
| 11 | Lineage | Lineage of the VOC |
| 12 | Mutation | Mutational status of the VOC |
| 13 | Dose 1 administered | Date Dose 1 administered |
| 14 | Dose 2 administered | Date Dose 2 administered |
| 15 | Dose 3 administered | Date Dose 3 administered |
| 16 | Dose 1 | Dose 1 received before infection diagnosis |
| 17 | Dose 2 | Dose 2 received before infection diagnosis |
| 18 | NITHA Partner | NITHA Partner in-charge of the community |
| 19 | fRHA | |
| 20 | Zone | Zone of residence |
| 21 | Subzone | Subzone |
| 22 | Episode Date | Episode Date |
| 23 | Occupation | Occupation |
| 24 | Exposure setting (e.g. household, school, workplace, travel, mass gathering, healthcare setting). | Exposure setting (e.g. household, school, workplace, travel, mass gathering, healthcare setting). |
| 25 | FNIHB Exposure | FNIHB Exposure |
| 26 | Crowded living condition | Crowded living condition |
| 27 | Risk Factor-Chronic Medical Condition - Other | Risk Factor-Chronic Medical Condition - Other |
| 28 | Risk Factor - Contact to a known case | Risk Factor - Contact to a known case |

| | | |
|---|---|---|
| 29 | Risk Factor – Immunocompromised-Related to underlying disease or treatment | Risk Factor - Immunocompromised- Related to underlying disease or treatment |
| 30 | Risk Factor - Occupation - Health Care Worker | Risk Factor - Occupation - Health Care Worker |
| 31 | Risk Factor - Travel - Outside of community | Risk Factor - Travel - Outside of community |
| 32 | Risk Factor - Travel outside of Saskatchewan but within Canada | Risk Factor - Travel outside of Saskatchewan but within Canada |
| 33 | Risk Factor - Travel Outside of Canada | Risk Factor - Travel Outside of Canada |
| 34 | Asymptomatic | Presence of symptoms |
| 35 | Symptom onset date | Date of Symptom onset |
| 36 | Fever | Symptoms - Fever |
| 37 | Cough | Symptoms - Cough |
| 38 | Sore Throat | Symptoms - Sore Throat |
| 39 | Shortness of breath | Symptoms - Breathing difficulty |
| 40 | Headache | Symptoms - Headache |
| 41 | Loss of taste | Symptoms - Loss of taste |
| 42 | Loss of smell | Symptoms - Loss of smell |
| 43 | Runny Nose | Symptoms - Rhinitis/Rhinorrhea |
| 44 | Arthralgia | Symptoms - Body pain (arthralgia, myalgia) |
| 45 | GI symptoms | Symptoms - GI symptoms (vomiting, nausea) |
| 46 | Diarrhea | Symptoms - Diarrhea |
| 47 | Fatigue | Symptoms - Fatigue |
| 48 | Other details | Symptoms - Nasal congestion |
| 49 | Isolation | Place isolation |
| 50 | Start date of isolation period | Start date of isolation period |
| 51 | Hospitalization | Hospitalization |
| 52 | Hospital | Name of Hospital |
| 53 | ICU | ICU admission |
| 54 | Admission date | Admission date |
| 55 | Discharge date | Discharge date |
| 56 | nCoV testing date | Days on admission |
| 57 | nCoV result (RRPL) | nCoV testing date |
| 58 | Confirmatory nCoV result (NML) reported | Confirmatory nCoV result (NML) reported |

| | | |
|---|---|---|
| 59 | End of monitoring period/Recovered | End of monitoring period/Recovered |
| 60 | Date deceased | Date deceased |
| 61 | Notes | Notes |

**Appendix D. Univariable logistics regression between Demographic factors, vaccination, symptoms, comorbidities, and COVID-19 hospitalization, ICU admission and death**

Table 1. Univariable logistics regression between Demographic factors, vaccination, symptoms, comorbidities, and COVID-19 hospitalization among the study cohort, March 2020–December 2022

| Variable | Odds Ratio | 95% CI | P > z | Log Like. | LR chi(1) | Prob >chi$^2$ | Pseudo R$^2$ |
|---|---|---|---|---|---|---|---|
| **Age Group** | | | | -922.40 | 215.19 | 0.00 | 0.11 |
| <65 | Ref | | | | | | |
| 65+ | 11.13 | 8.38 – 14.79 | **<0.01** | | | | |
| **Sex** | | | | -1029.51 | 0.96 | 0.33 | 0.00 |
| Female | Ref | | | | | | |
| Male | 1.142 | 0.88 – 1.49 | 0.33 | | | | |
| **Zone** | | | | -1020.91 | 18.17 | 0.00 | 0.01 |
| Far North | Ref | | | | | | |
| Central | | | | | | | |
| Far North East | 0.462 | 0.29 – 0.73 | **<0.01** | | | | |
| Far North West | 0.807 | 0.51 – 1.29 | 0.37 | | | | |
| North Central | 0.496 | 0.28 – 0.89 | **0.02** | | | | |
| North East | 0.743 | 0.44 – 1.27 | 0.28 | | | | |
| **Vaccination status** | | | | -1029.77 | 0.44 | 0.51 | <0.01 |
| Unvaccinated | Ref | | | | | | |
| Vaccinated | 0.91 | 0.70 – 1.19 | 0.51 | | | | |
| **Number of doses received** | | | | -462.04 | 0.04 | 0.83 | <0.01 |
| One | Ref | | | | | | |
| Two or more | 1.07 | 0.58 – 1.97 | 0.83 | | | | |
| **Months between last dose and infection** | | | | -461.19 | 1.175 | 0.42 | <0.01 |
| 1 – 6 | Ref | | | | | | |
| 6 – 12 | 0.99 | 0.57 – 1.72 | 0.96 | | | | |
| >12 | 2.45 | 0.72 – 8.05 | 0.14 | | | | |
| **Pandemic Wave** | | | | -1017.50 | 24.99 | 0.00 | 0.01 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Wave 1 | Ref | | | | | | |
| Wave 2 | 0.41 | 0.13 – 1.36 | 0.15 | | | | |
| Wave 3 | 0.61 | 0.18 – 2.08 | 0.43 | | | | |
| Wave 4 | 0.41 | 0.12 – 1.34 | 0.14 | | | | |
| Wave 5 | 0.19 | 0.53 – 0.67 | **0.01** | | | | |
| Subsequent | 0.85 | 0.24 – 3.02 | 0.80 | | | | |
| **Presence of symptoms** | | | | -647.25 | 175.19 | 0.00 | 0.12 |
| Asymptomatic | Ref | | | | | | |
| Symptomatic | 26.28 | 10.76 – 64.17 | <**0.01** | | | | |
| Unknown | 2.18 | 0.58 – 8.14 | 0.246 | | | | |
| **Presence of comorbidities** | | | | -985.91 | 88.17 | 0.00 | 0.04 |
| No | Ref | | | | | | |
| Yes | 3.80 | 2.91 – 4.97 | <**0.01** | | | | |
| **Comorbidity type** | | | | -325.64 | 148.83 | 0.00 | 0.19 |
| Substance use | Ref | | | | | | |
| DM | 16.67 | 8.72 – 31.87 | <**0.01** | | | | |
| CVD | 21.19 | 10.30 – 43.61 | <**0.01** | | | | |
| Liver & Kidney disease | 25.05 | 8.62 – 72.80 | <**0.01** | | | | |
| Lung disease | 10.35 | 4.10 – 26.13 | <**0.01** | | | | |
| Other | 20.87 | 8.56 – 50.91 | <**0.01** | | | | |

Table 2. Univariable logistic regression between Demographic factors, vaccination, symptoms, comorbidities, and ICU admission among the study cohort, March 2020–December 2022

| **Variable** | **Odds Ratio** | **95% CI** | **P > z** | **Log Like.** | **LR chi(1)** | **Prob >chi2** | **Pseudo $R^2$** |
|---|---|---|---|---|---|---|---|
| **Age Group** | | | | -140.80 | 0.39 | 0.53 | <0.01 |
| <65 | Ref | | | | | | |
| 65+ | 0.83 | 0.47 – 1.48 | 0.53 | | | | |
| **Sex** | | | | -141.71 | 0.15 | 0.70 | <0.01 |
| Female | Ref | | | | | | |
| Male | 1.12 | 0.64 – 1.95 | 0.70 | | | | |
| **Zone** | | | | - 139.129 | 5.32 | 0.26 | 0.02 |
| FNC | Ref | | | | | | |
| FNE | 0 .56 | 0.21 – 1.48 | 0.24 | | | | |
| FNW | 0.91 | 0.35 – 2.37 | 0.85 | | | | |
| NC | 1.61 | 0 .49 – 5.28 | 0.43 | | | | |
| NE | 1.07 | 0.36 – 3.16 | 0.91 | | | | |
| **Vaccination status at time of infection** | | | | -139.03 | 5.52 | 0.02 | 0.02 |
| Unvaccinated | Ref | | | | | | |
| Vaccinated | 0.50 | 0.28 – 0.91 | 0.02 | | | | |
| **Number of doses received** | | | | -54.60 | 0.46 | 0.50 | 0<0.01 |
| One | Ref | | | | | | |
| Two or more | 1.69 | 0.34 – 8.33 | 0.52 | | | | |
| **Months between last dose and infection** | | | | -53.86 | 0.25 | 0.62 | <0.01 |
| 1 – 6 | Ref | | | | | | |
| 6 – 12 | 0.71 | 0.18 – 2.78 | 0.63 | | | | |
| >12 | 1 | Empty | | | | | |
| **Pandemic Wave** | | | | -134.87 | 13.85 | 0.02 | 0.05 |
| Wave 1 | Ref | | | | | | |
| Wave 2 | 1.17 | 0.10 – 13.44 | 0.90 | | | | |
| Wave 3 | 0.78 | 0.06 – 9.74 | 0.85 | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Wave 4 | 0.86 | 0.07 – 10.02 | 0.91 | | | | |
| Wave 5 | 3.0 | 0.220 – 40.931 | 0.41 | | | | |
| Subsequent | 0.12 | 0.01 – 2.71 | 0.18 | | | | |
| **Presence of comorbidities** | | | | -985.91 | 88.17 | 0.00 | 0.04 |
| No | Ref | | | | | | |
| Yes | 1.31 | 0.75 – 2.29 | 0.35 | | | | |
| **Comorbidity type** | | | | -68.18 | 2.87 | 0.72 | 0.02 |
| Substance use | Ref | | | | | | |
| DM | 1.13 | 0.30 – 4.33 | 0.86 | | | | |
| CVD | 1.20 | 0.28 – 5.15 | 0.81 | | | | |
| Liver & Kidney disease | 2.00 | 0.27 – 14.78 | 0.50 | | | | |
| Lung disease | 0.29 | 0.26 – 3.20 | 0.31 | | | | |
| Other | 0.50 | 0.23 – 7.63 | 0.75 | | | | |

Table 3. Univariable logistics regression between Demographic factors, vaccination, symptoms, comorbidities, and death among study cohort, March 2020–December 2022

| Variable | Odds Ratio | 95% CI | P > z | Log Like. | LR chi(1) | Prob >chi2 | Pseudo $R^2$ |
|---|---|---|---|---|---|---|---|
| **Age Group (years)** | | | | -250.83 | 141.32 | <0.01 | 0.22 |
| <65 | Ref | | | | | | |
| 65+ | 35.37 | 19.54 – 64.01 | **<0.01** | | | | |
| **Sex** | | | | -318.10 | 6.78 | 0.01 | 0.01 |
| Female | Ref | | | | | | |
| Male | 2.09 | 1.09 – 3.69 | **0.01** | | | | |
| **Zone** | | | | -318.54 | 5.90 | 0.21 | 0.01 |
| FNC | Ref | | | | | | |
| FNE | 0.39 | 0.16 – 0.94 | **0.04** | | | | |
| FNW | 0.51 | 0.20 – 1.30 | 0.16 | | | | |
| NCZ | 0.51 | 0.17 – 1.54 | 0.23 | | | | |
| NEZ | 8.84 | 0.32 – 2.21 | 0.72 | | | | |
| **Vaccination status at time of infection** | | | | -314.93 | 12.12 | <0.01 | 0.02 |
| Unvaccinated | Ref | | | | | | |
| Vaccinated | 0.33 | 0.18 – 0.64 | **<0.01** | | | | |
| **Number of doses received** | | | | -78.37 | 6.19 | 0.01 | 0.04 |
| One dose | Ref | | | | | | |
| Two or more doses | 0.20 | 0.06 – 0.65 | **<0.01** | | | | |
| **Months between last dose and infection** | | | | -80.18 | 2.25 | 0.13 | 0.01 |
| 1 – 6 | Ref | | | | | | |
| 6 – 12 | 2.68 | 0.80 – 8.91 | 0.11 | | | | |
| >12 | 1 | Empty | | | | | |
| **Pandemic Wave** | | | | -318.57 | 5.22 | 0.27 | 0.01 |
| Wave 1 | Ref | | | | | | |
| Wave 2 | 2.74 | 0.37 – 20.26 | 0.32 | | | | |
| Wave 3 | 1.95 | 0.23 – 16.75 | 0.54 | | | | |
| Wave 4 | 1.86 | 0.25 – 14.06 | 0.55 | | | | |
| Wave 5 | 1.04 | 0.12 – 9.35 | 0.97 | | | | |
| **Presence of symptoms** | | | | -230.69 | 49.39 | <0.01 | 0.10 |
| Asymptomatic | Ref | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Symptomatic | 34.57 | 4.75 – 251.48 | **<0.01** | | | | |
| Unknown | 2.72 | 0.17 – 43.55 | 0.48 | | | | |
| **Presence of comorbidities** | | | | -295.31 | 52.37 | <0.01 | 0.08 |
| No | Ref | | | | | | |
| Yes | 7.78 | 4.40 – 13.78 | **<0.01** | | | | |
| **Comorbidity type** | | | | -130.04 | 81.38 | <0.01 | 0.24 |
| Substance use | Ref | | | | | | |
| DM | 45.43 | 5.88 – 350.79 | **<0.01** | | | | |
| CVD | 170.22 | 22.47 – 1292.97 | **<0.01** | | | | |
| Liver & Kidney disease | 41.22 | 2.51 – 676.511 | **0.01** | | | | |
| Lung disease | 14.27 | 0.88 – 230.30 | 0.06 | | | | |
| Other | 65.47 | 6.69 – 640.41 | **<0.01** | | | | |

Appendix E. Multivariable logistic regression with interaction terms between demographic factors, vaccination, symptoms, comorbidities, and COVID-19 hospitalization, ICU admission and death

Table 1. Adjusted multivariable logistic regression model with interaction terms, predictors of COVID-19 hospitalization among the study cohort; March 2020 – December 2022

| **Variable** | **Odds Ratio** | **Standard Error** | **95%CI** | **p-value** |
|---|---|---|---|---|
| **Age groups** | | | | |
| <65 | Ref | | | |
| 65+ | 15.33 | 3.43 | 9.89 – 23.76 | **<0.01*** |
| **Sex** | | | | |
| Female | Ref | | | |
| Male | 0.87 | 0.17 | 0.59 – 1.28 | 0.47 |
| **Zone** | | | | |
| Far North Central | Ref | | | |
| Far North East | 0.48 | 0.12 | 0.30 – 0.80 | **<0.01*** |
| Far North West | 0.62 | 0.16 | 0.38 – 1.04 | 0.68 |
| North Central | 0.60 | 0.19 | 0.32 – 1.12 | 0.11 |
| North East | 0.77 | 0.23 | 0.44 – 1.37 | 0.38 |
| **Vaccination status** | | | | |
| Unvaccinated | Ref | | | |
| One dose | 0.28 | 0.23 | 0.54 – 1.41 | 0.12 |
| Two or more doses | 0.88 | 0.23 | 0.52 – 1.47 | 0.62 |
| **Presence of symptoms** | | | | |

| | | | | |
|---|---|---|---|---|
| Asymptomatic | Ref | | | |
| Symptomatic | 3.35 | 0.57 | 2.39 – 4.68 | **<0.01*** |
| Unknown | 1.22 | 0.40 | 0.64 – 2.22 | 0.55 |
| **Presence of co-existing medical condition** | | | | |
| No | Ref | | | |
| Yes | 2.82 | 0.58 | 1.89 – 4.23 | **<0.01*** |
| **Age group*Vaccine doses received** | | | | |
| 65+*One dose | 1.30 | 0.93 | 0.32 – 5.29 | 0.72 |
| 65+*Two or more doses | 0.36 | 0.12 | 0.31 – 1.04 | 0.07 |
| **Sex*Vaccine doses received** | | | | |
| Male*One dose | 4.02 | 2.97 | 0.95 – 17.12 | 0.06 |
| Male*Two or more doses | 1.78 | 0.53 | 0.98 – 3.20 | 0.06 |
| **Presence of co-existing medical condition* Vaccine doses received** | | | | |
| Yes*One dose | 1.30 | 0.92 | 0.32 – 5.22 | 0.71 |
| Yes*Two or more doses | 0.57 | 0.17 | 0.31 – 1.04 | 0.07 |

*Ref = Reference category*
***** *Statistical test of Significance*

Log likelihood = -837.24 LR $chi^2$ = 385.50 Prob > $chi^2$ < 0.01
Number of observations = 8428 Pseudo $R^2$ = 0.19

Table 1b. Hosmer-Lemeshow goodness-of-fit test for multivariable model with interaction terms on predictors of hospitalization among COVID-19 cases

| Group | Prob | Obs_1 | Exp_1 | Obs_0 | Exp_0 | Total |
|---|---|---|---|---|---|---|
| 1 | <0.01 | 3 | 3.7 | 919 | 918.3 | 922 |
| 2 | <0.01 | 6 | 6.0 | 938 | 938.0 | 944 |
| 3 | <0.01 | 3 | 5.1 | 687 | 684.9 | 690 |
| 4 | <0.01 | 3 | 7.6 | 926 | 921.4 | 929 |
| 5 | <0.01 | 3 | 7.2 | 783 | 778.8 | 786 |
| 6 | 0.01 | 4 | 8.7 | 782 | 777.3 | 786 |
| 7 | 0.02 | 15 | 15.3 | 849 | 848.7 | 864 |
| 8 | 0.03 | 27 | 20.7 | 839 | 845.3 | 866 |
| 9 | 0.04 | 31 | 24.7 | 771 | 777.3 | 802 |
| 10 | 0.73 | 128 | 124.0 | 711 | 715.0 | 839 |

Number of observations =8,428; number of groups=10
Hosmer-Lemeshow chi2=12.69; Prob>chi2=0.12

Table 2. Adjusted multivariable logistic regression model with interaction terms, predictors of COVID-19 ICU admission among the study cohort; March 2020 – December 2022

| Variable | Odds Ratio | Standard Error | 95%CI | p-value |
|---|---|---|---|---|
| **Age groups** | | | | |
| <65 | Ref | | | |
| 65+ | 0.89 | 0.37 | 0.40 – 1.99 | 0.77 |
| **Sex** | | | | |
| Female | Ref | | | |
| Male | 0.75 | 0.29 | 0.35 – 1.61 | 0.46 |
| **Zone** | | | | |
| Far North Central | Ref | | | |
| Far North East | 0.52 | 0.27 | 0.18 – 1.46 | 0.22 |
| Far North West | 0.84 | 0.44 | 0.30 – 2.36 | 0.73 |
| North Central | 2.65 | 1.84 | 0.68 – 10.32 | 0.16 |
| North East | 0.88 | 0.52 | 0.28 – 2.81 | 0.83 |
| **Vaccination status** | | | | |
| Unvaccinated | Ref | | | |
| One dose | 2301 | $1.78*10^{9}$ | 0.0 – 0.0 | 0.99 |
| Two or more doses | 0.17 | 0.11 | 0.05 – 0.57 | **<0.01*** |
| **Presence of symptoms** | | | | |
| Asymptomatic | Ref | | | |
| Symptomatic | 1.53 | 0.60 | 0.71 – 3.31 | 0.28 |
| Unknown | 1.73 | 1.29 | 0.40 – 7.46 | 0.46 |
| **Presence of co-existing medical condition** | | | | |
| No | Ref | | | |
| Yes | 0.86 | 0.34 | 0.39 – 1.86 | 0.70 |
| **Age group*Vaccine doses received** | | | | |
| 65+*One dose | $6.85*10^{-7}$ | 0.00 | 0.0 – 0.0 | 0.99 |
| 65+*Two or more doses | 1.02 | 0.70 | 0.27 – 3.89 | 0.97 |
| **Sex*Vaccine doses received** | | | | |
| Male*One dose | $4.32*10^{-7}$ | 0.00 | 0.0 – 0.0 | 0.99 |
| Male*Two or more doses | 3.25 | 2.22 | 0.86 – 12.37 | 0.08 |
| **Presence of co-existing medical condition* Vaccine doses received** | | | | |
| Yes*One dose | 1 | (omitted) | | |
| Yes*Two or more doses | 2.31 | 1.53 | 0.63 – 8.47 | 0.21 |

*Ref = Reference category*

***** *Statistical test of Significance*

Log likelihood = -128.22 LR $chi^2$ = 22.36 Prob > $chi^2$ < 0.13

Number of observations = 219 Pseudo $R^2$ = 0.08

Table 3. Multivariable logistics regression with interaction terms between Demographic factors, vaccination, symptoms, comorbidities, and Disease outcome among the study cohort; March 2020 – December 2022

| Variable | Odds Ratio | SE | 95%CI | p-value |
|---|---|---|---|---|
| **Age groups (years)** | | | | |
| <65 | Ref | | | |
| 65+ | 46.78 | 17.58 | 22.39 – 97.72 | **<0.01** |
| **Sex** | | | | |
| Female | Ref | | | |
| Male | 1.74 | 0.63 | 0.85 – 3.55 | 0.13 |
| **Zone** | | | | |
| Far North Central | Ref | | | |
| Far North East | 0.36 | 0.18 | 0.13 – 0.98 | **0.045** |
| Far North West | 0.30 | 0.16 | 0.10 – 0.87 | **0.03** |
| North Central | 0.77 | 0.49 | 0.22 – 2.65 | 0.67 |
| North East | 1.14 | 0.65 | 0.37 – 3.48 | 0.82 |
| **Doses of vaccine received** | | | | |
| Unvaccinated | Ref | | | |
| One dose | 0.70 | 0.95 | 0.05 – 9.87 | 0.79 |
| Two or more doses | 0.16 | 0.17 | 0.02 – 1.33 | 0.09 |
| **Presence of co-existing medical condition** | | | | |
| No | Ref | | | |
| Yes | 5.36 | 2.00 | 2.59 – 11.12 | **<0.01** |
| **Age group*Vaccination status** | | | | |
| 65+*One dose | 1.47 | 1.81 | 0.13 – 16.31 | 0.75 |
| 65+*Two or more doses | 0.44 | 0.41 | 0.07 – 2.69 | 0.37 |
| **Presence of comorbidities*Vaccination status** | | | | |
| Yes*One dose | 0.56 | 0.59 | 0.70 – 4.44 | 0.58 |
| Yes*Two or more doses | 0.71 | 0.61 | 0.13 – 3.84 | 0.69 |
| **Sex*Vaccination status** | | | | |

| | | | | |
|---|---|---|---|---|
| Malee*One dose | 1.31 | 1.39 | 0.16 – 10.45 | 0.80 |
| Male*Two or more doses | 1.57 | 1.44 | 0.26 – 9.53 | 0.62 |

Ref = *Reference category*
***** *Statistical test of Significance*
*(empty)= Predicts failure perfectly*

Log likelihood = -205.22 LR chi2 = 232.55 Prob > chi2<0.001
Number of observations = 8428 Pseudo R2 = 0.36

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