This document is intended to enable health care providers to better understand the most significant risk factors associated with the development of severe illness or complications from COVID-19 among adults. For the purpose of this document, severe illness is defined as a case of COVID-19 that results in hospitalization, admission to intensive care, use of a ventilator, or death. The section on risk factors is followed by a section mentioning risk calculators and additional resources for patients and the general public.

This document does not cover children and youth, people experiencing symptoms that persist for more than four weeks (i.e. “long COVID”), or the emergence of new variants of concern. The information included in this document is current as of April 24, 2021. For resources to provide advice to patient please see this content, and for considerations related to vaccine and clinically most vulnerable status please refer to this page.

The information is based on available provincial, national, and international evidence. This document draws heavily on three high quality sources:

1) a study conducted by the British Columbia Centre for Disease Control (BCCDC) using the BC COVID-19 Cohort which integrates data on all individuals tested for COVID-19 in BC, including all diagnosed cases, medical visits, hospitalizations, emergency room visits, prescription drugs, some chronic conditions and mortality;
2) findings from the OpenSAFELY data, which covers 40% of all patients in England and holds patient data from electronic health records; and
3) the United States Centre for Disease Control evidence review of underlying medical conditions associated with an increased risk of developing severe illness from COVID-19.1,2

The studies that inform this document differ in the terminology used to quantify particular risks. Key terms used in this document to summarize relative risk include the following:

- Adjusted risk ratio (aRR) refers to the relative risk of hospitalization calculated using bivariate and multivariable Poisson regression models with robust error variance that adjusted for age, sex, and co-morbidities.
- Hazard ratio refers to the relative risk of mortality

Epidemiological Overview of COVID-19 in British Columbia

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Cumulatively, there have been 114,460 (2,223 per 100K population) confirmed or epidemiologically linked cases of COVID-19 in British Columbia as of April 10, 2021. In British Columbia, 4.9% of cases have required hospitalization and 1.3% of cases have resulted in death. These severe outcomes are disproportionately experienced by seniors of advanced age. The BCCDC produces weekly situation reports that provide a more in-depth look at provincial COVID-19 epidemiology.

Risk Factors

Age is by far the single most important risk factor for severe illness or complications from COVID-19 including mortality. The following risk factors discussed in this document are also associated with greater risk for severe illness:

Conditions

- Asthma
- Cancer
- Cardiovascular
- Chronic Kidney Disease
- Chronic Respiratory Disease
- Diabetes
- Down Syndrome
- Immunosuppression and Immunodeficiency
- Obesity
- Organ Transplant
- Pregnancy
- Sickle Cell Disease
- Substance Use

Other factors that warrant additional consideration

- Age
- Race, Ethnicity, Socio-Economic Factors and their Intersection
- Sex at Birth
- Other Populations that Warrant Special Consideration

Conditions

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Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

Adults of any age with one or more underlying medical conditions or comorbidities are at increased risk for severe illness from COVID-19. Comorbidities associated with the greatest risk of severe illness, defined as having an aRR above 2.5 based on provincial data and/or a mortality risk (hazard ratio) above 2.5 based on OpenSAFELY data, include those with chronic kidney disease with an eGFR < 30, down syndrome, and organ transplant. Other comorbidities associated with a greater risk of severe illness include cancer, cardiovascular disease, chronic respiratory disease, diabetes, gout, immunosuppression and immunodeficiency, obesity, pregnancy, and sickle cell disease. Appendix A provides a graphic representation of the risk factors for severe illness from COVID-19 identified using provincial data.

Table 1 below summarizes the relative risk of severe illness associated with specific comorbidities identified in either epidemiological data from British Columbia and/or findings from published literature or other jurisdictions.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Adjusted risk ratio* (British Columbia data)</th>
<th>Hazard ratio (OpenSAFELY data)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asthma</strong></td>
<td>1.27 (1.15-1.40)</td>
<td>1.13 (1.01–1.26)</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td>all cancer: 1.21 (1.08-1.34)</td>
<td>non-haematological: 1.72 (1.5-1.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>haematological: 2.8 (2.08-3.78)</td>
</tr>
<tr>
<td><strong>Cardiovascular Disease</strong></td>
<td>Heart Disease: Not statistically significant</td>
<td>1.17 (1.12-1.22)</td>
</tr>
<tr>
<td></td>
<td>History of Stroke: N/A</td>
<td>2.16 (2.06-2.27)</td>
</tr>
<tr>
<td><strong>Chronic Kidney Disease</strong></td>
<td>1.45 (1.29-1.64)</td>
<td>eGFR 30–60: 1.33 (1.28-1.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eGFR &lt; 30: 2.52 (2.33-2.72)</td>
</tr>
<tr>
<td><strong>Chronic Respiratory Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>1.45 (1.29-1.64)</td>
<td>Controlled: 1.31 (1.24-1.37)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uncontrolled: 1.95 (1.83-2.08)</td>
</tr>
<tr>
<td><strong>Down Syndrome</strong></td>
<td>N/A</td>
<td>10.39 (7.08-15.23)</td>
</tr>
<tr>
<td><strong>Immunosuppression</strong></td>
<td>1.57 (1.27-1.95)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Immunodeficiency</strong></td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMI 30-34.9: 1.05 (1.00-1.11)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMI 35-39.9: 1.4 (1.30-1.52)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMI 40+: 1.92 (1.72-2.13)</td>
<td></td>
</tr>
<tr>
<td><strong>Organ Transplant</strong></td>
<td>N/A</td>
<td>3.53 (2.77–4.49)</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Sickle Cell Disease</strong></td>
<td>N/A</td>
<td>Asplenia: 1.34 (0.98–1.83)</td>
</tr>
<tr>
<td><strong>Substance Use</strong></td>
<td>Injection Drug Use:</td>
<td>Smoking (former): 1.43 (1.37-1.49)</td>
</tr>
<tr>
<td></td>
<td>Problematic Alcohol Use:</td>
<td>Smoking (current): 1.14 (1.05-1.23)</td>
</tr>
</tbody>
</table>
Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

*Adjusted for age, sex, and co-morbidities

The risk of severe illness increases substantially among those with multiple comorbidities. In Canada, among hospitalized cases for whom clinical presentation was reported, 74% reported one or more comorbidities.\(^4\)

**Asthma:** People with asthma are at greater risk of developing severe illness. The BC study found that people with asthma had an aRR of 1.27 (1.15-1.40) to be hospitalized with COVID-19, while a sub-analysis of women of reproductive age found an aRR of 1.95 (1.42-2.68).\(^5\) The OpenSAFELY study showed that those with asthma and recent use of corticosteroids had a hazard ratio of 1.13 (1.01-1.26).\(^6\)

**Cancer:** People with a history of cancer are at greater risk of severe illness with the risk of illness increasing for those with a more recent diagnosis. The BC study shows that those with a history of cancer have an aRR of 1.21 (1.08-1.34) compared to those without a previous diagnosis.\(^7\) The OpenSAFELY study suggests that mortality risk increases more for those with a more recent diagnosis. The hazard ratio for those diagnosed with a non-haematological cancer within the past year is 1.72 (1.50-1.96) and for those diagnosed with a haematological malignancy 2.80 (2.08-3.78) within the past year compared to those with COVID-19 without a recent cancer diagnosis.\(^8\)

**Cardiovascular Disease:** People with chronic heart disease and those with a history of stroke are generally considered at greater risk of severe illness. The BC study found an association of hypertension, ischemic heart disease, myocardial infarction and stroke with hospitalization, but they were not statistically significant in the multivariate model. The OpenSAFELY study found that compared to those with no cardiac conditions, those with heart disease carry a hazard ratio of 1.17 (1.12–1.22), while those with a history of stroke had a mortality risk of 2.16 (2.06–2.27).\(^9\)

**Chronic Kidney Disease:** People with reduced kidney function or chronic renal disease are at greater risk of severe illness. The BC study found that having a chronic kidney disease was

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\(^7\) British Columbia Centre for Disease Control. (Unpublished). Risk factors for hospitalization among people with COVID-19 in British Columbia.


\(^9\) Ibid.
associated with an aRR of 1.45 (1.29-1.64) for hospitalization from COVID-19 compared to those without a chronic kidney disease. The OpenSAFELY study found that the risk of death increases with reductions in kidney function, as people with an eGFR 30–60 carry a hazard ratio of 1.33 (1.28–1.40) while those with an eGFR < 30 have a hazard ratio of 2.52 (2.33–2.72).\textsuperscript{10}

**Chronic Respiratory Disease:** The OpenSAFELY study found that people with chronic respiratory disease are at higher risk of death from COVID-19. The grouping they used for chronic respiratory disease excluded asthma. It included people with chronic obstructive pulmonary disease (COPD), fibrosing lung disease, bronchiectasis or cystic fibrosis. Those with a diagnosis of a chronic respiratory condition, compared to those without carried a hazard ratio of 1.63.

**Diabetes:** People with diabetes are at greater risk of severe illness. The BC study shows an aRR of 1.45 (1.29-1.64) for people with diabetes. The OpenSAFELY study shows that people with diabetes that is considered controlled (i.e. with HbA1c < 58 mmol mol\(^{-1}\) or 7.5%) are at less risk of severe illness than those whose condition is considered uncontrolled (i.e. with HbA1c ≥ 58 mmol mol\(^{-1}\) or 7.5%).\textsuperscript{1} Compared to people who do not have diabetes, people with controlled diabetes have a hazard ratio of 1.31 (1.24–1.37) while those with uncontrolled diabetes have a hazard ratio of 1.95 (1.83–2.08).\textsuperscript{11}

**Down Syndrome:** People with down syndrome are at much greater risk of developing severe illness. A recent UK study found that people with down syndrome had a hazard ratio of 10.39 (7.08-15.23) compared to others.\textsuperscript{12}

**Immunosuppression and Immunodeficiency:** People with immunosuppression or immunodeficiency are at increased risk of severe illness. The BC study shows an aRR of 1.57 (1.27-1.95) of hospitalization from COVID-19 for people with immunosuppression. A systematic review and meta-analysis also found that immunosuppression and immunodeficiency was associated greater risk of severe illness from COVID-19. Compared to others, people with immunosuppression had a hazard ratio of 3.29 (0.89-12.21) while people with immunodeficiency had a hazard ratio of 1.55 (0.70 to 3.45).\textsuperscript{13}

**Obesity:** Body mass index (BMI) is a predictor of severe illness as the risk of severe illness increases considerably for those with a BMI greater than 30 and is highest among those with a BMI greater

\textsuperscript{10} Ibid.

\textsuperscript{11} Ibid.


Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

than 40. Compared to people with a BMI of less than 30, those with a BMI between 30 and 34.9 have a hazard ratio of 1.05 (1.00–1.11), those with a BMI between 35 and 39.9 have a hazard ratio of 1.4 (1.30-1.52), and those with a BMI greater than 40 have a hazard ratio of 1.92 (1.72-2.13).

**Organ Transplants:** Prior recipients of organ transplants are significantly more likely to experience severe illness and have a hazard ratio of 3.53 (2.77–4.49) compared to those who have never undergone an organ transplant.

**Pregnancy:** Most pregnant women who become infected with COVID-19 will experience mild-to-moderate symptoms and many may be asymptomatic. However, data from five Canadian provinces including British Columbia show that pregnant women are more likely to require hospitalization (risk ratio of 5.33 [4.51-6.20]) than non-pregnant women of reproductive age. Both Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately 8-11% of pregnant women will require hospitalization for COVID-19-related morbidity and between 2-4% of pregnant women will require admission to intensive care. Pre-existing comorbidities, high maternal age, and high body mass index seem to be risk factors for severe COVID-19. Preterm birth rates are high in pregnant women with COVID-19 compared to pregnant women without the disease.

**Sickle Cell Disease:** People with sickle cell disease are at greater risk of severe illness due to their impaired immunity resulting from functional hyposplenism, systemic vasculopathy, which predisposes them to end organ dysfunction, and a high risk of thrombosis. The OpenSAFELY study shows that those with asplenia (i.e. included splenectomy or a spleen dysfunction, including sickle

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15 Ibid.
cell disease) have a hazard ratio of 1.34 (0.98–1.83).

Limited evidence suggests that people with thalassemia are also at greater risk of severe illness.

**Substance Use:** People with a history of substance use are at greater risk of severe illness or complications from COVID-19. The BC study found that injection drug use and problematic alcohol use were both associated with a greater risk of hospitalization. Injection drug use carries an aRR of 2.28 (2.18–3.09) while problematic alcohol use has an aRR of 1.21 (1.02–1.43). Both current and former cigarette smokers are at greater risk of severe illness or complications from COVID-19. The OpenSAFELY study found that compared to people who have never smoked (i.e. consumed fewer than 100 cigarettes lifetime), former smokers carry a hazard ratio of 1.43 (1.37–1.49) while current smokers have a hazard ratio of 1.14 (1.05–1.23). Smoking contributes to the development of comorbidities such as chronic respiratory disease that are strongly associated with severe illness or complications from COVID-19.

**Socio-economic, demographic, and other factors that warrant additional consideration**

**Age:** Age is by far the strongest predictor of hospitalization and mortality based on available data. The risk of severe illness and complications increases with age. Table 2 below provides a breakdown of relative risk of mortality by age cohort using provincial data for the period of September 1, 2020 to January 5, 2021.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Mortality Rate per 1,000,000</th>
<th>Relative Mortality Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-17 years</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>18-34 years</td>
<td>0.8</td>
<td>Comparison group</td>
</tr>
<tr>
<td>35-44 years</td>
<td>8.8</td>
<td>11x higher</td>
</tr>
<tr>
<td>45-54 years</td>
<td>25.5</td>
<td>30x higher</td>
</tr>
<tr>
<td>55-64 years</td>
<td>59.8</td>
<td>71x higher</td>
</tr>
<tr>
<td>65-74 years</td>
<td>238.2</td>
<td>284x higher</td>
</tr>
<tr>
<td>75-84 years</td>
<td>955.6</td>
<td>1,139x higher</td>
</tr>
<tr>
<td>85+ years</td>
<td>4,620.9</td>
<td>5,506x higher</td>
</tr>
</tbody>
</table>

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Compared to those in the 18 to 34 years of age cohort, people in the 35-44 years old group are 8.8x more at risk to die from COVID-19. As shown in Table 1, the mortality risk increases with every subsequent decade of age. Those who are 85 years of age and older are 5,506 times more likely to die from COVID-19 than those in than the comparison group. This is fairly similar to what was found in the United States.\textsuperscript{24}

In British Columbia, people 70 years of age and above are much more likely to experience severe illness as this cohort accounts for 42.3% of hospitalizations and 85.9% of deaths despite making up 13% of the population. The median age among decedents is 85. Almost two-thirds (64.9%) of all COVID-19 deaths in British Columbia have been associated with long-term care facility outbreaks.\textsuperscript{25}

It is important to note that COVID-19 still represents a significant risk to younger adults. Data from the United States show that 38% of the excess mortalities that occurred between March and July 2020 among those aged 25 to 44 were related to COVID-19.\textsuperscript{26}

**Race, Ethnicity, Socio-Economic Factors and their Intersection:** Limited data exists regarding the relationship between race, ethnicity, and socio-economic status and outcomes relating to COVID-19 in British Columbia. Available data from England suggest that people from all racial and ethnic groups are at greater risk of severe illness relative to those of white ethnicity. Compared to those with white ethnicity, the mortality risk reaches 1.48 (1.29-1.69) for people who are Black, 1.45 (1.32-1.58) for those of South Asian ethnicity, and 1.43 (1.11-1.84) for those of mixed ethnicity.\textsuperscript{27} This analysis did not separate ethnicity from material deprivation. Increased risk of severe disease for those of racial or ethnicity other than Caucasian, and those living in poverty is also reported in the US.\textsuperscript{28,29,30}


https://doi.org/10.3389/fsoc.2020.00047


https://doi.org/10.1093/cid/ciaa815
Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

In Canada, as reported in the Chief Public Health Officer’s report on the State of Public Health in Canada 2020, race, ethnicity, poverty, certain occupations and other factors affect COVID-19 outcomes and intersect.³¹

“There are overlapping and compounding risks related to sex, gender, racialization, income, housing, employment, and other socioeconomic factors. For example, racialization intersects with employment: in Canada, approximately 41% of meat processing workers are members of racialized groups, compared to 21% of the workforce in general. Elevated risk can also be shaped by the intersection of gender and racialization. For example, the vast majority of staff in nursing and residential care facilities, as well as home care, are women, including the majority of nurses' aides, orderlies and client service associates. From 1996 to 2016, the share of immigrants in these occupations grew more quickly than in all other occupations, from 22% to 36%. Of all Canadian workers in these positions in 2016, 31% were immigrant women and the proportions were higher in larger metropolitan areas such as Toronto, Vancouver, and Calgary where over 70% of these positions were filled by immigrants, the majority of these immigrant women. Further, 12% of all workers in these occupations were Black and 11% were Filipino despite Black and Filipino workers only making up 3% of workers in all other occupations.”

In the United Kingdom, the OpenSAFELY study showed that compared to the least deprived group, all other groups had higher risk of death, with a hazard ratio progressively increasing to 2.11 (1.98-2.25) for the most deprived of the five groups.³² This finding is reproduced in a large cohort study in patients requiring critical care for COVID-19 in Scotland.³³

One factor found to contribute to poorer outcomes is poor housing conditions, including overcrowding and homelessness as well as insufficient plumbing or kitchen facilities or high housing cost. At total, those factors were associated with a 42% higher risk of mortality in a recent

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Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

US study. A recent Ontario study found that people experiencing homelessness were over 20 times more likely to be hospitalized with COVID-19 (3.5 per 1,000 vs. 0.2/1,000), over 10 times more likely to be admitted into intensive care with COVID-19 (0.51 per 1,000 vs. 0.07/1,000), and over 5 times more likely to die within 21 days of a COVID-19 infection (0.34 per 1,000 vs. 0.05/1,000).

First Nations, Métis, and Inuit People: As stated in the Chief Public Health Officer’s report on the State of Public Health in Canada 2020, Indigenous people may also experience more severe illness or complications relating to COVID-19.

“First Nations, Inuit and Métis face social and economic challenges that intersect to increase their risk of contracting COVID-19 and experiencing serious illness. The lasting impacts of intergenerational trauma continue to influence the health of Indigenous peoples in Canada. Social and economic inequities persist, increasing risk related to COVID-19. This includes challenges such as lack of access to medical care, geographic isolation, inadequate and overcrowded housing, as well as low-income and food insecurity. Some communities are unable to comply with public health measures due to overcrowding and lack of a safe water supply, and a number of communities concurrently faced the risk of fire or flood evacuations as well as the pandemic. First Nations, Métis, and Inuit populations also experience higher rates of pre-existing health conditions, such as asthma and diabetes.”

The First Nations Health Authority has developed resources for health professionals to support the delivery of culturally safe and appropriate care for First Nations people and produces regular situation reports that provide a more in-depth look at COVID-19 epidemiology specific to First Nations.

Sex at Birth: Males are more likely to experience severe illness or complications from COVID-19. The BC study found males had an aRR of 1.29 (1.19-1.41). A recent study from England found that

Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

males had a mortality risk of 1.6 compared to females.\textsuperscript{37} In British Columbia, men account for 56% of hospitalizations and 54% of deaths.\textsuperscript{38} This is also consistent with studies from the United States.

**Other Populations that Warrant Special Consideration:** The BCCDC has also identified additional priority populations that may require special attention or additional support including:

- people living in rural and remote communities
- people living with disabilities
- people with development and/or behavioural disorders
- people who may be or are experiencing violence

For more information on some of these specific populations, visit: [http://www.bccdc.ca/health-info/diseases-conditions/covid-19/priority-populations](http://www.bccdc.ca/health-info/diseases-conditions/covid-19/priority-populations).

**Resources**

**Risk Quantification**

The British Medical Association has developed a risk stratification tool based on published literature incorporating epidemiological data across the world including age, sex, ethnicity, and comorbidities to predict risk of severe complications due to COVID-19 infection. The tool is intended to both quantify risk and assist team leaders when allocating roles within clinical departments and general practitioner practices. For more information, visit: [https://www.bma.org.uk/media/2768/bma-covid-19-risk-assessment-tool-july2020.pdf](https://www.bma.org.uk/media/2768/bma-covid-19-risk-assessment-tool-july2020.pdf)

The University of Oxford has developed an online risk assessment tool that incorporates a range of factors such as age, sex, ethnicity and existing medical conditions to predict risk of death or hospitalisation from COVID-19. The model is based on patient data from England and is not intended for use supporting or informing clinical decision-making. For more information, visit: [https://qcovid.org/](https://qcovid.org/).

**List of Contributors**


Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults

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This document was reviewed by the Public Health Reference Group and Public Health Leadership. This document was approved by the Clinical Reference Group, Public Health Reference Group, BCCDC COVID-19 Oversight Committee, Public Health Leadership, and the Ministry of Health.

References


Risk Factors Associated with Severe Illness or Complications due to COVID-19 Infection, for Adults


Appendix A: Risk Factors for Severe Illness from COVID-19 in British Columbia

- Sex (vs. female): Male
- Age (vs. 20-29 years): <20 years
- Age (vs. 20-29 years): 30-39 years
- Age (vs. 20-29 years): 40-49 years
- Age (vs. 20-29 years): 50-59 years
- Age (vs. 20-29 years): 60-69 years
- Age (vs. 20-29 years): 70-79 years
- Age (vs. 20-29 years): 80+ years
- Asthma
- Chronic kidney disease
- Diabetes
- Gout
- Injection drug use
- Problematic alcohol use
- Cancer
- Immunosuppression

Adjusted risk ratio for hospitalization