COVID-19 Scientific Advisory Group
Rapid Evidence Report

Topic: Is being immunosuppressed (in its various forms) associated with increased likelihood of recognized COVID-19 and/or increased disease severity?

1. **Is being immunosuppressed (in its various forms) associated with increased likelihood of recognized COVID-19?**
2. **Is being immunosuppressed (in its various forms) associated with worse disease severity (i.e., risk of hospitalization, ICU admission, death)?**

Immunosuppression may result from certain health conditions and/or therapies. For example, a patient's immune system may be deliberately suppressed in preparation for organ transplantation, to prevent rejection of the donor tissue. Common examples of immunosuppression include (but are not limited to):

a) Malignancies (including hematologic), autoimmune diseases, inflammatory diseases, and moderate to severe kidney failure
b) Transplantation (hematopoietic transplantation: allo/autologous and solid organ [lung, heart, liver, kidney, small bowel])
c) Using medications such as: corticosteroids (prednisone equivalent of >10mg/day), non-biologic disease-modifying agents, biologic disease-modifying agents, anti-rejection medications, chemotherapy, and other immunosuppressive medications
d) Primary immune deficiencies (antibody, cell mediated or combined).

Immunosuppressive conditions and/or therapies are defined similarly to definitions provided by Alberta Health Services Infection Prevention and Control (IPC), which can be accessed here. However, this report includes corticosteroids of prednisone equivalent of >10mg/day as immunosuppressive (given poor outcomes reported in COVID-19) compared to IPC's definition of prednisone equivalent of >20mg/day for two weeks.

Context

- As Alberta reduces restrictive community-based public health interventions as part of its relaunch strategy, the risk of SARS-CoV-2 transmission increases, especially in places where physical distancing might not be possible. This may include certain workplaces, in-person learning environments, and other places where groups congregate.
- Immunosuppressed patients are generally thought to be at increased risk of developing complications from infections, although not all patients who are immunosuppressed have elevated risk, or the same level of risk for all infections, and risk varies with the type and degree of immunosuppression and the type of infection.
- Questions have arisen about whether immunosuppressed patients are at increased risk of developing recognized COVID-19 or severe outcomes such as hospitalization, ICU admission, and death.
- SAG recently completed a complementary rapid evidence report assessing risk factors associated with the development of severe outcomes in COVID-19. The report focuses on age, co-morbid conditions, and pregnancy and is available on the AHS web site.
- The purpose of this review is to assess and summarize the medical literature describing risks of developing COVID-19 (SARS-CoV2 infection) and the likelihood that severe outcomes will ensue (e.g. hospitalization, need for mechanical ventilation, or death) in immunosuppressed patients.
- This review is not intended to provide guidance on management of immunosuppressive diseases and therapies during the COVID-19 pandemic or treatment of COVID-19 in immunosuppressed patients. In addition, this review is not intended to generate hypotheses on interactions between COVID-19 and immunosuppressive diseases or therapies.

September 9, 2020

Key Messages from the Evidence Summary

- The actual risk of recognized COVID-19 in immunosuppressed patients may be underestimated because patients who would typically be considered at high risk likely adopted protective measures early and rigorously, and potentially because of limited testing during early phases of the pandemic, although these groups may also have had higher testing rates. .
- The limited evidence that is available suggests that patients in some immunosuppressed states appear to be at increased risk for recognized COVID-19 or increased disease severity, however, available studies are subject to bias due to potential confounding factors (documented COVID-19 risks such as age, obesity, co-morbidities) without appropriate matched controls. As such, it is difficult to determine whether this increased risk is driven by the immunosuppressive state). Furthermore, there is limited quantitative data on COVID-19 in immunosuppressed patients and such, there is insufficient available information to assess risk in many conditions/therapies. There is also limited data assessing the additive risk of COVID-19 or severity in immunosuppressed patients with co-morbidities or complications that develop secondary to their primary condition (eg: CKD secondary to ANCA-vasculitis, diabetes secondary to chronic corticosteroid use).
- The current assessment of risk for specific immunosuppressed patient populations are summarized in the table below with a brief comment on the quality of available evidence (further discussion is available in the text of this report). Here we define low strength associations as OR <1.67 or HR <1.5; moderate strength associations are defined as OR 1.68-3.47 or HR/RR 1.5-2.5; and high strength associations are defined as OR>3.47 or HR/RR >2.5. Additional detail on risk factors for specific populations follows the table. Pediatric data is excluded from this table due to insufficient available information (see below). Inflammatory arthritis includes rheumatoid arthritis, psoriatic arthritis, and seronegative spondyloarthropathy. Systemic rheumatic illnesses include SLE, CTD, inflammatory myositis, sarcoidosis, and Raynaud's phenomenon. There is limited data on vasculitis.

Condition	**Studies identifying increased risk of recognized of COVID-19 (# studies addressing question)**	**Studies identifying increased risk of COVID-19 disease severity (# studies addressing question)**	**Comments on available evidence** *(see Summary of Evidence page 8 for details)*
Active Cancer	Yes – Possible (low strength association) (1)	Yes (moderate strength association) (6)	One study assessing risk of recognized COVID-19 with low strength association. Moderate quality evidence assessing risk of severe COVID-19 with moderate strength association. One meta-analysis showing increased mortality in lung and hematological malignancies with moderate strength association.
Autoimmune Diseases			
Inflammatory Bowel Disease	No (1)	Insufficient Data (0)	One study reported a lower age-adjusted incidence of recognized COVID-19 in IBD patients compared with the general population. There was no population-level data on risk of COVID-19 disease severity with IBD although an unmatched cohort of IBD patients had high-strength association (with wide confidence intervals) of pneumonia and death in patients with active IBD (compared to remission).
Psoriasis	Insufficient data (1)	Insufficient data (1)	Although one study reported increased recognised COVID-19 and hospitalization patients with psoriasis and on biologic therapy compared to the general population, there was no adjustment for any potential confounders (and patients with psoriasis are more likely to have vascular co-morbidities).
Inflammatory Arthritis	Insufficient data (0)	Insufficient Data (2)	There was no population-level data assessing risk of recognized COVID-19 in rheumatic diseases. A matched case-control study of hospitalised patients did show a moderate strength association with ICU admission/mechanical ventilation in patients with rheumatic diseases, but there was an over-representation of
Systemic Rheumatic Illness	Insufficient data (0)	Yes (2) (moderate	

		strength association, specific diseases)	systemic lupus erythematosus, active rheumatic disease, and ILD/sleep apnea in the hospitalized population. Contributions of those factors was not formally assessed. One unmatched cohort had a high strength association of hospitalization in systemic connective tissue disease (e.g. systemic lupus erythematosus, systemic sclerosis) although the confidence interval was wide (but did not cross 1). As such, patients with inflammatory arthritis do not appear to be at increased risk of COVID-19 severity based on current data. Studies formally comparing risk of recognized COVID-19 or severity stratified by active disease compared to remission are not available.
Multiple Sclerosis	Insufficient data (0)	Insufficient data (0)	There was no population-level data assessing risk of recognised COVID-19 or severity in patients with multiple sclerosis.
Transplantation			
Solid organ	Insufficient data (0)	Insufficient data (0)	There was no population-level data assessing risk of recognized COVID-19 in patients with organ transplants although there have been reports of COVID-19 in these patients. An observational cohort of liver transplant patients reported doubled age- and gender-matched incidence ratios of COVID-19 compared to the general population but risk was not calculated. A single small case control study of transplant patients (predominantly renal) did not show an association between transplantation and severe COVID-19.
Hematological	Insufficient data (0)	Insufficient data (0)	
Chronic Kidney Disease			
Renal Replacement Therapy	Yes (2) (moderate –high association)	Yes (3) (moderate association)	One population study had a moderate-level association between recognized COVID-19 and CKD (reported as a binary: yes/no) while another had a high-level association between renal replacement therapy and recognized COVID-19. Three unmatched cohort studies reported moderate-strength associations between CKD and severe COVID-19 although studies did not stratify CKD by stage or renal replacement. Risk factors for severe COVID-19 in CKD were assessed only in hemodialysis patients.
No Renal Replacement Therapy	Yes – Possible (low strength association) (1)	Yes (3) (moderate association)	
Chronic Liver Disease	Insufficient data (0)	Insufficient data (0)	There was no population-level data on risk of recognized COVID-19 in chronic liver disease but one observational cohort of hospitalised patients with COVID-19 identified a low-strength association between mortality and moderate-severe liver disease.
Primary Immune Deficiencies	Insufficient data (0)	Insufficient data (0)	There was no population-level data on risk of recognized COVID-19 or severity in primary immune deficiencies, although there have been case reports in patients with these conditions.

- Not unexpectedly, previously identified risk factors for severe COVID-19 including age, male gender, obesity, smoking, and other co-morbidities (hypertension, CVD, diabetes) appear to be associated with increased risk of severe COVID-19 outcomes in immunosuppressed patients as well. These factors are often described in immunocompromised patients in cohort studies assessing risk factors for severe COVID-19 and likely confound the results. Additional identified disease and therapy specific factors are mentioned below.
- **Patients with active cancer:** Patients with hematological malignancies and lung cancers appear to be at increased risk for severe disease compared to other malignancies. Relapsing or progressive cancer, functional impairment, lymphopenia <0.5/L (at baseline), and severe hypogammaglobulinemia <4g/L (at baseline particularly in in multiple myeloma) are associated with an increased risk of severe COVID-19 in active cancer patients with moderate-high strength associations from unmatched observational cohorts.
- **Patients with autoimmune diseases:** As a group, these patients do not appear to be at increased risk for recognized COVID-19; however, the presence of certain risk factors in these conditions appear to be associated with severe COVID-19 outcomes (see below). However, epidemiological studies have not addressed differences in disease type routinely (e.g., SLE patients are likely at higher risk of complications) and other subtleties in therapy or co-morbidities.

- **In patients with IBD,** active IBD and corticosteroids are associated with an increased risk of severe COVID-19 outcomes.
- **In patients with psoriasis:** there is no published cohort data assessing outcomes of COVID-19 although a number of registries are collecting information.
- **In patients with rheumatic diseases,** systemic rheumatic diseases (SLE, CTD, inflammatory myositis, sarcoidosis, Raynaud's phenomenon), prednisone >10mg/day, and co-morbidities (ILD and CKD) are associated with an increased risk of severe COVID-19 outcomes. Continuation of therapies used to control these diseases may therefore reduce the risk of hospitalization and other severe outcomes.
- **In patients with multiple sclerosis,** increased disability and progressive MS are associated with increased risk of severe COVID-19 outcomes.

- **Transplant patients:** In solid organ transplant recipients, transplant specific factors (eg: organ transplanted, time post-transplant, level of immunosuppression) were not associated with risk of COVID-19 severity (although age, gender, and co-morbidities were associated with COVID-19 severity among patients with solid organ transplants).
- **Patients with chronic kidney disease:** The majority of data was available from patients on renal replacement therapy. Severe COVID-19 outcomes in patients on hemodialysis appears to be associated with previously defined risk factors (age, co-morbidities), and severe symptoms at onset. One study identified patients with longer hemodialysis vintage to be at increased risk of mortality.

Immunosuppressive Medications

The impact of immunosuppression-inducing therapies on risk of recognized COVID-19 or disease severity (hospitalization, ICU admission, and death) is summarized in the table below. The majority of these data is from cohorts of patients with specific conditions who were on these therapies (ie: cohorts were not specifically selected for immunosuppressive medications).

Therapy	Risk of recognized COVID-19 or disease severity	Comments on available evidence
Corticosteroids	There appears to be increased risk of recognized COVID-19 and disease severity with corticosteroid use, most likely at doses >10mg/day prednisone equivalent.	Corticosteroid use had a high strength association with risk of recognized COVID-19 in an unmatched cohort of a small number of patients with immune-mediated inflammatory diseases, however, dose was not specified and confidence intervals were wide. With respect to disease severity, corticosteroid use had moderate strength associations with increased disease severity in active cancer, IBD, and rheumatic diseases. Studies in active cancer and IBD unmatched cohorts either did not specify corticosteroid dose or only analyzed risk with prednisone >20mg/day. One study in a cohort of rheumatic patients analyzed severity with prednisone >10mg/day and noted a moderate strength association with hospitalization.
Chemotherapy	There does not appear to be an association with COVID-19 severity in analysis of chemotherapeutic treatment within 4 weeks of COVID-19 diagnosis	Evidence from two observational cohort studies without matched controls.
Immune Checkpoint Inhibitors	Conflicting information/Further information needed	Association with COVID-19 severity in one observational cohort, but sub-group analysis showed this only in lung cancer (which was also noted to increase severity). Two other observational cohorts did not find an association
Conventional Synthetic Disease Modifying Drugs (eg: methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, azathioprine, 5-ASA)	There does not appear to be an association with csDMARDs and COVID-19 severity. (Unmatched cohort studies)	In unmatched cohort studies, csDMARDs were not associated with risk of COVID-19 severity. In one unmatched cohort of IBD patients, 5-ASA/sulfasalazine was associated with a composite of ICU admission, ventilator use, and/or death but this was not seen in the other IBD cohort study. Furthermore, it is unclear if these patients had increased IBD activity, co-morbidities or corticosteroid use compared to patients who were on other therapies. Data assessing risk in individual DMARDs in a controlled manner was not available.

Biologic Disease Modifying Drugs *Examples (specific agents, not inclusive)* TNF-inhibitors (infliximab/Remicade, adalimumab/Humira, golimumab/Simponi, certolizumab/Cimzia, etanercept/Enbrel) IL-1 Inhibitors (anakinra/Kineret, canakinumab/Ilaris) IL-6 inhibitors (tocilizumab/Actemra, sarilumab/Kevzara) IL-12/23 inhibitors (ustekinumab/Stelara) IL-17 inhibitors (secukinumab/Cosentyx, ixekizumab/Taltz, brodalumab/Siliq) IL-23 inhibitors (guselkumab/Tremfya, risankizumab/Skyrizi) integrin antagonists (vedolizumab/Entyvio) B-cell depleting therapies (rituximab/Rituxan, ocrelizumab/Ocrevus)	There does not appear to be an association with risk of either recognized COVID-19 or high COVID severity overall. There may be reduced severity of COVID-19 with bDMARD use (unmatched cohort studies.) **Although there are studies ongoing looking at bDMARD use in to treat inflammatory manifestations of severe COVID-19 lung disease these medication should not be presumed to protect against infection.*	Assessment of recognized COVID-19 is from one Italian population-based study with low numbers of COVID-19 in patients on bDMARDs. The impact of physical distancing measures in infection risk in this study is unclear. Unmatched cohort studies have not shown an association with bDMARDs and recognized COVID-19. bDMARDs (as a whole) do not appear to be associated with severe COVID-19 in unmatched cohorts of patients with autoimmune disease. In an unmatched cohort of IBD patients on bDMARDs, there was no association with COVID-19 severity, but in an unmatched cohort of rheumatic patients, there was reduced hospitalization with bDMARD use. TNF-inhibitors were the highest percentage of bDMARDs included in these studies. COVID-19 has been described in patients on B-cell depleting therapies (such as rituximab) and there is no signal for increased disease severity within the context of larger epidemiological studies; however, numbers are. Furthermore, malignancy dosing of B-cell depletion therapy has not been well studied. There is insufficient information on cyclophosphamide.
Targeted Synthetic Disease Modifying Drugs (eg: JAK-inhibitors such as tofacitinib/Xeljanz, bariticinib/Olumiant, upadacitinib/Rinvoq, ruxolitinib/Jakavi)	There does not appear to be an association with risk of recognized COVID-19 (population based study, low numbers) or severity (unmatched cohort studies).	Assessment of recognized COVID-19 is from one Italian population-based study with low numbers of COVID-19 in patients on tsDMARDs. The impact of physical distancing measures in infection risk in this study is unclear. Unmatched cohort studies have not shown an association with bDMARDs and COVID-19 or severity and one unmatched cohort reported a reduced risk of hospitalization with tsDMARD use.
Disease Modifying Therapies used in the treatment of multiple sclerosis (and not included above; eg: fingolimod)	There does not appear to be an association with risk of COVID-19 severity. ((unmatched cohort studies).	One unmatched cohort showed no association between disease modifying therapy for MS and COVID-19 severity on multivariate analysis and one unmatched cohort showed reduced hospitalization for COVID-19 in MS patients on disease modifying therapy on univariate analysis.
Induction Anti-rejection Therapies (eg: anti-thymocyte globulin, alemtuzumab)	Further information needed	There was no published information on risk of recognized COVID-19 or severity with induction doses of anti-rejection therapies.
Maintenance Anti-rejection Therapies (eg: mycophenolate, calcineurin inhibitors)	Conflicting information/Further information needed	Anti-rejection therapies were not associated with mortality in a global cohort of transplant patients but mycophenolate was associated with a composite of respiratory support, ICU admission, and/or death in a smaller (n=111) cohort of liver transplant patients. Majority of patients in this cohort were male, older, and/or had significant co-morbidities, therefore, further information on mycophenolate is needed.

Pediatric Population

- There is insufficient information on immunosuppressed pediatric patients with limited descriptive studies of small unmatched cohorts.

- There may be increased incidence of COVID-19 in pediatric cancer patients, although mainly mild disease has been noted.
- There is no data on risk of COVID-19 or severity in pediatric patients with autoimmune diseases.
- Published evidence of COVID-19 in transplant patients were limited to case reports with no assessment of risk of infection or severity.
- There is no data on COVID-19 in pediatric patients with chronic kidney disease.

Committee Discussion

Overall, the committee was in agreement that available evidence on risk of COVID-19 in immunosuppressed populations was limited by significant flaws in study designs, small sample sizes, bias due to confounding factors, and heterogeneity of available data. They acknowledged that although certain immunosuppressed populations appear to be at increased risk of recognized COVID-19 or severe outcomes, it is difficult to disentangle the risks associated with the presence of confounders (eg: higher age, comorbid conditions) and as such a much of the data was insufficient to deriving anything more than preliminary conclusions. The tables provided in the evidence summary were updated to better reflect the amount of insufficient data, provide brief comments on available data, and to optimize readability based on condition/therapy.

Given the limitations of data available, the committee was unable to provide concrete recommendations regarding risk management of immunosuppressed patients as pandemic restrictions are lifted (eg: whether enhanced public health strategies are required or if patients at increased risk should be provided medical notes for workplace avoidance). To better reflect nuances involved in the discussion, the practical recommendations provide considerations for physicians where formal recommendations could not be made. Due to the limitations of available evidence, questions will remain about whether additional strategies in the workplace are required to reduce risk for immunosuppressed populations.

The committee expressed a desire for studies with appropriately matched controls and increased stratification to better assess the risk of COVID-19 and severe outcomes. The research gaps section was formulated based on this discussion.

There was overall agreement within the committee with the findings presented in this report.

Recommendations

1. Immunosuppressed patients should continue to follow physical distancing measures and hand hygiene measures as recommended by Alberta Health where possible.
   Rationale: Patients with immunosuppressed conditions are being diagnosed with COVID-19 and the degree of community risk may be underestimated given broad early adoption of physical distancing in these populations. Patients with cancer and chronic kidney disease appear to be at increased risk of developing recognized COVID-19.
2. Immunosuppressed patients should continue on prescribed disease therapy, unless otherwise directed by their healthcare provider.
   Rationale: Broadly, immunosuppressive therapy does not appear to be associated with increased risk of COVID-19 infection or severe outcomes. However, increased disease activity, particularly when increased doses of corticosteroids are used, appears to be associated with more severe COVID-19 outcomes. Optimal disease control should be a goal.
3. Patients should not abruptly discontinue corticosteroid use. However, healthcare providers should consider additional disease-modification therapy, where necessary, to successfully taper steroid use (to the lowest possible dose without risking a disease flare), with a goal to achieve disease control and reduce any excess risk of COVID-19 infection and severity.
   Rationale: Corticosteroids at doses greater than prednisone 10mg/day chronically appear to be associated with increased COVID-19 infection and severe outcomes. Furthermore, active IBD appears to be associated independent of steroid dose with severe COVID-19 outcomes.
4. Since age and some comorbidities are associated with severe COVID-19 outcomes, individual assessment of immunosuppressed patients should, whenever possible, include risk of recognized

COVID-19 and severe outcomes, taking into account age, underlying illness, co-morbidities, and chronic therapy (including corticosteroid use).
Rationale: Risk of recognized and severe COVID-19 varies based on underlying disease, disease activity, corticosteroid use, age, and co-morbidities (CVD, HTN, ILD, severity of chronic kidney disease).

Practical Considerations

- Actual risk of recognized COVID-19 or severe outcomes is likely under-estimated in this report due to broad adoption of early physical distancing measures by patients who would typically be considered at high risk for infection and limited testing during early phases of the pandemic.
- The majority of available studies were observational cohort studies with limited evidence utilizing appropriately matched controls in immunosuppressed patients. These study designs are likely a reflection of the speed with which COVID-19 information is being disseminated to provide information globally and will likely evolve as more information is available over a longer time period. Given the study designs, there is significant confounding by other risk factors (age, gender, co-morbidities) and direct contribution of immunosuppression to risk in COVID-19 cannot be determined at this time.
- With the recognition that risk behavior in immunosuppressed populations may have been modified and the inability to stratify risk assessment because of insufficient data (e.g. disease severity, monotherapy vs combination therapy), the following statements may be considerations when assessing risk of recognized COVID-19 and/or severity in the immunosuppressed populations. These suggestions are based on the limited available evidence and reasonable inferences based on similarities and differences in immunosuppressed conditions and/or therapies:
    - Patients with active cancer should be considered to be at increased risk of COVID-19 and severe outcomes based on the limited data available. Hematologic and lung cancers should be considered highest risk of severe COVID-19 outcomes among patients with active cancer. In additional to previously identified risk factors, relapsing or progressive cancers, functional disability, lymphopenia <0.5/L, and severe hypogammaglobulinemia <4g/L should be considered to increase the risk of severe COVID-19.
    - Young patients with autoimmune disease in remission without additional medical co-morbidities (see below) are likely not at increased risk of severe outcomes of COVID-19.
        - The following risk factors should be considered to be associated with an increased risk of severe COVID-19 outcomes in patients with autoimmune disease: older age (>65), co-morbidities (obesity, chronic lung disease, cardiovascular disease, hypertension), active or progressive autoimmune disease, systemic rheumatologic disease (e.g. SLE, CTD)
    - Chronic kidney disease should be considered to be associated with increased risk of COVID-19 and severe outcomes, especially in patients who are on renal replacement therapy.
    - Corticosteroid use: more data on risk of COVID-19 in corticosteroid use stratified by dose is needed. In the interim, chronic (> 14 days) corticosteroid use of prednisone equivalent >10mg/day are considered to be associated with an increased risk of recognized COVID-19 and severe outcomes.
    - The available evidence suggests that other immunosuppressive therapies are not associated with increased risk of COVID-19 or severe outcomes, although this does not include the risk of developing other non-COVID-19 related infections. There is limited data on individual therapies, and more data on the risks of COVID-19 in these populations as COVID-19 is expected restrictions are lifted.

Advice for patients:

- Immunosuppressed patients considered to be at increased risk for recognized COVID-19 or severe outcomes on the basis of this review should be advised to
  (1) follow recommended guidelines for physical distancing and hand hygiene
  (2) take additional measures (e.g., use of medical masks and eye protection if distancing is not possible) where there is a high risk of COVID-19 transmission, particularly if they live or work in higher-transmission, higher-risk settings or in communities under a COVID-19 watch as determined by Public Health.

- Recommendations regarding workplace avoidance cannot be made based on the results of this report, although this may change as restrictions are lifted and more information is available. In the interim, physicians should consider requesting reasonable workplace accommodations in patients identified to be at increased risk for recognized COVID-19 or severe outcomes as discussed above.
- It is beyond the scope of this review to discuss management of immunosuppressive conditions following exposure to COVID-19 or a positive COVID-19 diagnosis.
- It is beyond the scope of this review to assess mechanisms for altered COVID-19 risks in patients with immunosuppressive conditions.

Strength of Evidence

Evidence from primary literature was largely consistent between articles and is corroborated by the included grey literature. Most included studies were peer-reviewed, and all included studies are applicable to the population in Alberta.

Limitations of this review

This review is limited by small sample sizes in some studies, primarily due to the rarity of some immunosuppressive conditions. Population-based studies assessing the risk of COVID-19 with specific immunosuppressive conditions/therapies and comparing risk to the general population are limited, and the actual risk of COVID-19 may be underestimated due to limited testing during early phases of the pandemic and broad adoption of preventative measures in the immunosuppressed population. Data on pediatric patients was very limited. Published articles are subject to bias due to the presence of potential confounding factors (eg: age, obesity, co-morbidities) and the absence of appropriately matched controls. We included some studies that were not discovered on original literature search or did not meet inclusion criteria to illustrate subtleties of risk amongst immunosuppressed patients. Given the short turn-around time for this report and to ensure applicability to Alberta, included studies required assessment of European or North American patients and publication in English. Thus, relevant studies may be missing from this review. Due to the nature of COVID-19 literature, one included study was a pre-print and did not undergo the peer-review process.

Research Gaps

Well-designed studies comparing immunosuppressed patients with appropriately matched controls to reduce the risk of confounding are needed for true estimation of risk. Furthermore, the majority of data assess immunosuppressive conditions in a binary fashion (eg: presence or absence of disease). More robust data is needed in assessing risk within the immunosuppressed population including stratification based on disease activity and amount of immunosuppressive therapy (eg: induction vs maintenance, monotherapy vs combination therapy). Finally, Canadian data is needed to assess the risk of recognized COVID-19 in immunosuppressed populations in the context of our healthcare system.

Summary of Evidence

Fifty-one articles were included in the narrative synthesis below, of which 39 were identified from the initial literature search results of 623 articles. Additional included articles were discovered from recommended articles on PubMed, reference lists of included articles, and on recommendation from reviewers involved with this report. The full search strategy is described in the appendix. Abstracts were reviewed by the writer to ensure analyzed studies fulfilled inclusion and exclusion criteria (also outlined in the appendix). Eight articles describing grey literature were included *ad hoc*. Evidence is summarized based on immunosuppressive disease category, and the grey literature complements results reported in the primary literature, lending credibility to the findings of this review. Unless otherwise mentioned, data in pediatric patients was lacking in the immunosuppressed population.

Evidence from secondary and grey literature

Credible policies and guidelines regarding risk of COVID-19 and severity were identified through major medical societies associated with immunosuppressive conditions.

Cancer patients
The American Society of Clinical Oncology (General Information about COVID-19 & Cancer, 2020) states that incidence of COVID-19 is higher in patients with cancer compared to the general population, and cancer patients are at increased risk of severe complications and mortality. Hematological cancers (including leukemia, lymphoma, and multiple myeloma) were specifically identified as being associated with increased hospitalization based on data from the USA, United Kingdom, and Turkey. Furthermore, they deemed patients with hematological cancers to be at increased risk of mortality based on an analysis from China that showed increased risk of death in hematological malignancies (primarily acute myeloid leukemia, acute lymphoblastic leukemia, plasma cell myeloma, and non-Hodgkin's lymphoma). Lung cancer was also mentioned as being specifically associated with increased mortality based on one published report of high rates of mortality in lung cancer patients in New York.

IBD and rheumatic disease patients
With respect to inflammatory diseases, the American Gastroenterological Association Clinical Practice Update (Rubein et al., 2020) states that there is no baseline increased risk of COVID-19 in patients with IBD, but it is unclear if bowel wall inflammation is a risk factor for COVID-19 infection. The American College of Rheumatology (Mikuls et al., 2020) did not identify risk factors for poor outcomes with COVID-19 that are specific to rheumatic disease; however, it acknowledged that age and select co-morbidities that are associated with poor outcomes in preliminary studies are frequently overrepresented in patients with rheumatic diseases.

Transplant patients
The American Society of Transplantation (2019-nCOV (Coronavirus): FAQs for Organ Transplantation, 2020) acknowledges that data on transplant patients with COVID-19 is limited, and risk factors for severe disease have not been fully characterized. It notes that risk factors (e.g., renal dysfunction, diabetes, cardiac disease, lung disease, and obesity) for severe COVID-19 in normal hosts are common in transplant patients.

In the pediatric population (Downes et al., 2020), the American Society of Transplantation states that there is no evidence to suggest that pediatric solid organ transplant recipients get COVID-19 more often than other children; however, the limited number of reports of pediatric SOT recipients with COVID-19 are insufficient to determine if this is truly the case. However, pediatric SOT patients should be managed as a higher-risk population when it comes to school re-entry decisions and they provide further information to facilitate this. Based mostly on experience with other respiratory viruses in the pediatric SOT population, and considering risk factors for severe COVID-19 infection in other populations, they suggest the following factors may increase the risk of severe COVID-19 in pediatric SOT recipients: (i) having undergone transplantation in the last 3-6 months, (ii) receiving high doses of immunosuppression (especially in the setting of acute/subacute rejection), and (iii) having other medical conditions such as diabetes, obesity, or certain lung conditions.

Patients with chronic kidney disease
The Immunonephrology Working Group of the European Renal Association-European Dialysis and Transplant Association (Anders et al., 2020) recommends patients with immune-mediated kidney disease be considered at risk to experience a more severe disease course of COVID-19. Individual risk assessment may assist decision-making for more or less rigid preventative measures or disease-related interventions. Highest risk for COVID-19 complications in immune-mediated kidney disease were reported as:

- Age >60 years
- Male gender
- Active disease
- Extrarenal solid organ involvement, especially lung or heart
- eGFR <30mL/min
- Nephrotic syndrome or massive proteinuria
- Severe hypogammaglobulinemia (< 4 g/L)
- Several and poorly controlled co-morbidities
- High dose or combination immunosuppressive therapy

- Symptomatic COVID-19 infection

These recommendations also provide assistance in managing immune-mediated kidney disease patients who have been exposed to/develop COVID-19; however, this information is beyond the scope of this report.

The Canadian Society of Nephrology COVID-19 Rapid Response Team (White et al., 2020) recommends that questions on whether patients with chronic kidney disease (CKD) be advised to refrain from working be handled on a case-by-case basis. Although CKD patients appear to be at increased risk of severe COVID-19 infection, there is insufficient evidence to determine whether patients with CKD Stage IV and V not on dialysis (eGFR<30mls/min) and who are not on immunosuppression are at increased risk of infection. Furthermore, advanced age and co-morbidities that increase risk of COVID-19 infection and severity are prevalent in CKD.

Chronic Liver Disease patients
In a position paper (Boettler et al., 2020), the European Association for the Study of the Liver and the European Society of Clinical and Microbiology and Infectious Diseases report patients with chronic liver disease do not appear to be overrepresented in cohorts of patients with COVID-19; however, there is a recognized shortage of appropriate studies.

Evidence from the primary literature

Forty epidemiological articles were identified that evaluated associations between immunosuppressive conditions and therapies (as defined above) and recognized COVID-19 or COVID-19 outcomes. Studies were required to assess populations in North America and Europe to be considered applicable to the population in Alberta. For the purpose of this review, severe COVID-19 infection is defined as hospitalization, ICU admission, invasive ventilation, and/or death. The literature described is divided into major immunosuppressive categories below. Low strength associations are defined as OR <1.67 or HR <1.5; moderate strength associations are defined as OR 1.68-3.47 or HR/RR 1.5-2.5; and high strength associations are defined as OR>3.47 or HR/RR >2.5.

Overall, cancer and CKD appear to be associated with increased risk of recognized COVID-19 infections. Immunosuppressive conditions appear to be associated with increased risk of severe COVID-19 outcomes, but the risk is not the same within each category and varies with underlying diagnosis. Age, co-morbidities, disability, and disease activity were most likely to be associated with increased risk of severe COVID-19. Immunosuppressive therapy, with the exception of prednisone >10mg/day, was not associated with increased risk of severe COVID-19 outcomes. The majority of studies included significant confounding factors, thus it is difficult to estimate risk directly attributable to the immunosuppressed state in these patients.

Malignancy and cancer therapy (including chemotherapy and immune checkpoint inhibitors)

Thirteen articles were identified that measured associations between cancer and risk of developing COVID-19, risk of severe COVID-19 outcomes, or factors associated with severe outcomes.

Research Question 1
Only one study was identified that assessed risk of COVID-19 in patients with cancer compared to those without cancer at a population level. In this Italian study (Montopoli et al., 2020), an increased risk of COVID-19 in males with cancer compared to those without cancer was noted with an odds ratio of 1.79 (95% CI: 1.62-1.98). Subgroup analysis showed increased risk of COVID-19 infection in prostate cancer patients not on androgen deprivation therapy compared to those on it (OR 4.04, 95% CI 1.55-10.69) and in patients with other tumors compared to those on androgen deprivation therapy for prostate cancer (OR 4.86, 95% CI 1.88-12.56).

Risk of COVID-19 in pediatric cancers compared to the general population is unavailable, but a Spanish study (de Rojas et al., 2020) estimated a 1.3% prevalence of recognized COVID-19 in the pediatric cancer population in Madrid compared to 0.8% in the general pediatric population.

Research Question 2
Two meta-analyses assessing multi-national populations (including USA and Europe) were identified that assessed the risk of severe COVID-19 disease in patients with cancer compared to those without cancer. Patients

with cancer were at increased risk of death with COVID-19 compared to patients without cancer, although in one meta-analysis (Venkatesulu et al., 2020), increased risk was not present in subgroup analysis of patients in USA or Europe. This meta-analysis, however, included studies with significant heterogeneity and inconsistent measured outcomes. Furthermore, overall mortality and geographical subgroup analysis was not corrected for age and other co-morbidities. In three other studies of patients in North America or Europe, cancer was associated with increased risk of COVID-19 mortality. In the pre-print meta-analysis (Venkatesulu et al., 2020), subgroup analysis based on type of malignancy revealed an increased risk of mortality with hematological malignancies (OR 2.39, 95% CI 1.17-4.87) and lung cancer (OR 1.83, 95% CI 1.00-3.37) compared to other types of cancer. Subgroup analysis of treatment modalities did not show increased risk of mortality with chemotherapy, immunotherapy, radiotherapy, or targeted therapy, although specific regimens were not evaluated. In the second meta-analysis (Giannakoulis et al., 2020), subgroup analysis of the 8 studies that assessed mortality in patients >65 years age, all-cause mortality was not different in patients with COVID-19 and cancer compared to patients with COVID-19 without cancer (RR 1.06, 95% CI 0.79-1.41, p=0.71). A small US cohort (Suleyman et al., 2020) showed an increased risk of mechanical ventilation with cancer in COVID-19.

There is limited data for the pediatric population; however, in one small Italian cohort (Bisogno et al., 2020) of 26 pediatric patients with an active hematological or solid organ malignancy who were diagnosed with COVID-19, the majority had mild infection and only one patient required oxygen support.

Table 1: Association between malignancy and severe COVID-19 outcomes using multivariable analysis

Reference	Jurisdiction	Study Design	Study Size (Cancer patients)	Outcome (No cancer)	Association
Docherty et al., 2020	United Kingdom	Observational cohort – hospitalized patients	20,133 (1,743)	Death	HR 1.13 (1.02-1.24)
Fabio et al., 2020	Italy	Observational cohort – hospitalized patients	410 (22)	Death	HR 2.32 (1.15-4.67)
Giannakoulis et. al., 2020	Multi-national (China, US, Italy, UK, Iran)	Meta-analysis	46,499 (1,776)	Mortality	RR 1.66 (1.33-2.07)
				ICU admission	RR 1.56 (1.31-1.87)
Mehta et al., 2020	United States	5:1 (no cancer: cancer) age and gender-matched case control	1,308 (218)	Death	OR 2.45
Suleyman et al., 2020	United States	Observational cohort – hospitalized patients	463 (49)	Mechanical ventilation	2.5 (1.2-5.0)
Venkatesulu et al., 2020	Multi-national (China, US, Europe)	Meta-analysis	181,323 (23,736)	Death	OR 2.54 (1.47-4.42)

Six studies reported risk factors for severe disease in patients with cancer and included patients in North America or Europe. Hematological malignancy, lung cancer, relapsing cancer, progressive cancer, male gender, increased age, functional impairment, lymphopenia (< 700 cells/mm^3 at baseline), severe hypogammaglobulinemia (at baseline in multiple myeloma), and other co-morbidities (CVD, diabetes, hypertension) were associated with increased risk of severe COVID-19 in patients with cancer. Two studies (Kuderer et al., 2020 and Lee et al., 2020) assessed risk of severe disease with anti-cancer therapy within 4 weeks prior to the diagnosis of COVID-19 and did not find an association with chemotherapy, immunotherapy, hormonal therapy, or targeted therapy. One study (Robilotti et al., 2020) did report increased risk of severe disease with immune checkpoint inhibitor (ICI) therapy; however, subgroup analysis based on type of malignancy showed this risk with ICI use in lung cancer only. It is unknown if this risk was secondary to SARS-CoV-2 infection or if there was acute lung injury secondary to ICI therapy. Furthermore, lung cancer was noted independently to increase the risk of severe respiratory illness. This study also assessed a composite of lymphopenia (<0.5/L) or corticosteroids (prednisone >20mg/day or equivalent) as associated with an increased risk of hospitalization. Poor performance status, based on ECOG scores, was also associated with increased risk of death in patients with cancer (Kuderer et al., 2020). There is a

scarcity of evidence assessing specific anti-cancer regimens including specific chemotherapeutic agents (and doses) and immune check point inhibitors.

*Table 2: Factors associated with increased severity of COVID-19 in adult cancer patients on multivariable analysis (*Univariate analysis in Lee et al., 2020 and Wang et al., 2020)*

Reference	Jurisdiction	Study Design	Study Size	Malignancy	Outcome	Risk Factors
Assaad et al., 2020	France	Observational cohort – cancer patients	302	Mixed (77.5% Solid Tumours; 22.5% Hematological)	Death	Male gender (HR 2.75, 1.91-3.59) Karnofsky performance status < 60 (HR 4.87, 3.87-5.87) Relapsing cancer (HR 3.05, 1.83-4.87) Respiratory symptoms (HR 5.09, 4.11-6.07) Lymphopenia <700/uL (HR 3.05, 2.19-2.91)
Garassino et al., 2020	Multi-national	Observational cohort – thoracic cancer patients	200	Thoracic (76% NSCLC)	Death	Smoking (OR 3.18, 1.11-9.06)
Kuderer et al., 2020	Multi-national (USA, Canada, Spain)	Observational cohort – cancer patients	928	Mixed (82% Solid tumours, 22% Hematological)	Death	Age, per 10 years (OR 1.84, 1.53-2.21) Male gender (OR 1.63, 1.07-2.48) Former smoker (OR 1.60, 1.03-2.47) 2 or more co-morbidities (2 comorbidities OR 4.50, 1.33-15.28; >4 co-morbidities OR 3.55, 1.03-12.30) Present cancer (Stable/Response to treatment OR 1.79, 1.09-2.95; Progressive cancer OR 5.20, 2.77-9.77) ECOG 2 (OR 3.89, 2.11-7.18) ECOG 3 or 4 (OR 5.66, 2.79-11.47)
Lee et al., 2020*	UK	Observational cohort – cancer patients	800	Mixed (Solid Tumours 73%, Hematological 22%)	Death	Age (OR 9.42, 6.56-10) Male gender (OR 1.67, 1.19-2.34) Hypertension (OR 1.95, 1.36-2.80) Cardiovascular disease (OR 2.32, 1.47-3.64)
Robilotti et al., 2020	USA	Observational cohort – cancer patients	423	Mixed (Solid Tumours 76%; Hematological 24%)	Hospitalization	Hematologic cancer (OR 2.49, 1.35-4.67) Chronic lymphopenia or corticosteroids (OR 1.85, 1.06-3.24) Immune checkpoint inhibitor (OR 2.84, 1.24-6.72)
					High-flow O_2/ Mechanical ventilation	Age >65 (OR 1.67, 1.07-2.60) Immune checkpoint inhibitor (OR 2.74, 1.37-5.46) Lung cancer (OR 3.31, 1.68-6.52)
Wang et al., 2020*	United States	Observational cohort – plasma cell disorder patients	58	Multiple myeloma	Hospitalization	Age >70 (OR 7.74, 1.51-78.12) Male gender (OR 3.7, 1.08-13.81) High CV risk (OR 3.42, 1.01-12.4) Diabetes (OR 6.18, 1.19-62.84) Lymphopenia <0.5 x 10^9/L (OR ∞, 0.99-∞)
					Death	Race (non-White) (OR 10.49, 1,35-481.76) Severe Hypogammaglobulinemia (IgG <400mg/dL) (OR 7.80, 0.97-97.75)

Autoimmune/Autoinflammatory Disease including immunomodulatory therapy (including DMT, csDMARDs, bDMARDs, tsDMARDs)

Fifteen articles were identified that measured associations between autoimmune disease and therapies and risk of developing COVID-19, risk of severe COVID-19 outcomes, or factors associated with severe outcomes. The majority of data on rheumatic disease was in patients with inflammatory arthritis (eg: rheumatoid arthritis, psoriatic arthritis, seronegative spondyloarthropathy) and limited data was available specifically for systemic rheumatic illnesses (SLE, CTD, inflammatory myositis, sarcoidosis, Raynaud's phenomenon). Some studies included a small number of patients with autoinflammatory syndromes including Adult Onset Still's Disease and Familial Mediterranean Fever; however, these were analyzed together with other rheumatic diseases. There were no published studies on pediatric autoinflammatory syndromes.

Research Question 1

Three population-based studies assessed the risk of COVID-19 in patients with autoimmune or autoinflammatory diseases. In a single-centre study from Madrid (Taxonera et al., 2020), 12 of 1,918 IBD patients were diagnosed with COVID-19. IBD patients had a lower adjusted incidence ratio of COVID-19 (OR 0.74, 95% CI 0.70-0.77) and a similar associated mortality ratio (OR 0.95, 95% CI 0.84-1.06) compared to the general population. Approximately 18% of patients were on azathioprine and 16% were on biologic therapy (predominantly TNF inhibitors (TNFi)) in this study. An Italian report on the risk in patients on biologics or small molecules for psoriasis (Damiani et al., 2020) found an increased risk of testing positive for COVID-19 (OR 3.43, 95% CI 2.25-5.73) compared to the general population; however, there was no report on or adjustment for likely confounding factors (such as age and co-morbidities). As such, this report may overestimate the risk of recognized COVID-19 in psoriasis patients. Another study (Salvarani et al., 2020) assessing patients on bDMARDs and tsDMARDs compared to all patients in the Reggio Emilia region of Italy found no statistically significant difference in positive COVID-19 tests or hospitalization.

Three studies evaluated risk factors for increased risk of recognized COVID-19 infection in patients with autoimmune/inflammatory diseases. Previously identified risk factors for COVID-19 (including increased age, hypertension, and obesity) were associated with an increased risk of COVID-19 in patients with rheumatic diseases (Fredi et al., 2020). In immune-mediated inflammatory diseases (Haberman et al., 2020), biologic medications (eg: TNFi, IL17 inhibitors, IL12/23 inhibitors, IL23 inhibitor), JAK inhibitors, and mesalamine were not associated with an increased risk of COVID-19 infection. Prednisone was associated with increased risk of recognized COVID-19 in immune mediated inflammatory diseases (Haberman et al., 2020), however, doses were not specified and risk was not stratified by dose. In one study of European patients with multiple sclerosis (Dalla Costa et al., 2020), secondary progressive MS had a reduced risk of COVID-19 symptoms compared to relapsing-remitting MS. Although there was a trend toward increased risk of COVID-19 symptoms with cladribine/alemtuzumab use, the overall rate of COVID-19 testing (n=10) and positive tests (n=4) in this population was low and no conclusions can be made.

A retrospective analysis (via database screening) of 6228 autoimmune rheumatic disease patients in Hubei showed an overall infection COVID infection rate of 0.43% in the assessed rheumatic patient cohort (Zhong et al, 2020). There were 42 rheumatic patient households with a COVID case (lab confirmed or clinically diagnosed) identified - in these households the rheumatic patients OR of infection was 2.68 versus household members without rheumatic disease but exposure risks and disease activity as a risk were not assessed. The study period encompassed the main epidemic curve in Hubei. However, without a population based comparator (outside of the higher risk household contact situation) these data do not establish a comparative risk for rheumatic patients and risk reduction practices and relative testing rates are not described.

Table 3: Factors associated with increased risk of COVID-19 in autoimmune and autoinflammatory disease

Reference	Jurisdiction	Study Design	Study Size	Disease	Outcome (compared to no COVID-19 unless specified)	Risk Factors
Fredi et al., 2020	Italy	Observational cohort	1525	Rheumatic diseases (IA, Vasculitis,	Confirmed COVID-19 (compared to suspected)	Age >65 (OR 4.4, 1.9-9.9) Arterial hypertension (OR 2.8, 1.3-6.1)

				CTD, and Still's disease)		Obesity (OR 11.0, 1.3-83.4)
Haberman et al., 2020	USA	Observational cohort	86	IMID (RA, PsA, AS, IBD, PsO, related disorders)	Suspected and confirmed COVID-19	Prednisone (OR 27.41, 1.77-424.42)
					Confirmed COVID-19	Prednisone (OR 44.45, 1.37-536.32) Methotrexate (OR 27.8, 1.37-562.32; Not adjusted for acute medication use such as steroids)
Dalla Costa et al., 2020	Italy, Spain, Denmark	Observational cohort	399	Multiple sclerosis	COVID-19 defined as fever or anosmia/ ageusia and any other COVID-19 symptoms or respiratory symptoms and 2 other COVID-19 symptoms	Increased risk on cladribine/ alemtuzumab (OR 3.78, 1.00-15.93)
					COVID-19 defined as fever and any other COVID-19 symptom or cough/dyspnea and anosmia/ageusia	Increased risk on cladribine/ alemtuzumab (OR 4.87, 1.10-21.04)

Research Question 2

Three studies were identified and assessed risk of severe COVID-19 disease in patients with autoimmune disease compared to those without autoimmune disease. These were single-country studies with two assessing the Italian population and one based out of the United States. Patients with psoriasis on biologics and small molecules were at increased risk for hospitalization, but not ICU admission or death, in an Italian study (Damiani et al., 2020); however, the analysis was unadjusted and did not account for likely confounding factors. Patients with rheumatic diseases were not at increased risk of death (D' Silva et al., 2020 and Fredi et al., 2020) or hospitalization (D'Silva et al., 2020) but did have an increased risk of ICU and mechanical ventilation (D'Silva et al., 2020) with an odds ratio of 3.11 (1.07-9.05) compared to patients with COVID-19 without rheumatic diseases. In this study, patients with rheumatic diseases were also more likely to have baseline interstitial lung disease and obstructive sleep apnea. Thirty-seven percent of patients had rheumatoid arthritis and 19% had a diagnosis of systemic lupus erythematosus (higher than expected). Furthermore, of the hospitalized patients included in the study with rheumatic disease and COVID-19, 63% of these patients had active rheumatic disease. Although not formally assessed, elevated rheumatic disease activity, overrepresentation of SLE in patient cohort, and increased lung disease may have contributed to elevated risk of ICU admission and mechanical ventilation in rheumatic patients with COVID-19. In a small US cohort (Wallace et al., 2020) of patients with SLE (n=5) compared to other rheumatic diseases (n=31), SLE patients had much higher hospitalization (80% vs 19%), mechanical ventilation (60% vs 13%), and death (20% vs 0%).

A global cohort (Gianfrancesco et al., 2020) reported an increased risk of hospitalization with prednisone >10mg/day but similar doses of prednisone were not associated with a composite of ICU, mechanical ventilation, or death in a smaller Italian study (Scire et al., 2020). Studies assessing rheumatic disease did not find increased risk with use of csDMARDs, bDMARDs/tsDMARDs, combination csDMARDs and bDMARDS, or prednisone <10mg/day. The COVID-19 Global Rheumatology Alliance Registry (Gianfrancesco et al., 2020) reported a reduced risk of hospitalization with bDMARD/tsDMARD use. This may be due to reduction of pro-inflammatory cytokines with these medications with downstream reduction of cytokine storm, although studies of bDMARDs and tsDMARDs for treatment of COVID-19 are underway. There was no specific evidence regarding the risk of cyclophosphamide in rheumatic diseases with COVID-19.

Table 4: Association between autoimmune diseases and severe COVID-19 outcomes (* Damiani et al., 2020 reported unadjusted OR)

Reference	Jurisdiction & Disease	Study Design	Study Size (Autoimmune Disease)	Outcome (No autoimmune disease)	Association
Damiani et al., 2020*	Italy, Psoriasis on biologics and small molecules	Unmatched case control	10, 061, 767 (1193)	Hospitalization	OR 3.59 (1.49-8.63)
				ICU admission	None
				Death	None
D'Silva et al., 2020	USA, Rheumatic disease (RA, SLE, PMR, spondyloarthritis, myositis)	2:1 (no rheumatic disease vs rheumatic) age, gender, and diagnosis date-matched case control	156 (52)	Hospitalization	None
				ICU admission/Mechanical ventilation (Adjusted for age, BMI, smoking, number of comorbidities)	OR 3.11 (1.07-9.05)
				Death	None
Fredi et al., 2020	Italy	2:1 hospitalized (no rheumatic vs rheumatic) age, gender, and admission month-matched case control	88 (26)	Death	None

Seven studies reported risk factors for severe disease in patients with autoimmune diseases and included patients in North America or Europe. There was published information on inflammatory bowel disease, rheumatic diseases, and multiple sclerosis. Two dermatology registries (Mahil et al., 2020) have been set up to gather observational data on COVID-19 outcomes in patients with psoriasis (PsOProtect) and atopic dermatitis (SECURE-AD), but these have yet to publish reports, although preliminary data showed no increased risk in these patients.

In inflammatory bowel disease, age, active IBD, increasing co-morbidities, and corticosteroids were associated with increased risk of severe COVID-19. Ulcerative colitis was associated with increased risk of COVID-19 pneumonia but not death in a small study (Bezzio et al., 2020). Active IBD continued to increase the risk of COVID-19 pneumonia and death in a statistically significant manner even after adjusting for corticosteroid therapy (Bezzio et al., 2020). A global study (Brenner et al., 2020) reported an increased risk of severe disease with 5-ASA/Sulfasalazine use but this was not seen in the smaller Italian study (Bezzio et al., 2020). TNFi and other immunosuppressive therapy were not associated with increased risk of COVID-19 severity in patients with inflammatory bowel disease.

Two studies assessed risk factors in multiple sclerosis and found age, obesity, increased disability, and progressive multiple sclerosis were associated with more severe COVID-19. Disease-modifying therapy was not associated with hospitalization (Parrotta et al., 2020) and in a univariate analysis, patients on disease-modifying therapy had a statistically significant lower risk of severe disease (Louapre et al., 2020).

*Table 5: Factors associated with increased severity of COVID-19 in autoimmune and autoinflammatory disease patients on multivariable analysis (*Univariate analysis in Bezzio et al., 2020 and Parrotta et al., 2020)*

Reference	Jurisdiction	Study Design	Study Size	Disease	Outcome	Risk Factors
Bezzio et al., 2020*	Italy	Observational cohort	79	Inflammatory bowel disease	COVID-19 pneumonia	Age >65 (OR 5.81, 1.15-29.66) Charlson Comorbidity Index >1 (OR 2.91, 1.06-9.21) Ulcerative Colitis diagnosis (OR 2.72, 1.06-6.99) Active IBD (OR 10.25, 2.11-49.73)
					Death	Age >65 (OR 19.6, 2.95-130.6)

						Charlson Comorbidity Index >1 (OR 16.66, 1.80-153.9) Active IBD (OR 8.45, 1.26-56.56)
Brenner et al., 2020	Global	Observational cohort	525	Inflammatory bowel disease	Composite of ICU admission, Ventilator use, and/or death	Increased age (OR 1.04, 1.01-1.06) ≥2 comorbidities (OR 2.87, 1.1-7.8) Systemic corticosteroids (OR 6.87, 2.3-20.5) 5-ASA/Sulfasalazine (OR 3.14, 1.3-7.7)
Freites et al., 2020	Spain	Observational cohort	123	Rheumatic diseases (IA, vasculitis, CTD, etc)	Hospitalization	Age (OR 1.08, 1.4-1.13) Systemic autoimmune conditions (OR 3.55, 1.30-9.67)
Gianfrancesco et al., 2020	Global	Observational cohort	600	Rheumatic diseases (IA, Vasculitis, CTD, Gout, Sarcoidosis, etc)	Hospitalization	Age >65 (OR 2.56, 1.52-4.04) HTN or CVD (OR 1.86, 1.23-2.81) Lung disease (OR 2.48, 1.55-3.98) Renal insufficiency (OR 3.02, 1.21-7.54) Prednisone >10mg/day (OR 2.05, 1.06-3.96)
Scire et al., 2020	Italy	Observational cohort	232	Rheumatic diseases	Composite of ICU, Mechanical ventilation, or Death	No increased risk with immunosuppressive therapy
Louapre et al., 2020	France	Observational cohort	347	Multiple sclerosis	Severity score ≥ 3 (Hospitalization or worse)	Age (OR 1.85, 1.39-2.46) Obesity (OR 2.99, 1.03-8.70) EDSS 3-5.5 (OR 3.48, 1.55-7.84) EDSS ≥6 (OR 6.33, 2.78-14.39)
Parrotta et al., 2020*	USA	Observational cohort	76	Multiple Sclerosis and related disorders	Hospitalization	Age (95% CI 1.22-17.11) Progressive MS (OR 4.11, 1.21-13.97) Ambulatory assistance/Non-ambulatory (OR 4.27, 1.38-13.27) Obesity (OR 6.25, 1.90-20.50)

Transplantation including anti-rejection medications

There was limited data available on transplant patients and COVID-19. Only four studies were identified that assessed associations between organ transplant recipients and COVID-19.

Research Question 1

There were no population-level studies on the risk of COVID-19 in transplant patients. Current data is limited to case series with small numbers reporting descriptive statistics. COVID-19 has been reported in patients with kidney (Husain et al., 2020), liver (Webb et al., 2020), heart (Holzhauser et al., 2020), lung (Aigner et al., 2020), and bone marrow transplants (Kanellopoulos et al., 2020). These case reports describe presenting symptoms similar to the general population with a wide range of outcomes including mild disease, hospitalization, ICU admission, mechanical ventilation, and death. An observational cohort study (Colmenero et al., 2020) of 111 liver transplant patients in Spain reported doubled standardized (age- and gender-matched) incidence rates of COVID-19 in liver transplant patients compared to the general Spanish population during the study time, although risk ratios were not calculated. Larger studies are needed to determine the risk of COVID-19 in transplant patients compared to the general population.

Data on COVID-19 and pediatric transplant patients are also limited to case reports. However, a previous multi-centre study (Danziger-Isakov et al., 2019) reported hospital-associated respiratory virus infection commonly in the first year after solid organ transplant and an association with younger age at transplant, although coronavirus infections were not evaluated in this study. Hospitalized respiratory virus infections (Fisher et al., 2018) were also

commonly diagnosed following hematopoietic stem cell transplant, although coronavirus infections were uncommon (6 patients with no deaths).

Research Question 2

A single-centre case-control study from the United States (Chaudhry et al., 2020) assessed outcomes of COVID-19 in hospitalized solid organ transplant (n=35) recipients compared to hospitalized COVID-19 patients without transplants (n=100). There was no difference between groups in the primary outcome (composite of ICU admission, mechanical ventilation, or death), or independently assessed secondary outcomes of ICU admission, mechanical ventilation, or death. Most of the transplants included in this study were renal transplants. The study initially described characteristics of 35 hospitalized solid organ transplant recipients and 12 non-hospitalized solid organ transplant recipients with COVID-19, but it did not assess risks of hospitalization or other severe outcomes within organ transplants. Interestingly, of the 5 heart and 4 lung transplant recipients included in the study, all were hospitalized. Compared to kidney and liver transplant, heart and lung transplants often require higher doses of induction and maintenance immunosuppressive therapy (Clinical Guidelines for Transplant Medications, 2019).

Two studies reported risk factors for death in patients with solid organ transplants and included patients in North America or Europe. Increased death was associated with increased age, co-morbidities (congestive heart failure, chronic lung disease, obesity), lymphopenia (<0.5/L), elevated IL-6 levels, and abnormal chest imaging at baseline. In kidney transplant patients (Cravedi et al., 2020) with COVID-19, a higher baseline eGFR was associated with reduced in-hospital mortality (OR 0.97, 0.93-0.99). In the global study (Kates et al., 2020) time post-transplant, thoracic vs other transplants, and level of immunosuppression was not associated with mortality. However, a prospective cohort of liver transplant recipients in Spain (Colmenero et al., 2020) reported a relative risk of 3.94 (95% CI 1.59-9.74) of severe COVID-19 (composite of respiratory support, ICU admission, and/or death) in liver transplant patients on mycophenolate. This risk was not seen with calcineurin inhibitors or other immunosuppressive medications in this study. It is worth noting 51% of patients in this study were on mycophenolate and over half were over 65, male, and/or had multiple co-morbidities.

Although there is no data on post-hematopoietic stem cell transplants with COVID-19, a previous analysis of human coronaviruses (Eichenberger, 2018) showed age >50 (OR 3.63, 1.16-11.35), corticosteroids within 30 days of diagnosis (OR 2.00, 1.00-8.88), and low serum albumin (OR 3.94, 1.09-14.22) were associated with increased risk of progression to lower respiratory tract infection. Hypogammaglobulinemia (< 6 g/L) in patients following stem cell transplant increase risk of infection, especially with encapsulated bacteria (Espinoza et al., 2018).

Table 6: Factors associated with increased severity of COVID-19 in organ transplant recipient patients on multivariable analysis

Reference	Jurisdiction	Study Design	Study Size	Transplant	Outcome	Risk Factors
Colmenero et al., 2020	Spain	Observational cohort	111	Liver	Composite of respiratory support, ICU admission, and/or death	Male gender (RR 2.49, 1.14-5.41) Charlson Comorbidity (RR 1.28, 1.05-1.56) Mycophenolate (RR 3.94, 1.59-9.74)
Cravedi et al., 2020	USA, Spain, Italy	Observational cohort	144	Kidney (All hospitalized)	Death	Age >60 (OR 1.07, 1.02-1.14) Respiratory rate >20 (OR 6.88, 1.63-41.98) Elevated IL-6 level (OR 1, 1-1.01)
Kates et al., 2020	Global	Observational cohort	482	Solid organ (66% kidney, 15.1% liver, 11.8% heart, 6.2% lung)	Death	Age >65 (OR 3.0, 1.7-5.5) Congestive heart failure (OR 3.2, 1.4-7.0) Chronic lung disease (OR 2.5, 1.2-5.2) Obesity (OR 1.9, 1.0-3.4) Lymphopenia (OR 1.9, 1.1-3.9) Abnormal chest imaging (OR 2.9, 1.1-7.5)

Chronic Kidney Disease

Nine articles were identified that measured associations between CKD and the risk of developing COVID-19, risk of severe outcomes, or factors associated with severe outcomes. These studies either reported CKD in a binary fashion (yes/no) or they reported on severe CKD treated with renal replacement therapy. Data specifically on patients with mild chronic kidney disease (such as CKD Stage I and II) was unavailable.

Research Question 1

Two population-based studies assessing the risk of COVID-19 in patients with CKD were identified. In a primary care study from the UK (Lusignan et al., 2020), increased risk of COVID-19 occurred in CKD identified in a binary fashion (CKD was defined as either yes or no). A much higher odds ratio of recognized COVID-19 was reported in an Italian population-based study (Manganaro et al., 2020) for patients on renal replacement therapy.

Table 7: Incidence of COVID-19 in the CKD population compared to the general population

Reference	Jurisdiction	Study Design	Study Size (CKD patients)	Outcome (No renal disease)	Association
Lusignan et al., 2020	United Kingdom	Cross-Sectional	3,802 (207)	COVID-19 in CKD	OR 1.91 (1.31-2.78)
Manganaro et al., 2020	Italy	Cross-Sectional	4,482,072 (5793)	COVID-19 in renal replacement therapy (HD, PD, graft)	OR 13.43 (11.27-16.00)

One study assessed risk factors for increased COVID-19 in a cohort of hemodialysis patients. This single-centre cohort study of 1530 patients receiving dialysis (Corbett et al., 2020) found a univariable HR of 1.11 (1.02-1.21) and a multi-variable HR of 1.09 (0.99-1.20) for time to COVID-19 with increased age (per decade increase).

Research Question 2

Three studies were identified that assessed risk of severe COVID-19 independently in patients with CKD compared to those with no pre-existing renal disease in a European or North American population. ICU admission, mechanical ventilation, in-hospital mortality, and death all increased in patients with CKD. Argenziano et al included patients with CKD who were on dialysis and patients who were not on dialysis, although exact numbers of either population was not documented and analysis was conducted in CKD patients as a whole. The other two studies did not define CKD beyond presence or absence of the condition.

Table 8: Association between CKD and severe COVID-19 outcomes. Included studies used multivariable analysis

Reference	Jurisdiction	Study Design	Study Size (CKD patients)	Outcome (No renal disease)	Association
Argenziano et al., 2020	United States	Observational cohort - patients treated at a centre in New York City	1,000 (137)	Death	HR 1.61 (1.06-2.43)
Docherty et al., 2020	United Kingdom	Observational cohort – hospitalized patients	20,122 (2830)	In-hospital mortality	HR 1.28 (1.18-1.39)
Suleyman et al., 2020	USA	Observational cohort – hospitalized patients	463 (182)	ICU admission	OR 2.0 (1.3-3.3)
				Mechanical ventilation	OR 2.4 (1.4-4.2)

Risk factors for increased COVID-19 severity in patients on hemodialysis were assessed in three studies and included age, co-morbidities (ischemic heart disease, chronic respiratory disease), and symptoms at onset (fever, dyspnea, cough). A French cohort (Chawki et al., 2020) reported immunosuppressive therapy with increased risk for death in hemodialysis patients with COVID-19, but did not specify the type of immunosuppressive therapy. Studies involving other immunosuppression-inducing conditions have shown increased risk of death with corticosteroids but not with steroid-sparing immunosuppressants. A small Spanish study (Goicoechea et al., 2020) of hemodialysis patients found that the only baseline risk factor for increased in-hospital death was longer hemodialysis vintage. Baseline co-morbidities were not associated with a risk of in-hospital mortality, but this

study contained relatively few patients. No studies assessing patients with CKD not on renal replacement therapy were identified.

Table 9: Factors associated with increased severity of COVID-19 in CKD patients on multivariable analysis

Reference	Jurisdiction	Study Design	Study Size	Disease Severity	Outcome	Risk Factors
Alberici et al., 2020	Italy	Observational cohort	94	Hemodialysis	ARDS	Age >70 (OR 1.1, 1-1.15) Ischemic heart disease (OR 7.5, 1.6-36.3) Fever at onset (OR 17, 4.5-64) Shortness of breath (OR 20, 3.6-79.3)
					Death	Fever at onset (OR 18.7, 2.4-146) Cough at onset (OR 3, 1.02-17.6) CRP at onset >50mg/L (OR 5.6, 1.6-23.5)
Chawki et al., 2020	France	Observational cohort	248	Hemodialysis	Death	Age (OR 1.04, 1.01-1.09) Facility living (OR 17.29, 3.95-75.6) Chronic respiratory failure (OR 7.47, 1.18-47.39) Immunosuppressive therapy (OR 8.32, 2.19-31.55) Dyspnea at onset (OR 3.14, 1.24-7.96)
Goicoechea et al., 2020	Spain	Observational cohort	36	Hemodialysis	Death (In Hospital)	Longer hemodialysis vintage (OR 1.008, 1.001-1.015)

Miscellaneous Conditions

Chronic Liver Disease

There is limited data on risks of COVID-19 in patients with chronic liver disease or cirrhosis that are applicable to the Albertan population. A large UK prospective cohort (Docherty et al., 2020) identified an increased risk of mortality in hospitalized COVID-19 patients with moderate to severe chronic liver disease (identified in 301 of 17360 patients) COVID-19 on multivariate analysis (HR 1.51, 95% CI 1.21-1.88).

Primary Immune Deficiencies

There are no epidemiological studies on the risk of COVID-19 in patients with primary immune deficiencies including X-linked agammaglobulinemia, combined variable immune deficiency, severe combined immune deficiency, IgA deficiency, and other humoral immune deficiencies. Intact cell-mediated immunity is likely more important than humoral immunity in response to SARS-CoV-2 infection. Patients with X-linked agammaglobulinemia (although diagnosed with COVID-19) had mild infections (Sorasina et al., 2020). A patient with combined variable immunodeficiency (Fill et al., 2020) required hospitalization with mechanical ventilation due to complications from COVID-19. More data is needed in primary immune deficiencies, although epidemiological data may remain insufficient due to the rarity of these conditions.

Evolving Evidence

The bulk of the evidence in this report is specific to COVID-19; however, study sizes are limited due to small numbers of reported COVID-19 in patients with immunosuppressive conditions. Evidence regarding risk factors associated with these conditions may change as further data becomes available or as more patients with immunosuppressive conditions return to work and school. Immunosuppressive medications, with the exception of prednisone >10mg/day, are not associated with increased risk of COVID-19 or severe outcomes; however, risk may change with results of studies currently underway to assess immunosuppressive medications as treatment for hyperinflammatory states in COVID-19. Theoretically, bDMARDs and tsDMARDs may have a reduced risk of severe COVID-19 outcomes as they block pro-inflammatory cytokine release or signaling, which reduces the cytokine storm responsible for outcomes such as acute respiratory distress syndrome.

Date question received by advisory group: August 5, 2020

Date report submitted to committee: August 27, 2020

Date of first assessment: September 9, 2020

(If applicable) Date of re-assessment: N/A

Authorship and Committee Members

This report was written by Shahna Tariq and primary review was completed by Mohamed Osman. Secondary review of this report was completed by Lynora Saxinger, Catherine Burton, Robert Gniadecki, Daniel Muruve, Jan Willem Cohen Tervaert, and Nicola Wright. The full Scientific Advisory Group was involved in discussion and revisions of the document: Braden Manns (co-chair), Lynora Saxinger (co-chair), John Conly, Alexander Doroshenko, Nelson Lee, Elizabeth MacKay, Andrew McRae, James Talbot, Shelley Duggan, Jeremy Slobodan, Brandie Walker, and Nathan Zelyas.

COVID-19 Scientific Advisory Group
Rapid Evidence Report

Appendix

List of Abbreviations

AHS: Alberta Health Services
AS: Ankylosing Spondylitis
bDMARD: Biologic Disease-Modifying Antirheumatic Drug
CKD: Chronic kidney disease
COVID-19: Coronavirus Disease-2019csDMARD: Conventional Synthetic Disease-Modifying Antirheumatic Drug
CTD: Connective tissue disease
CVD: Cardiovascular disease
DMT: Disease Modifying Therapy
ECOG: Eastern Cooperative Oncology Group
EDSS: Expanded Disability Status Scale
HD: Hemodialysis
HTN: Hypertension
IA: Inflammatory arthritis
IBD: Inflammatory Bowel Disease
ICU: Intensive Care Unit
IMID: Immune-Mediated Inflammatory Disease
KRS: Knowledge Resource Services
MS: Multiple Sclerosis
NSCLC: Non-Small Cell Lung Carcinoma
OR: Odds Ratio
PD: Peritoneal Dialysis
PsA: Psoriatic Arthritis
PsO: Psoriasis
RA: Rheumatoid Arthritis
RR: Relative Risk
RT-PCR: Reverse Transcription Polymerase Chain Reaction
SAG: Scientific Advisory Group
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
TNFi: Tumour Necrosis Factor inhibitor
tsDMARD: Targeted Synthetic Disease-modifying Antirheumatic Drug

Methods

Literature Search

A literature search was conducted by Joycelyn Jaca from Knowledge Resources Services (KRS) within the Knowledge Management Department of Alberta Health Services. KRS searched databases for articles published from [state dates of publications of interest], and included: OVID Medline, CINAHL, and PubMed. The full search strategy is included below. Briefly, the search strategy involved combinations of keywords and subject headings including:

- Hematologic malignancies: Leukemia, Lymphoma, Multiple myeloma
- Other malignancies: Colon cancer, Lung cancer, Breast cancer, Skin cancer, Melanoma, Adenocarcinoma
- Autoimmune diseases:
    - Gastrointestinal: Inflammatory bowel disease, Ulcerative colitis, Crohn's Disease, Autoimmune hepatitis, Primary biliary cirrhosis
    - Rheumatic: Rheumatoid arthritis, Psoriatic arthritis, Enteropathic arthritis, Ankylosing spondylitis, Spondyloarthropathy, Spondyloarthritis, Vasculitis, Granulomatosis

with polyangiitis, Microscopic polyangiitis, Eosinophilic granulomatosis with polyangiitis, giant cell arteritis, Takayasu's arteritis, polyarteritis nodosa, polymyalgia rheumatica, dermatomyositis, polymyositis, anti-synthetase syndrome, systemic sclerosis, scleroderma, Sjogren's syndrome, mixed connective tissue disease, connective tissue disease, Behcet's disease, IgA vasculitis, ANCA-vasculitis, Juvenile idiopathic arthritis
    - Pulmonary: Interstitial lung disease, Interstitial lung disease with autoimmune features, Non-specific interstitial pneumonia, Usual interstitial pneumonia
    - Neurologic: Multiple sclerosis, Myasthenia gravis, Guillain-Barre syndrome, Chronic inflammatory demyelinating polyneuropathy
    - Dermatologic: Psoriasis, Discoid lupus, Pyoderma gangrenosum, hidradenitis suppurativa
    - Renal: IgA nephritis, Glomerulonephritis
- Autoinflammatory diseases: Adult onset Still's disease, Familial Mediterranean Fever, CAPS (Cryopyrin-Associated Autoinflammatory Syndromes), TRAPS (Tumor Necrosis Factor Receptor-Associated Periodic Syndrome), PAPA (Pyogenic Arthritis, Pyoderma gangrenosum and Acne), CANDLE (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature Syndrome)
- Primary Immune Deficiencies: X-linked agammaglobulinemia, Combined variable immune deficiency, Severe combined variable immune deficiency, IgA deficiency, IgG subclass deficiency
- Chronic infections: HIV, Hepatitis B, Hepatitis C
- Other: Chronic liver failure, cirrhosis, chronic renal failure, chronic kidney disease, dialysis, intermittent hemodialysis, peritoneal dialysis
- Transplants:
    - Solid organ transplant: Lung transplant, Kidney transplant, Liver transplant, Cardiac (or heart) transplant
    - Bone marrow: Stem cell transplant, Hematopoietic stem cell transplant, Autologous stem cell transplant, Allogenic stem cell transplant, CAR T-cell therapy, CAR T-cell transplant
- Medications:
    - Steroids: Corticosteroids, Prednisone, Dexamethasone, Methylprednisolone, Hydrocortisone, Budesonide
- Conventional DMARDs: Methotrexate, leflunomide, sulfasalazine, azathioprine, hydroxychloroquine (or Plaquenil), 5-ASA, mesalamine, pentaza, mesalazine, mycophenolate
- Biologics:
    - TNF-inhibitors: Remicade (infliximab), Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab pegol) and Simponi (golimumab)
    - IL-1 inhibitors: anakinra, canakinumab
    - IL-6 inhibitors: tocilizumab
    - IL-17 inhibitiors: secukinumab, ixekizumab, brodalumab
    - IL-12/23 inhibitors: ustekinumab
    - IL-23 inhibitors: guselkumab, risankizumab, tildrakizumab
    - Anti-CD20 therapy: rituximab, ocrelizumab, obinutuzumab, ofatumumab, Ublituximab
    - Integrin blockers: vedolizumab
- JAK inhibitors: tofacitinib, baricitinib, upadacitinib, ruxolitinib
- Others: abatacept, aprelimast
- Immune checkpoint inhibitors: pembrolizumab, ipilimumab, nivoloumab
- Calcineurin inhibitors: tacrolimus, sirolimus, cyclosporine
- Transplant induction agents: Atgam, anti-thymocyte globulin, alemtuzumab
- Others: Cyclophosphamide, fingolimod
- Specific chemotherapeutic agents: Vincristine, vinblastine, paclitaxel, bleomycin, daunorubicin, doxirubicin, etoposide, ibrutinib, cytarabine, 5-fluorouracil, tamoxifen, anastrazole, letrozole, azacitidine, cisplatin, carboplatin, docetaxel, epirubicin, fludarabine, gemcitabine, fluorouracil, ifosfamide, lenalidomide, bortezomib, thalidomide, goserelin, leuprolide, mercaptopurine, triretinoin, bendamustine, melphalan, capecitabine
- Chemotherapy regimens: CHOP, CHOP-R, ABVD

Articles identified by KRS in their search were initially screened by title against the inclusion/exclusion criteria listed in Table 1 below. 623 articles were identified by KRS with references and abstracts provided for further review. 584 were excluded from the review in accordance with the inclusion/exclusion criteria stated below. Twelve additional articles that met inclusion criteria below were identified subsequently based on review of recommended articles on PubMed, reference lists, and recommendations by the reviewers of this report.

Table 1. Inclusion and exclusion criteria for results of the literature search

Inclusion Criteria	Exclusion Criteria
- Epidemiological studies describing association between defined immunosuppressive condition/therapy and COVID-19 infection or severity - Measure of association is calculated in primary studies - In primary literature, study population must include patients from Europe and North America - Case series ≥20 patients, Observational studies, Systematic reviews, Meta-analyses, Grey literature, Pre-prints - Published in 2019 or later	- Article is not from a credible source - Article does not have a clear research question or issue - Presented data/evidence is not sufficient to address the research questions - Article is not in English - Case reports, Case series <20 patients, Commentary, Narrative review, Modelling studies, Editorial - No measure of association calculated or only descriptive statistics reported - Main purpose of article is to generate hypotheses for increased/decreased risk or provide guidance on management of patients with COVID-19 - Studies assessing immunosuppressive therapy as treatment for COVID-19

Critical Evaluation of the Evidence

Exclusion criteria for study quality were adapted from the Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018). Potential articles were evaluated on three criteria: 1) Peer reviewed or from a reputable source; 2) Clear research question or issue; 3) Whether the presented data/evidence is appropriate to address the research question. Preprints and non peer-reviewed literature (such as commentaries and letters from credible journals) are not excluded out of hand due to the novelty of COVID-19 and the speed with which new evidence is available.

Table 10 below is a narrative summary of the body of evidence included in this review. The categories, format, and suggested information for inclusion were adapted from the Oxford Centre for Evidence-Based Medicine, the Cochrane Library, and the AGREE Trust (Urwin, Gavinder & Graziadio, 2020; Viswanathan et al, 2012; Wynants et al., 2020; Brouwers et al., 2010).

Table 10. Narrative overview of the literature included in this review.

	Description
Volume	Thirty-nine articles from the body of primary literature and eight from the grey literature were included in this review. Of the primary literature, 2 meta-analyses (1 was pre-print) were included and the rest were observational studies (mix of case series, retrospective cohort, and prospective cohort). All the observational studies were peer-reviewed. The grey literature was derived from reputable medical societies.
Quality	Generally, included studies were of moderate quality. The majority of included literature reported associations following multivariable analysis, reducing the risk for confounders

	and increasing the quality of the studies. However, There was a limited number of studies with appropriately matched controls used in comparison and these would have been important in significantly reducing bias from confounding. Time frames in studies was 28 days and may be too short to appropriately assess mortality-related outcomes. Sample sizes of the studies included vary greatly due to the nature of the immunosuppressive conditions included and number of controls available. However, this does not vastly affect the quality of included studies due to the consistent methods of statistical analysis.
Applicability	Association studies are applicable to the population in Alberta as comparable populations were selected for in the inclusion criteria (such as European and North American populations).
Consistency	Although some confidence intervals were quite large due to variations in study size, data for specific factors assessed were relatively consistent across studies.

Search Strategy

Neoplasms

CINAHL

S5	S1 AND S2 AND S3 AND S4
S4	"likelihood functions" OR "increased likelihood" OR "risk factors" OR Risk OR "Risk Assessment" OR "Odds Ratio" OR Probability OR "Severity of illness Index" OR "Disease susceptibility"
S3	“Hematologic Neoplasms” OR Leukemia OR Lymphoma OR “Multiple Myeloma” OR “Colonic Neoplasms” OR “Lung Neoplasms” OR “Breast Neoplasms” OR “Skin Neoplasms” OR Melanoma OR Adenocarcinoma OR Neoplasms
S2	Mortality OR “Respiration, Artificial” OR "mechanical ventilat*" OR “Critical Care” OR “Intensive Care Units” OR Hospitalization OR "hospital admission*"
S1	((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND ((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND DT 20191201-20300101)

Medline

Database: Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily <1946 to August 06, 2020>

Search Strategy:

---

1 exp Coronavirus/ (25078)

2 exp Coronavirus Infections/ (25877)

3 (coronaviru* or corona viru* or ncov* or n-cov* or novel cov* or COVID-19 or COVID-19 or COVID-2019 or COVID2019 or SARS-COV-2 or SarsCOV-2 or sarscov2 or sarscov19 or SARS-COV-19 or SARSCOV-19 or Sars-cov-2019 or sarscov2019 or sarscov-2019 or severe acute respiratory syndrome coronaviru* or severe acute respiratory syndrome cov 2 or severe acute respiratory syndrome or severe acute respiratory disease or 2019ncov or 2019 ncov).mp. (41734)

4 or/1-3 (44027)

5 exp Mortality/ (382671)
6 exp Respiration, Artificial/ (77072)
7 "mechanical ventilat*".mp. (42827)
8 exp Critical Care/ (57958)
9 exp Intensive Care Units/ (84739)
10 exp Hospitalization/ (240690)
11 "hospital admission*".ti. (4624)
12 or/5-11 (776088)
13 exp Hematologic Neoplasms/ (21146)
14 exp Leukemia/ (232208)
15 exp Lymphoma/ (171719)
16 exp Multiple Myeloma/ (41173)
17 exp Colonic Neoplasms/ (74742)
18 exp Lung Neoplasms/ (233037)
19 exp Breast Neoplasms/ (292640)
20 exp Skin Neoplasms/ (125174)
21 exp Melanoma/ (95085)
22 exp Adenocarcinoma/ (379927)
23 exp Neoplasms/ (3348104)
24 or/13-23 (3348104)
25 4 and 12 and 24 (76)
26 limit 25 to english language (76)
27 limit 26 to humans (74)
28 limit 27 to yr="2019 - 2020" (65)

PubMed

#11	Search: #7 AND #10 Filters: Humans, English
#10	Search: "likelihood functions" [MeSH] OR "increased likelihood" [tiab] OR "risk factors" [MesH] OR Risk [MeSH] OR "Odds Ratio" [MeSH] OR Probability [MeSH] OR "Severity of illness" [MeSH] Filters: Humans, English
#7	Search: #1 AND #2 #3 Filters: Humans, English, from 2019 - 2020
#6	Search: #1 AND #2 #3 Filters: Humans, from 2019 - 2020
#5	Search: #1 AND #2 #3 Filters: from 2019 - 2020
#4	Search: #1 AND #2 #3
#3	Search: "Hematologic Neoplasms" [MeSH] OR Leukemia [MeSH] OR Lymphoma [MeSH] OR "Multiple Myeloma" [MeSH] OR "Colonic Neoplasms" [MeSH] OR "Lung Neoplasms" [MeSH] OR "Breast Neoplasms" [MeSH] OR "Skin Neoplasms" [MeSH] OR Melanoma [MeSH] OR Adenocarcinoma OR Neoplasms [MeSH]
#2	Search: Mortality [MeSH] OR "Respiration, Artificial" [MeSH] OR "mechanical ventilat*" [tiab] OR "Critical Care" [MeSH] OR "Intensive Care Units" [MeSH] OR Hospitalization OR "hospital admission*" [tiab]
#1	Search: Coronavirus [MeSH] OR "Coronavirus Infections" [MeSH] OR 2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])

Autoimmune Diseases

CINAHL

S40	S1 AND S33 AND S39
S39	S34 OR S35 OR S36 OR S37 OR S38
S38	(MH "Hospitalization+")
S37	(MH "Intensive Care Units+")
S36	(MH "Critical Care+")
S35	(MH "Respiration, Artificial+") OR (MH "Ventilators, Mechanical")
S34	(MH "Mortality+")
S33	S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32
S32	(MH "Glomerulonephritis+")
S31	(MH "Hidradenitis Suppurativa")
S30	(MH "Hidradenitis+")
S29	(MH "Pyoderma Gangrenosum")
S28	(MH "Lupus Erythematosus, Cutaneous") OR (MH "Lupus Erythematosus, Systemic+")
S27	(MH "Psoriasis+")
S26	"chronic inflammatory demyelinating polyneuropathy"
S25	(MH "Myasthenia Gravis")
S24	(MH "Idiopathic Interstitial Pneumonias+")
S23	(MH "Lung Diseases, Interstitial+")
S22	(MH "Arthritis, Juvenile Rheumatoid")
S21	(MH "Behcet's Syndrome")
S20	(MH "Connective Tissue Diseases+")
S19	(MH "Sjogren's Syndrome")
S18	(MH "Scleroderma, Systemic+")
S17	(MH "Polymyositis+")
S16	(MH "Dermatomyositis")
S15	(MH "Takayasu Arteritis") OR (MH "Polyarteritis Nodosa")
S14	(MH "Microscopic Polyangiitis") OR "granulomatosis with polyangiitis"
S13	(MH "Vasculitis+") OR (MH "Giant Cell Arteritis") OR (MH "Behcet's Syndrome")

S12	(MH "Spondylarthritis+")
S11	(MH "Spondylarthropathies+")
S10	(MH "Spondylitis, Ankylosing")
S9	(MH "Arthritis+") OR (MH "Arthritis, Rheumatoid+") OR (MH "Arthritis, Psoriatic") OR (MH "Spondylarthritis+")
S8	(MH "Liver Cirrhosis+")
S7	(MH "Hepatitis, Autoimmune") OR (MH "Guillain-Barre Syndrome+") OR (MH "Hepatitis C+")
S6	"chron's disease"
S5	(MH "Colitis, Ulcerative")
S4	(MH "Inflammatory Bowel Diseases+")
S3	MH inflammatory bowel disease
S2	MH autoimmune diseases
S1	((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND ((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND DT 20191201-20300101)

Medline
Database: Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily <1946 to August 06, 2020>
Search Strategy:
---
1 exp Coronavirus/ (25078)
2 exp Coronavirus Infections/ (25877)
3 (coronaviru* or corona viru* or ncov* or n-cov* or novel cov* or COVID-19 or COVID-19 or COVID-2019 or COVID2019 or SARS-COV-2 or SarsCOV-2 or sarscov2 or sarscov19 or SARS-COV-19 or SARSCOV-19 or Sars-cov-2019 or sarscov2019 or sarscov-2019 or severe acute respiratory syndrome coronaviru* or severe acute respiratory syndrome cov 2 or severe acute respiratory syndrome or severe acute respiratory disease or 2019ncov or 2019 ncov).mp. (41734)
4 or/1-3 (44027)
5 exp Mortality/ (382671)
6 exp Respiration, Artificial/ (77072)
7 "mechanical ventilat*".mp. (42827)
8 exp Critical Care/ (57958)
9 exp Intensive Care Units/ (84739)
10 exp Hospitalization/ (240690)
11 "hospital admission*".ti. (4624)
12 or/5-11 (776088)
13 exp Inflammatory Bowel Diseases/ (80859)
14 exp Colitis, Ulcerative/ (34508)
15 exp Crohn Disease/ (38854)

16 exp Hepatitis, Autoimmune/ (3563)
17 exp Liver Cirrhosis, Biliary/ (8067)
18 exp Arthritis, Rheumatoid/ (112960)
19 exp Arthritis, Psoriatic/ (6125)
20 exp Arthritis/ (259325)
21 enteropathic arthritis.ti. (22)
22 exp Spondylitis, Ankylosing/ (14690)
23 exp Spondylarthropathies/ (24134)
24 exp Spondylarthritis/ (26137)
25 exp Vasculitis/ (95351)
26 exp Granulomatosis with Polyangiitis/ or exp Microscopic Polyangiitis/ (7266)
27 exp Giant Cell Arteritis/ (6462)
28 exp Takayasu Arteritis/ (3950)
29 exp Polyarteritis Nodosa/ (6047)
30 exp Polymyalgia Rheumatica/ (2521)
31 exp Dermatomyositis/ (7889)
32 exp Polymyositis/ (9301)
33 "anti-synthetase syndrome".ti. (75)
34 exp Scleroderma, Systemic/ (20559)
35 exp Sjogren's Syndrome/ (12779)
36 exp Mixed Connective Tissue Disease/ (1636)
37 exp Connective Tissue Diseases/ (304509)
38 exp Behcet Syndrome/ (9110)
39 exp Arthritis, Juvenile/ (10412)
40 exp Lung Diseases, Interstitial/ (55789)
41 "interstitial pneumonia".ti. (2602)
42 exp Multiple Sclerosis/ (58826)
43 exp Myasthenia Gravis/ (15479)
44 exp Guillain-Barre Syndrome/ (5089)
45 "chronic inflammatory demyelinating polyneuropathy".ti. (750)
46 exp Psoriasis/ (40065)
47 exp Lupus Erythematosus, Discoid/ (3177)
48 exp Pyoderma Gangrenosum/ (2149)
49 exp Hidradenitis/ or exp Hidradenitis Suppurativa/ (2017)
50 exp Glomerulonephritis, IGA/ or exp Glomerulonephritis/ (47400)
51 or/13-50 (800165)
52 4 and 12 and 51 (38)
53 limit 52 to (english language and humans and yr="2019 -Current") (33)

PubMed

#22	Search: #1 AND #2 AND #3 AND #4 Filters: Humans, English
#4	Search: "likelihood functions" [MeSH] OR "increased likelihood" [tiab] OR "risk factors" [MesH] OR Risk [MeSH] OR "Risk Assessment" [MeSH] OR "Odds Ratio" [MeSH] OR Probability [MeSH] OR "Severity of illness Index" [MeSH] OR "Disease susceptibility" [MeSH] Filters: Humans, English, from 2018 - 2020
#3	Search: "Autoimmune Diseases" [MeSH] OR "Inflammatory Bowel Diseases" [MeSH] OR "Colitis, Ulcerative" [MeSH] OR "Crohn Disease" [MeSH] OR "Hepatitis, Autoimmune" [MeSH] OR "Liver Cirrhosis, Biliary" [MeSH] OR "Arthritis, Rheumatoid" [MeSH] OR "Arthritis, Psoriatic [MeSH]" OR Arthritis OR "enteropathic arthritis" [tiab] OR "Spondylitis, Ankylosing" [MeSH] OR Spondylarthropathies [MeSH] OR Spondylarthritis [MeSH] OR Vasculitis [MeSH] OR "Granulomatosis with Polyangiitis" [MeSH] OR "Microscopic Polyangiitis" [MeSH] OR "Giant Cell Arteritis" [MeSH] OR "Takayasu Arteritis" [MeSH] OR "Polyarteritis Nodosa [MeSH]" OR

	"Polymyalgia Rheumatica" [MeSH] OR Dermatomyositis [MeSH] OR Polymyositis [MeSH] OR "anti-synthetase syndrome" [tiab] OR "Scleroderma, Systemic" [MeSH] OR "Sjogren's Syndrome" [MeSH] OR "Mixed Connective Tissue Disease" [MeSH] OR "Connective Tissue Diseases" [MeSH] OR "Behcet Syndrome" [MeSH] OR "Arthritis, Juvenile" [MeSH] OR "Lung Diseases, Interstitial" [MeSH] OR "interstitial pneumonia" [MeSH] OR "Multiple Sclerosis" [MeSH] OR "Myasthenia Gravis" [MeSH] OR "Guillain-Barre Syndrome" [MeSH] OR "chronic inflammatory demyelinating polyneuropathy" [tiab] OR Psoriasis [MeSH] OR "Lupus Erythematosus, Discoid" [MeSH] OR "Pyoderma Gangrenosum" [MeSH] OR Hidradenitis [MeSH] OR "Hidradenitis Suppurativa" [MeSH] OR "Glomerulonephritis, IGA" [MeSH Filters: Humans, English
#2	Search: Mortality [MeSH] OR "Respiration, Artificial" [MeSH] OR "mechanical ventilat*" [tiab] OR "Critical Care" [MeSH] OR "Intensive Care Units" [MeSH] OR Hospitalization OR "hospital admission*" [tiab]
#1	Search: Coronavirus [MeSH] OR "Coronavirus Infections" [MeSH] OR 2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])

Autoinflammatory and Chronic Diseases
CINAHL

S31	S1 AND S7 AND S29
S30	S1 AND S7 AND S29
S29	S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28
S28	(MH "Dialysis+") OR (MH "Peritoneal Dialysis+") OR (MH "Hemodialysis+")
S27	(MH "Kidney Failure, Chronic+") OR (MH "Renal Insufficiency, Chronic+")
S26	(MH "Liver Failure+") OR "end stage liver disease"
S25	(MH "Hepatitis C+") OR (MH "Hepatitis B+")
S24	(MH "Acquired Immunodeficiency Syndrome")
S23	(MH "Human Immunodeficiency Virus+") OR (MH "HIV Infections+")
S22	"chronic infection"
S21	"IgG deficiency"
S20	"iga deficiency"
S19	(MH "Common Variable Immunodeficiency") OR (MH "Severe Combined Immunodeficiency")
S18	(MH "Primary Immunodeficiency Diseases")
S17	"chronic atypical neutrophilic dermatosis"
S16	"chronic atypical neutrophilic dermatosis"
S15	"pyogenic arthritis"
S14	(MH "Pyoderma Gangrenosum")

S13	(MH "Acne Vulgaris")
S12	(MH "Tumor Necrosis Factor Receptor-Associated Periodic Syndrome") OR (MH "Tumor Necrosis Factor")
S11	(MH "Still's Disease, Adult-Onset")
S10	(MH "Cryopyrin-Associated Periodic Syndromes+")
S9	"familial mediterranean fever"
S8	(MH "Hereditary Autoinflammatory Diseases+") OR "autoinflammatory diseases"
S7	S2 OR S3 OR S4 OR S5 OR S6
S6	(MH "Hospitalization+")
S5	(MH "Intensive Care Units+")
S4	(MH "Critical Care+")
S3	(MH "Respiration, Artificial+") OR (MH "Ventilators, Mechanical")
S2	(MH "Mortality+")
S1	((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND ((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND DT 20191201-20300101)

Medline
Database: Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily <1946 to August 06, 2020>
Search Strategy:
---

1 exp Coronavirus/ (25078)
2 exp Coronavirus Infections/ (25877)
3 (coronaviru* or corona viru* or ncov* or n-cov* or novel cov* or COVID-19 or COVID-19 or COVID-2019 or COVID2019 or SARS-COV-2 or SarsCOV-2 or sarscov2 or sarscov19 or SARS-COV-19 or SARSCOV-19 or Sars-cov-2019 or sarscov2019 or sarscov-2019 or severe acute respiratory syndrome coronaviru* or severe acute respiratory syndrome cov 2 or severe acute respiratory syndrome or severe acute respiratory disease or 2019ncov or 2019 ncov).mp. (41734)
4 or/1-3 (44027)
5 exp Mortality/ (382671)
6 exp Respiration, Artificial/ (77072)
7 "mechanical ventilat*".mp. (42827)
8 exp Critical Care/ (57958)
9 exp Intensive Care Units/ (84739)
10 exp Hospitalization/ (240690)
11 "hospital admission*".ti. (4624)
12 or/5-11 (776088)

13 exp Hereditary Autoinflammatory Diseases/ or exp Familial Mediterranean Fever/ or exp Cryopyrin-Associated Periodic Syndromes/ (13684)
14 exp Still's Disease, Adult-Onset/ (1353)
15 exp Receptors, Tumor Necrosis Factor, Type I/ or exp Receptors, Tumor Necrosis Factor/ (48746)
16 exp Acne Vulgaris/ or exp Pyoderma Gangrenosum/ (13699)
17 Pyogenic Arthritis.ti. (116)
18 "chronic atypical neutrophilic dermatosis".ti. (6)
19 "autoinflammatory disease*".ti. (390)
20 exp Primary Immunodeficiency Diseases/ (12875)
21 exp Agammaglobulinemia/ (6366)
22 exp Common Variable Immunodeficiency/ or exp Autoimmune Diseases/ or exp Severe Combined Immunodeficiency/ (483295)
23 exp IgA Deficiency/ (1675)
24 exp IgG Deficiency/ (866)
25 "Chronic infection*".ti. (1382)
26 exp HIV/ (98870)
27 exp Acquired Immunodeficiency Syndrome/ (76311)
28 exp Hepatitis C/ or exp Hepatitis B/ (111838)
29 exp End Stage Liver Disease/ (2909)
30 exp Liver Failure/ (25318)
31 exp Fibrosis/ (160243)
32 exp Liver Cirrhosis/ (89318)
33 exp Kidney Failure, Chronic/ (93501)
34 exp Renal Insufficiency, Chronic/ (115086)
35 exp Renal Dialysis/ or exp Renal Replacement Therapy/ or exp Kidney Failure, Chronic/ (247093)
36 exp Peritoneal Dialysis/ (26153)
37 or/13-36 (1243567)
38 4 and 12 and 37 (82)
39 limit 38 to (english language and humans and yr="2019 -Current") (61)

PubMed

#5	Search: #1 AND #2 AND #3 AND #4 Filters: Humans, English
#4	Search: "Autoinflammatory Disease*" [tiab] OR "Familial Mediterranean Fever" [MeSH] OR "Cryopyrin-Associated Periodic Syndromes" [MeSH] OR "Still's Disease, Adult-Onset" [MeSH] OR "Receptors, Tumor Necrosis Factor, Type I" [MeSH] OR "Receptors, Tumor Necrosis Factor" [MeSH] OR "Acne Vulgaris" [MeSH] OR "Pyoderma Gangrenosum" [MeSH] OR "Pyogenic Arthritis" [tiab] OR "chronic atypical neutrophilic dermatosis" [tiab] OR "Primary Immunodeficiency Diseases" [MeSH] OR Agammaglobulinemia [MeSH] OR "Common Variable Immunodeficiency" [MeSH] OR "Severe Combined Immunodeficiency" [MeSH] OR "IgA Deficiency" [MeSH] OR "IgG Deficiency" [MeSH] OR "Chronic infection" [tiab] OR HIV [MeSH] OR "Acquired Immunodeficiency Syndrome" [MeSH] OR "Hepatitis C" [MeSH] OR "Hepatitis B" [MeSH] OR "End Stage Liver Disease" [MeSH] OR "Liver Failure" [MeSH] OR Fibrosis [MeSH] OR "Liver Cirrhosis" OR "Kidney Failure, Chronic" OR "Renal Insufficiency, Chronic" [MeSH] OR "Renal Dialysis" [MeSH] OR "Renal Replacement Therapy" [MeSH] OR "Kidney Failure, Chronic" [MeSH] OR "Peritoneal Dialysis" [MeSH] Filters: Humans, English
#3	Search: "likelihood functions" [MeSH] OR "increased likelihood" [tiab] OR "risk factors" [MesH] OR Risk [MeSH] OR "Risk Assessment" [MeSH] OR "Odds Ratio" [MeSH] OR Probability [MeSH] OR "Severity of illness Index" [MeSH] OR "Disease susceptibility" [MeSH] Filters: Humans, English, from 2018 - 2020

#2	Search: Mortality [MeSH] OR "Respiration, Artificial" [MeSH] OR "mechanical ventilat*" [tiab] OR "Critical Care" [MeSH] OR "Intensive Care Units" [MeSH] OR Hospitalization OR "hospital admission*" [tiab]
#1	Search: Coronavirus [MeSH] OR "Coronavirus Infections" [MeSH] OR 2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])

Transplants
CINAHL

S15	S1 AND S7 AND S13
S14	S1 AND S7 AND S13
S13	S8 OR S9 OR S10 OR S11 OR S12
S12	"CAR T-cell transplant"
S11	"CAR T-cell transplant"
S10	"car t-cell therapy"
S9	"allogenic stem cell transplant"
S8	(MH "Transplantation+") OR (MH "Lung Transplantation+") OR (MH "Kidney Transplantation+") OR (MH "Heart-Lung Transplantation") OR (MH "Bone Marrow Transplantation, Allogeneic") OR (MH "Heart Transplantation+") OR (MH "Bone Marrow Transplantation, Autologous") OR (MH "Hematopoietic Stem Cell Transplantation") OR (MH "Bone Marrow Transplantation+")
S7	S2 OR S3 OR S4 OR S5 OR S6
S6	(MH "Hospitalization+")
S5	(MH "Intensive Care Units+")
S4	(MH "Critical Care+")
S3	(MH "Respiration, Artificial+") OR (MH "Ventilators, Mechanical")
S2	(MH "Mortality+")
S1	((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND ((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND DT 20191201-20300101)

Medline
Database: Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily <1946 to August 06, 2020>
Search Strategy:
---
1 exp Coronavirus/ (25078)

2 exp Coronavirus Infections/ (25877)
3 (coronaviru* or corona viru* or ncov* or n-cov* or novel cov* or COVID-19 or COVID-19 or COVID-2019 or COVID2019 or SARS-COV-2 or SarsCOV-2 or sarscov2 or sarscov19 or SARS-COV-19 or SARSCOV-19 or Sars-cov-2019 or sarscov2019 or sarscov-2019 or severe acute respiratory syndrome coronaviru* or severe acute respiratory syndrome cov 2 or severe acute respiratory syndrome or severe acute respiratory disease or 2019ncov or 2019 ncov).mp. (41734)
4 or/1-3 (44027)
5 exp Mortality/ (382671)
6 exp Respiration, Artificial/ (77072)
7 "mechanical ventilat*".mp. (42827)
8 exp Critical Care/ (57958)
9 exp Intensive Care Units/ (84739)
10 exp Hospitalization/ (240690)
11 "hospital admission*".ti. (4624)
12 or/5-11 (776088)
13 exp Transplantation/ (514206)
14 exp Organ Transplantation/ (209813)
15 exp Lung Transplantation/ (16137)
16 exp Kidney Transplantation/ (95395)
17 exp Liver Transplantation/ (56459)
18 exp Heart Transplantation/ (35526)
19 exp Bone Marrow Transplantation/ or exp Hematopoietic Stem Cell Transplantation/ (86238)
20 exp Stem Cell Transplantation/ or exp Hematopoietic Stem Cell Transplantation/ (82366)
21 "autologous stem cell transplant".ti. (310)
22 exp Transplantation, Autologous/ (49950)
23 "allogenic stem cell transplant".ti. (11)
24 exp Immunotherapy, Adoptive/ (9164)
25 or/13-24 (522025)
26 4 and 12 and 25 (46)
27 limit 26 to (english language and humans and yr="2019 -Current") (33)

PubMed

#27	Search: #1 AND #2 AND #20 AND #25 Filters: Humans, English, from 2019 - 2020
#5	Search: #1 AND #2 AND #3 AND #4 Filters: Humans, English
#4	Search: Transplantation [MeSH] OR "Organ Transplantation" [MeSH] OR "Lung Transplantation" [MeSH] OR "Kidney Transplantation" [MeSH] OR "Liver Transplantation" [MeSH] OR "Heart Transplantation" [MeSH] OR "Bone Marrow Transplantation" [MeSH] OR "Hematopoietic Stem Cell Transplantation" [MeSH] OR "Stem Cell Transplantation" [MeSH] OR "Hematopoietic Stem Cell Transplantation" [MeSH] OR "autologous stem cell transplant" [tiab] OR "Transplantation, Autologous" [MeSH] OR "allogenic stem cell transplant" [tiab] OR "Immunotherapy, Adoptive" [MeSH] Filters: Humans, English
#3	Search: "likelihood functions" [MeSH] OR "increased likelihood" [tiab] OR "risk factors" [MesH] OR Risk [MeSH] OR "Risk Assessment" [MeSH] OR "Odds Ratio" [MeSH] OR Probability [MeSH] OR "Severity of illness Index" [MeSH] OR "Disease susceptibility" [MeSH] Filters: Humans, English, from 2018 - 2020
#2	Search: Mortality [MeSH] OR "Respiration, Artificial" [MeSH] OR "mechanical ventilat*" [tiab] OR "Critical Care" [MeSH] OR "Intensive Care Units" [MeSH] OR Hospitalization OR "hospital admission*" [tiab]

#1	Search: Coronavirus [MeSH] OR "Coronavirus Infections" [MeSH] OR 2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])

Medications
CINAHL

S82	S74 AND S75 AND S81
S81	S76 OR S77 OR S78 OR S79 OR S80
S80	(MH "Hospitalization+")
S79	(MH "Intensive Care Units+")
S78	(MH "Critical Care+")
S77	(MH "Respiration, Artificial+") OR (MH "Ventilators, Mechanical")
S76	(MH "Mortality+")
S75	((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND ((MH "Coronavirus+") or coronavirus* or covid) AND (wuhan or beijing or shanghai)) OR (("novel coronavirus*" AND ((MH "China") or China)) OR TI coronavirus* OR (((MH pneumonia) or pneumonia) AND Wuhan) OR ((D614G or "Covid-19" or COVID-19 or "2019-nCoV" or "SARS-CoV-2" or (MH Coronavirus Infections))))) AND DT 20191201-20300101)
S74	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73
S73	(MH "Fluorouracil")
S72	(MH "Cytarabine")
S71	"Ibrutinib"
S70	(MH "Etoposide")
S69	(MH "Doxorubicin+")
S68	(MH "Daunorubicin+")
S67	(MH "Bleomycins")
S66	(MH "Paclitaxel")
S65	(MH "Vinblastine")
S64	(MH "Vincristine")
S63	(MH "Antineoplastic Agents, Combined")

S62	(MH "Chemotherapy, Cancer+") OR (MH "Antineoplastic Agents, Combined")
S61	(MH "Cyclophosphamide+")
S60	"Alemtuzumab"
S59	(MH "Antilymphocyte Serum")
S58	(MH "Cyclosporine")
S57	(MH "Sirolimus")
S56	(MH "Tacrolimus")
S55	(MH "Nivolumab")
S54	(MH "Ipilimumab")
S53	"Pembrolizumab"
S52	(MH "Immune Checkpoint Inhibitors+")
S51	(MH "Tocilizumab")
S50	"Canakinumab"
S49	"Interleukin 1 Receptor Antagonist Protein"
S48	"Aprelimast"
S47	(MH "Abatacept")
S46	"Ruxolinitib"
S45	"Upadacinib"
S44	"Baricinitib"
S43	"Tofacinitib"
S42	"Tofacinitib"
S41	(MH "Janus Kinase Inhibitors")
S40	"Vedolizumab"
S39	"Integrin blockers"
S38	"Antigens, CD20"
S37	"Ublituximab"
S36	"Ofatumumab"
S35	"Obinutuzumab"
S34	"Ocrelizumab"
S33	(MH "Rituximab")

S32	"Tildrakizumab"
S31	"Risankizumab"
S30	"Guselkumab"
S29	"Ustekinumab"
S28	"Brodalumab"
S27	"Ixekizumab"
S26	"Secukinumab"
S25	(MH "Golimumab")
S24	(MH "Certolizumab Pegol")
S23	(MH "Adalimumab")
S22	(MH "Etanercept")
S21	(MH "Infliximab")
S20	(MH "Tumor Necrosis Factor Inhibitors")
S19	(MH "Biological Products+")
S18	(MH "Mycophenolate Mofetil")
S17	(MH "Mesalamine")
S16	"5-ASA"
S15	(MH "Hydroxychloroquine")
S14	(MH "Azathioprine")
S13	(MH "Sulfasalazine")
S12	(MH "Leflunomide")
S11	(MH "Methotrexate")
S10	(MH "Tumor Necrosis Factor Inhibitors")
S9	(MH "Antirheumatic Agents+")
S8	(MH "Budesonide")
S7	(MH "Hydrocortisone")
S6	(MH "Methylprednisolone")
S5	(MH "Dexamethasone")
S4	(MH "Prednisone")
S3	(MH "Adrenal Cortex Hormones+")

S2	(MH "Antineoplastic Agents+")
S1	(MH "Immunosuppressive Agents+")

Medline
Database: Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations and Daily <1946 to August 07, 2020>
Search Strategy:
---
1 exp Coronavirus/ (25240)
2 exp Coronavirus Infections/ (26114)
3 (coronaviru* or corona viru* or ncov* or n-cov* or novel cov* or COVID-19 or COVID-19 or COVID-2019 or COVID2019 or SARS-COV-2 or SarsCOV-2 or sarscov2 or sarscov19 or SARS-COV-19 or SARSCOV-19 or Sars-cov-2019 or sarscov2019 or sarscov-2019 or severe acute respiratory syndrome coronaviru* or severe acute respiratory syndrome cov 2 or severe acute respiratory syndrome or severe acute respiratory disease or 2019ncov or 2019 ncov).mp. (42170)
4 or/1-3 (44463)
5 exp Mortality/ (382742)
6 exp Respiration, Artificial/ (77084)
7 "mechanical ventilat*".mp. (42841)
8 exp Critical Care/ (57965)
9 exp Intensive Care Units/ (84754)
10 exp Hospitalization/ (240722)
11 "hospital admission*".ti. (4627)
12 or/5-11 (776227)
13 exp Immunosuppressive Agents/ (315843)
14 exp Antineoplastic Agents/ (1099652)
15 exp Adrenal Cortex Hormones/ (396189)
16 exp Prednisone/ (39371)
17 exp Dexamethasone/ (51354)
18 exp Methylprednisolone/ (19471)
19 exp Hydrocortisone/ (73154)
20 exp Budesonide/ (4513)
21 exp Antirheumatic Agents/ (426730)
22 exp Tumor Necrosis Factor Inhibitors/ (555)
23 exp Methotrexate/ (37901)
24 exp Leflunomide/ (1512)
25 exp Sulfasalazine/ (4113)
26 exp Azathioprine/ (14628)
27 exp Hydroxychloroquine/ (3436)
28 5-ASA.ti. (168)
29 exp Mesalamine/ (3472)
30 Mycophenolate.ti. (3494)
31 exp Biological Products/ (569455)
32 TNF-inhibitors.ti. (277)
33 exp Infliximab/ (10250)
34 exp Etanercept/ (5846)
35 exp Adalimumab/ (5367)
36 exp Certolizumab Pegol/ (603)
37 Golimumab.ti. (379)
38 Secukinumab.ti. (525)
39 Ixekizumab.ti. (217)

40 Brodalumab.ti. (99)
41 exp Ustekinumab/ (1044)
42 Guselkumab.ti. (89)
43 Risankizumab.ti. (43)
44 Tildrakizumab.ti. (45)
45 exp Rituximab/ (14677)
46 Ocrelizumab.ti. (91)
47 Obinutuzumab.ti. (214)
48 Ofatumumab.ti. (211)
49 Ublituximab.ti. (10)
50 exp Antigens, CD20/ (4130)
51 Integrin blockers.ti. (1)
52 Vedolizumab.ti. (483)
53 exp Janus Kinase Inhibitors/ (375)
54 Tofacinitib.ti. (1)
55 Baricinitib.ti. (0)
56 Upadacinib.ti. (0)
57 Ruxolinitib.ti. (0)
58 exp Abatacept/ (2900)
59 Aprelimast.ti. (0)
60 exp Interleukin 1 Receptor Antagonist Protein/ (5137)
61 Canakinumab.ti. (234)
62 tocilizumab.ti. (1429)
63 Immune checkpoint inhibitors.ti. (1344)
64 Pembrolizumab.ti. (1251)
65 exp Ipilimumab/ (1911)
66 Nivoloumab.ti. (0)
67 exp Tacrolimus/ (15912)
68 exp Sirolimus/ (20079)
69 exp Cyclosporine/ (29285)
70 exp Antilymphocyte Serum/ (11778)
71 exp Alemtuzumab/ (1969)
72 exp Cyclophosphamide/ (53600)
73 exp Drug Therapy/ (1359397)
74 exp Antineoplastic Combined Chemotherapy Protocols/ (140424)
75 exp Vincristine/ (23200)
76 exp Vinblastine/ (12593)
77 exp Paclitaxel/ (26735)
78 exp Bleomycin/ (15372)
79 exp Daunorubicin/ (64476)
80 exp Doxorubicin/ (56722)
81 exp Etoposide/ (16658)
82 Ibrutinib.ti. (1019)
83 exp Cytarabine/ (14648)
84 exp Fluorouracil/ (46673)
85 or/13-84 (3143392)
86 4 and 12 and 85 (247)
87 limit 86 to (english language and yr="2019 -Current") (167)

PubMed

#4	Search: #1 AND #2 AND #3 Filters: Humans, English, 2019-2020

#3	Search: "Immunosuppressive Agents" [MeSH] OR "Antineoplastic Agents" [MeSH] OR "Adrenal Cortex Hormones" [MeSH] OR Prednisone [MeSH] OR Dexamethasone [MeSH] OR Methylprednisolone [MeSH] OR Hydrocortisone [MeSH] OR Budesonide [MeSH] OR "Antirheumatic Agents" [MeSH] OR "Tumor Necrosis Factor Inhibitors" [MeSH] OR Methotrexate [MeSH] OR Leflunomide [MeSH] OR Sulfasalazine [MeSH] OR Azathioprine [MeSH] OR Hydroxychloroquine [MeSH] OR 5-ASA [tiab] OR Mesalamine [MeSH] OR Mycophenolate [MeSH] OR "Biological Products" [MeSH] OR TNF-inhibitors [tiab] OR Infliximab [MeSH] OR Etanercept [MeSH] OR Adalimumab [MeSH] OR "Certolizumab Pego"l [MeSH] OR Golimumab [tiab] OR Secukinumab [tiab] OR Ixekizumab [tiab] OR Brodalumab [tiab] OR Ustekinumab [tiab] OR Guselkumab [tiab] OR Risankizumab [tiab] OR Tildrakizumab [tiab] OR Rituximab [MeSH] OR Ocrelizumab [tiab] OR Obinutuzumab [tiab] OR Ofatumumab [tiab] OR Ublituximab [tiab] OR "Antigens, CD20" [MeSH] OR "Integrin blockers" [tiab] OR Vedolizumab [tiab] OR "Janus Kinase Inhibitors" [MeSH] OR Tofacinitib [tiab] OR Baricinitib [tiab] OR Upadacinib [tiab] OR Ruxolinitib [tiab] OR Abatacept [MeSH] OR Aprelimast [tiab] OR "Interleukin 1 Receptor Antagonist Protein" [MeSH] OR Canakinumab [tiab] OR tocilizumab [tiab] OR "Immune checkpoint inhibitors" [tiab] OR Pembrolizumab [tiab] OR Ipilimumab [MeSH] OR Nivoloumab [tiab] OR Tacrolimus [MeSH] OR Sirolimus [MeSH] OR Cyclosporine [MeSH] OR "Antilymphocyte Serum" [MeSH] OR Alemtuzumab [MeSH] OR Cyclophosphamide [MeSH] OR Chemotherapy [tiab] OR "Antineoplastic Combined Chemotherapy Protocols" [MeSH] OR Vincristine [MeSH] OR Vinblastine [MeSH] OR Paclitaxel [MeSH] OR Bleomycin [MeSH] OR Daunorubicin [MeSH] OR Doxorubicin [MeSH] OR Etoposide [MeSH] OR Ibrutinib [tiab] OR Cytarabine [MeSH] OR Fluorouracil [MeSH] Filters: Humans, English, from 2019 - 2020
#2	Search: Mortality [MeSH] OR "Respiration, Artificial" [MeSH] OR "mechanical ventilat*" [tiab] OR "Critical Care" [MeSH] OR "Intensive Care Units" [MeSH] OR Hospitalization OR "hospital admission*" [tiab] Filters: Humans, English
#1	Search: Coronavirus [MeSH] OR "Coronavirus Infections" [MeSH] OR 2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) AND 2019/12[PDAT]:2030[PDAT]) Filters: Humans, English

Reference List

Aigner, C., Dittmer, U., Kamler, M., Collaud, S., & Taube, C. (2020). COVID-19 in a lung transplant recipient. *The Journal of Heart and Lung Transplantation*, 39(6), 610-611. Retrieved from: https://doi.org/10.1016/j.healun.2020.04.004

Alberici, F., Delbarba, E., Manenti, C., Econimo, L., Valerio, F., Pola, A., Maffei, C., Possenti, S., Lucca, B., Cortinovis, R., Terlizzi, V., Zappa, M., Sacca, C., Pezzini, E., Calcaterra, E., Piarulli, P., Guerini, A., Boni, F., Gallico, A., … Scolari, F. (2020). A report from the Brescia Renal COVID Task Force on the clinical characteristics and short-term outcome of hemodialysis patients with SARS-CoV-2 infection. *Kidney International*, 98(1), 20–26. Retrieved from: https://doi.org/10.1016/j.kint.2020.04.030

Anders, H.-J., Bruchfeld, A., Fernandez Juarez, G. M., Floege, J., Goumenos, D., Turkmen, K., van Kooten, C., Tesar, V., & Segelmark, M. (2020). Recommendations for the management of patients with immune-mediated kidney disease during the severe acute respiratory syndrome coronavirus 2 pandemic. *Nephrology, Dialysis, Transplantation*, 35(6), 920–925. Retrieved from: https://doi.org/10.1093/ndt/gfaa112

Argenziano, M. G., Bruce, S. L., Slater, C. L., Tiao, J. R., Baldwin, M. R., Barr, R. G., . . . Chen, R. (2020). Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: Retrospective case series. *BMJ*, 369, m1996. Retrieved from: https://dx.doi.org/10.1136/bmj.m1996

Assaad, S., Avrillon, V., Fournier, M., Mastroianni, B., Russias, B., Swalduz, A., . . . Blay, J. (2020). High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-COV-2 on RT-PCR. *European Journal of Cancer*, 135, 251-259. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7275994/

Bezzio, C., Saibeni, S., Variola, A., Allocca, M., Massari, A., Gerardi, V., Casini, V., Ricci, C., Zingone, F., Amato, A., Caprioli, F., Lenti, M. V., Vigano, C., Ascolani, M., Bossa, F., Castiglione, F., Cortelezzi, C., Grossi, L., Milla, M., … (IG-IBD), I. G. for the S. of I. B. D. (2020). Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. *Gut*, 69(7), 1213–1217. Retrieved from: http://dx.doi.org/10.1136/gutjnl-2020-321411

Bisogno, G., Provenzi, M., Zama, D., Tondo, A., Meazza, C., Colombini, A., . . . Cesaro, S. (2020). Clinical Characteristics and Outcome of Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Italian Pediatric Oncology Patients: A Study From the Infectious Diseases Working Group of the Associazione Italiana di Oncologia e Ematologia Pediatrica. Journal of the Pediatric Infectious Diseases Society. Retrieved from: https://doi.org/10.1093/jpids/piaa088

Boettler, T., Marjot, T., Newsome, P. N., Mondelli, M. U., Maticic, M., Cordero, E., . . . Berg, T. (2020). Impact of COVID-19 on the care of patients with liver disease: EASL-ESCMID position paper after 6 months of the pandemic. *JHEP Reports*. Retrieved from: https://doi.org/10.1016/j.jhepr.2020.100113

Brenner, E. J., Ungaro, R. C., Gearry, R. B., Kaplan, G. G., Kissous-Hunt, M., Lewis, J. D., . . . Kappelman, M. D. (2020). Corticosteroids, But Not TNF Antagonists, Are Associated With Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results From an International Registry. *Gastroenterology*. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32425234/

Brouwers, M. C., Kho, M. E., Browman, G. P., Burgers, J. S., Cluzeau, F., Feder, G., Fervers, B., Graham, I. D., Grimshaw, J., Hanna, S. E., Littlejohns, P., Makarski, J., Zitzelsberger, L., & AGREE Next Steps Consortium (2010). AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, *182*(18), E839–E842. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3001530/

Chaudhry, Z. S., Williams, J. D., Vahia, A., Fadel, R., Acosta, T. P., Prashar, R., . . . Alangaden, G. J. (2020). Clinical characteristics and outcomes of COVID-19 in solid organ transplant recipients: A cohort study. *American Journal of Transplantation*. Retrieved from: https://doi.org/10.1111/ajt.16188

Chawki, S., Buchard, A., Sakhi, H., Dardim, K., Sakhawi, K. E., Chawki, M., . . . Attias, P. (2020). Treatment Impact on COVID-19 evolution in hemodialysis patients. *Kidney International*. Retrieved from: https://doi.org/10.1016/j.kint.2020.07.010

Clinical Guidelines for Transplant Medications. (2019). Retrieved on August 20, 2020 from: http://www.transplant.bc.ca/Documents/Health%20Professionals/Clinical%20guidelines/Clinical%20Guidelines%20for%20TRANSPLANT%20MEDICATIONS.pdf

Colmenero, J., Rodríguez-Perálvarez, M., Salcedo, M., Arias-Milla, A., Muñoz-Serrano, A., Graus, J., . . . Pons, J. A. (2020). Epidemiological pattern, incidence and outcomes of COVID-19 in liver transplant patients. *Journal of Hepatology*. Retrieved from: https://doi.org/10.1016/j.jhep.2020.07.040

Corbett, R. W., Blakey, S., Nitsch, D., Loucaidou, M., Mclean, A., Duncan, N., & Ashby, D. R. (2020). Epidemiology of COVID-19 in an Urban Dialysis Center. *Journal of the American Society of Nephrology*, 31(8), 1815-1823. Retrieved from: https://doi.org/10.1681/asn.2020040534

Cravedi, P., Mothi, S. S., Azzi, Y., Haverly, M., Farouk, S. S., Pérez-Sáez, M. J., . . . Riella, L. V. (2020). COVID-19 and kidney transplantation: Results from the TANGO International Transplant Consortium. *American Journal of Transplantation*. Retrieved from: https://doi.org/10.1111/ajt.16185

Dalla Costa G, Leocani L, Montalban X, et al. Real-time assessment of COVID-19 prevalence among multiple sclerosis patients: a multicenter European study. *Neurol Sci*. 2020;41(7):1647-1650. Retrieved from: https://europepmc.org/article/med/32617741

Damiani, G., Pacifico, A., Bragazzi, N. L., & Malagoli, P. (2020). Biologics increase the risk of SARS - CoV -2 infection and hospitalization, but not ICU admission and death: Real-life data from a large cohort during red-zone declaration. *Dermatologic Therapy*. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32356577/

Danziger-Isakov, L., Steinbach, W. J., Paulsen, G., Munoz, F. M., Sweet, L. R., Green, M., . . . Fisher, B. T. (2018). A Multicenter Consortium to Define the Epidemiology and Outcomes of Pediatric Solid Organ Transplant Recipients With Inpatient Respiratory Virus Infection. *Journal of the Pediatric Infectious Diseases Society*, 8(3), 197-204. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/29538674/

Docherty, A. B., Harrison, E. M., Green, C. A., Hardwick, H. E., Pius, R., Norman, L., . . . Semple, M. G. (2020). Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. *BMJ*, M1985. Retrieved from: https://doi.org/10.1136/bmj.m1985

Downes, K. J., Danziger-Isakov, L. A., Cousino, M. K., Green, M., Michaels, M. G., Muller, W. J., . . . Ardura, M. I. (2020). Return to School for Pediatric Solid Organ Transplant Recipients in the United States During the COVID-19 Pandemic: Expert Opinion on Key Considerations and Best Practices. *Journal of the Pediatric Infectious Diseases Society*. Retrieved on August 25, 2020 from: https://doi.org/10.1093/jpids/piaa095

D'Silva KM, Serling-Boyd N, Wallwork R, et al. Clinical characteristics and outcomes of patients with coronavirus disease 2019 (COVID-19) and rheumatic disease: a comparative cohort study from a US 'hot spot' [published online ahead of print, 2020 May 26]. *Ann Rheum Dis*. Retrieved from: https://doi.org/10.1136/annrheumdis-2020-217888

Eichenberger, E. M., Soave, R., Zappetti, D., Small, C. B., Shore, T., Besien, K. V., . . . Satlin, M. J. (2018). Incidence, significance, and persistence of human coronavirus infection in hematopoietic stem cell transplant recipients. *Bone Marrow Transplantation*, 54(7), 1058-1066. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/30385869/

Espinoza, J. L., Wadasaki, Y., & Takami, A. (2018). Infection Complications in Hematopoietic Stem Cells Transplant Recipients: Do Genetics Really Matter? *Frontiers in Microbiology*, 9. Retrieved from: https://doi.org/10.3389/fmicb.2018.02317

Fabio, C., Antonella, C., Patrizia, R., Francesco, D. C., Annalisa, R., Laura, G., . . . Alberto, Z. (2020). Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. *Clinical Immunology*.108509. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32535188/

Fill, L., Hadney, L., Graven, K., Persaud, R., & Hostoffer, R. (2020). The clinical observation of a patient with common variable immunodeficiency diagnosed as having coronavirus disease 2019. *Annals of Allergy, Asthma & Immunology*, 125(1), 112-114. Retrieved from: https://doi.org10.1016/j.anai.2020.04.033

Fisher, B. T., Danziger-Isakov, L., Sweet, L. R., Munoz, F. M., Maron, G., Tuomanen, E., . . . Steinbach, W. J. (2018). A Multicenter Consortium to Define the Epidemiology and Outcomes of Inpatient Respiratory Viral Infections in Pediatric Hematopoietic Stem Cell Transplant Recipients. *Journal of the Pediatric Infectious Diseases Society*, 7(4), 275-282. Retrieved from: https://doi.org/10.1093/jpids/pix051

Fredi, M., Cavazzana, I., Moschetti, L., Andreoli, L., Franceschini, F., Airò, P., . . . Zingarelli, S. (2020). COVID-19 in patients with rheumatic diseases in northern Italy: A single-centre observational and case–control study. *The Lancet Rheumatology*. Retrieved from: https://doi.org/10.1016/S2665-9913(20)30169-7

Freites, D., Leon, L., Mucientes, A., Rodriguez-Rodriguez, L., Font, J., Madrid, A., . . . Abasolo, L. (2020). Risk factors for hospital admission related to COVID-19 in inflammatory rheumatic diseases. *Annals of the Rheumatic Diseases*. Retrieved from: https://doi.org/10.1101/2020.05.14.20101584

Garassino, M. C., Whisenant, J. G., Huang, L., Trama, A., Torri, V., Agustoni, F., . . . Horn, L. (2020). COVID-19 in patients with thoracic malignancies (TERAVOLT): First results of an international, registry-based, cohort study. *The Lancet Oncology*, 21(7), 914-922. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7292610/

General Information about COVID-19 & Cancer. (2020, August 14). Retrieved on August 15, 2020 from: https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/general-information-about-covid-19

Gianfrancesco, M., Hyrich, K. L., Al-Adely, S., Carmona, L., Danila, M. I., Gossec, L., Izadi, Z., Jacobsohn, L., Katz, P., Lawson-Tovey, S., Mateus, E. F., Rush, S., Schmajuk, G., Simard, J., Strangfeld, A., Trupin, L., Wysham, K. D., Bhana, S., Costello, W., … Alliance, C.-19 G. R. (2020). Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Annals of the Rheumatic Diseases*, 79(7), 859–866. Retrieved from: https://europepmc.org/article/med/32471903

Giannakoulis, V. G., Papoutsi, E., & Siempos, I. I. (2020). Effect of Cancer on Clinical Outcomes of Patients With COVID-19: A Meta-Analysis of Patient Data. *JCO Global Oncology,* (6), 799-808. Retrieved from: https://ascopubs.org/doi/full/10.1200/GO.20.00225

Goicoechea, M., Sanchez Camara, L. A., Macias, N., Munoz de Morales, A., Rojas, A. G., Bascunana, A., Arroyo, D., Vega, A., Abad, S., Verde, E., Garcia Prieto, A. M., Verdalles, U., Barbieri, D., Delgado, A. F., Carbayo, J., Mijaylova, A., Acosta, A., Melero, R., Tejedor, A., … Aragoncillo, I. (2020). COVID-19: clinical course and outcomes of 36 hemodialysis patients in Spain. *Kidney International*, 98(1), 27–34. Retrieved from: https://doi.org/10.1016/j.kint.2020.04.031

Haberman R, Axelrad J, Chen A, et al. Covid-19 in immune-mediated inflammatory diseases — case series from New York. *N Engl J Med* 2020;383:85-8. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32348641/

Holzhauser, L., Lourenco, L., Sarswat, N., Kim, G., Chung, B., & Nguyen, A. B. (2020). Early experience of COVID-19 in 2 heart transplant recipients: Case reports and review of treatment options. *American Journal of Transplantation*. Retrieved from: https://doi.org/10.1111/ajt.15982

Hong, Quan Nha et al. (2018). The Mixed Methods Appraisal Tool (MMAT) Version 2018 for Information Professionals and Researchers'. 1 Jan. 2018 : 285 – 291. Retrieved from: http://mixedmethodsappraisaltoolpublic.pbworks.com/w/file/fetch/127916259/MMAT_2018_criteria-manual_2018-08-01_ENG.pdf

Husain, S. A., Dube, G., Morris, H., Fernandez, H., Chang, J., Paget, K., . . . Mohan, S. (2020). Early Outcomes of Outpatient Management of Kidney Transplant Recipients with Coronavirus Disease 2019. *Clinical Journal of the American Society of Nephrology*, 15(8), 1174-1178. Retrieved from: https://doi.org/10.2215/CJN.05170420

Kanellopoulos, A., Ahmed, M. Z., Kishore, B., Lovell, R., Horgan, C., Paneesha, S., . . . Nikolousis, E. (2020). COVID-19 in bone marrow transplant recipients: Reflecting on a single centre experience. *British Journal of Haematology*, 190(2). Retrieved from: https://doi.org/10.1111/bjh.16856

Kates, O. S., Haydel, B. M., Florman, S. S., Rana, M. M., Chaudhry, Z. S., Ramesh, M. S., . . . Limaye, A. P. (2020). COVID-19 in solid organ transplant: A multi-center cohort study. *Clinical Infectious Diseases*. Retrieved from: https://doi.org/10.1093/cid/ciaa1097

Kuderer, N. M., Choueiri, T. K., Shah, D. P., Shyr, Y., Rubinstein, S. M., Rivera, D. R., Shete, S., Hsu, C.-Y., Desai, A., de Lima Lopes, G. J., Grivas, P., Painter, C. A., Peters, S., Thompson, M. A., Bakouny, Z., Batist, G., Bekaii-Saab, T., Bilen, M. A., Bouganim, N., … Consortium, C.-19 and C. (2020). Clinical impact of COVID-19 on

patients with cancer (CCC19): a cohort study. *Lancet*, 395(10241), 1907–1918. Retrieved from: http://europepmc.org/article/MED/32473681

Lee, L. Y. W., Cazier, J. B., Starkey, T., Turnbull, C. D., Team, U. K. C. C. M. P., Kerr, R., & Middleton, G. (2020). COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet*, 395(10241), 1919–1926. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32473682/

Louapre C, Collongues N, Stankoff B, et al. Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis [published online ahead of print, 2020 Jun 26]. *JAMA Neurol*. 2020;e202581. Retrieved from: https://jamanetwork.com/journals/jamaneurology/fullarticle/2767776

Lusignan, S. D., Dorward, J., Correa, A., Jones, N., Akinyemi, O., Amirthalingam, G., . . . Hobbs, F. D. (2020). Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: A cross-sectional study. *The Lancet Infectious Diseases*. Retrieved from: https://doi.org/10.1016/s1473-3099(20)30371-6

Mahil, S., Yiu, Z., Mason, K., Dand, N., Coker, B., Wall, D., . . . Smith, C. (2020). Global reporting of cases of COVID-19 in psoriasis and atopic dermatitis: An opportunity to inform care during a pandemic. *British Journal of Dermatology*, 183(2), 404-406. Retrieved from: https://doi.org/10.1111/bjd.19161

Manganaro, M., Baldovino, S., & SIN, W. group of the P. and A. V. S. of the. (2020). First considerations on the SARS-CoV-2 epidemic in the Dialysis Units of Piedmont and Aosta Valley, Northern Italy. *Journal of Nephrology*, 33(3), 393–395. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32277423/

Mehta, V., Goel, S., Kabarriti, R., Cole, D., Goldfinger, M., Acuna-Villaorduna, A., . . . Verma, A. (2020). Case fatality rate of cancer patients with COVID-19 in a New York hospital system. *Cancer Discovery*. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32357994

Mikuls, T. R., Johnson, S. R., Fraenkel, L., Arasaratnam, R. J., Baden, L. R., Bermas, B. L., . . . Saag, K. G. (2020). American College of Rheumatology Guidance for the Management of Rheumatic Disease in Adult

Parrotta, E., Kister, I., Charvet, L., Sammarco, C., Saha, V., Charlson, R. E., Howard, J., Gutman, J. M., Gottesman, M., Abou-Fayssal, N., Wolintz, R., Keilson, M., Fernandez-Carbonell, C., Krupp, L. B., & Zhovtis Ryerson, L. (2020). COVID-19 outcomes in MS: Observational study of early experience from NYU Multiple Sclerosis Comprehensive Care Center. *Neurology(R) Neuroimmunology & Neuroinflammation*, 7(5). Retrieved from: https://doi.org/10.1212/NXI.0000000000000835

Patients During the COVID-19 Pandemic: Version 1. *Arthritis & Rheumatology*, 72(8), 1241-1251. Retrieved from: https://doi.org/10.1002/art.41301

Montopoli, M., Zumerle, S., Vettor, R., Rugge, M., Zorzi, M., Catapano, C., . . . Alimonti, A. (2020). Androgen-deprivation therapies for prostate cancer and risk of infection by SARS-CoV-2: A population-based study (N = 4532). *Annals of Oncology*, 31(8), 1040-1045. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7202813/

Rojas, T. D., Pérez-Martínez, A., Cela, E., Baragaño, M., Galán, V., Mata, C., . . . Madero, L. (2020). COVID-19 infection in children and adolescents with cancer in Madrid. *Pediatric Blood & Cancer*, 67(7). Retrieved from: https://doi.org/10.1002/pbc.28397

Robilotti, E. V., Babady, N. E., Mead, P. A., Rolling, T., Perez-Johnston, R., Bernardes, M., . . . Kamboj, M. (2020). Determinants of COVID-19 disease severity in patients with cancer. *Nature Medicine*, 26(8), 1218-1223. Retrieved from: https://doi.org/10.1038/s41591-020-0979-0

Rubin, D. T., Feuerstein, J. D., Wang, A. Y., & Cohen, R. D. (2020). AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Commentary. *Gastroenterology*, 159(1), 350-357. Retrieved from: https://doi.org/10.1053/j.gastro.2020.04.012

Salvarani, C., Bajocchi, G., Mancuso, P., Galli, E., Muratore, F., Boiardi, L., Catanoso, M., Pipitone, N., Cassone, G., Girolimetto, N., Croci, S., Cimino, L., Gradellini, F., Beltrami, M., Di Lernia, V., Dolci, G., Massari, M., Marata, A. M., Costantini, M., & Giorgi Rossi, P. (2020). Susceptibility and severity of COVID-19 in patients treated with bDMARDS and tsDMARDs: a population-based study. *Annals of the Rheumatic Diseases*, 79(7), 986–988. Retrieved from: http://dx.doi.org/10.1136/annrheumdis-2020-217903

Scire, C. A., Carrara, G., Zanetti, A., Landolfi, G., Chighizola, C., Alunno, A., Andreoli, L., Caporali, R., Gerli, R., Sebastiani, G. D., Valesini, G., Sinigaglia, L., & Rheumatology, I. R. of the I. S. for. (2020). COVID-19 in rheumatic diseases in Italy: first results from the Italian registry of the Italian Society for Rheumatology (CONTROL-19). *Clinical and Experimental Rheumatology*, 38(4), 748–753. Retrieved from: https://www.clinexprheumatol.org/article.asp?a=15906

Soresina, A., Moratto, D., Chiarini, M., Paolillo, C., Baresi, G., Focà, E., . . . Badolato, R. (2020). Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover. *Pediatric Allergy and Immunology*, 31(5), 565-569. Retrieved from: https://doi.org/10.1111/pai.13263

Suleyman, G., Fadel, R. A., Malette, K. M., Hammond, C., Abdulla, H., Entz, A., . . . Brar, I. (2020). Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Network Open*, 3(6). Retrieved from: https://doi.org/10.1001/jamanetworkopen.2020.12270

Taxonera, C., Sagastagoitia, I., Alba, C., Manas, N., Olivares, D., & Rey, E. (2020). 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. *Alimentary Pharmacology & Therapeutics*, 52(2), 276–283. Retrieved from: https://doi.org/10.1111/apt.15804

2019-nCOV (Coronavirus): FAQs for Organ Transplantation. (2020, August 14). Retrieved on August 15, 2020 from: https://www.myast.org/sites/default/files/COVID-19%20FAQ%20Tx%20Centers%206.18.2020.pdf

Urwin, S; Gavinder K, Graziadio S. (2020). What prognostic clinical risk prediction scores for COVID-19 are currently available for use in the community setting? Centre for Evidence-Based Medicine. Retrieved from: https://www.cebm.net/covid-19/what-prognostic-clinical-risk-prediction-scores-for-covid-19-are-currently-available-for-use-in-the-community-setting/

Venkatesulu, B. P., Chandrasekar, V. T., Giridhar, P., Advani, P., Sharma, A., Hsieh, C. E., . . . Krishnan, S. (2020). A systematic review and meta-analysis of cancer patients affected by a novel coronavirus. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7265691/

Viswanathan, M., Ansari, M. T., Berkman, N. D., Chang, S., Hartling, L., McPheeters, M., ... & Treadwell, J. R. (2012). Assessing the risk of bias of individual studies in systematic reviews of health care interventions. In *Methods guide for effectiveness and comparative effectiveness reviews [Internet]*. Agency for Healthcare Research and Quality (US). Retrieved from: https://www.ncbi.nlm.nih.gov/books/NBK91433/

Wallace, B., Washer, L., Marder, W., & Kahlenberg, J. M. (2020). Patients with lupus with COVID-19: University of Michigan experience. *Annals of the Rheumatic Diseases*. Retrieved from: https://doi.org/10.1136/annrheumdis-2020-217794

Wang, B., Van Oekelen, O., Mouhieddine, T. H., Del Valle, D. M., Richter, J., Cho, H. J., Richard, S., Chari, A., Gnjatic, S., Merad, M., Jagannath, S., Parekh, S., & Madduri, D. (2020). A tertiary center experience of multiple myeloma patients with COVID-19: lessons learned and the path forward. *Journal of Hematology & Oncology*, 13(1), 94. Retrieved from: https://europepmc.org/article/med/32577702

Webb, G. J., Moon, A. M., Barnes, E., Barritt, A. S., & Marjot, T. (2020). Determining risk factors for mortality in liver transplant patients with COVID-19. *The Lancet Gastroenterology & Hepatology*, 5(7), 643-644. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7182520/

White, C. A., Kappel, J. E., Levin, A., Moran, S. M., Pandeya, S., & Thanabalasingam, S. J. (2020). Management of Advanced Chronic Kidney Disease During the COVID-19 Pandemic: Suggestions From the Canadian Society of Nephrology COVID-19 Rapid Response Team. *Canadian Journal of Kidney Health and Disease*, 7, 1-8. Retrieved from: https://doi.org/10.1177%2F2054358120939354

Wynants, L., Van Calster, B., Bonten, M. M., Collins, G. S., Debray, T. P., De Vos, M., ... & Schuit, E. (2020). Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal. *BMJ*, *369*. Retrieved from https://www.bmj.com/content/369/bmj.m1328.long

Zhong J, Shen G, Yang H, Huang A, Chen X, Dong L, et al. COVID-19 in patients with rheumatic disease in Hubei province, China: A multicentre retrospective observational study. Lancet Rheumatol. 2020;9913(20):1–8. Retrieved from https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30227-7/fulltext