Summary of Evidence Related to
the Risk of Other Infections in the Context of COVID-19
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COVID-19 Literature Report Team:
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Severe COVID-19 is associated with critical illness and immune dysregulation, both of which have been previously associated with increased risk of nosocomial infection. The care of COVID-19 patients has required dramatic changes to usual hospital practices and heightened concern for infection control practices. **This document is a brief summary of published evidence related to the effect of the COVID-19 pandemic on non-COVID infections. Included are manuscripts published in peer-reviewed journals or on pre-print servers through March 10, 2021.** This summary does not consider the second order effects of increased antibiotics associated with COVID-19 on antimicrobial resistance. References summarized in this report were drawn from the COVID-19 Literature Report (Lit Rep) team database. **References that appeared in the daily Lit Rep are marked with an asterisk***, and the summary is shown in the annotated bibliography below.

Executive Summary

- **Contamination of improperly used personal protective equipment likely contributed to an outbreak of nosocomial infection with *Candida auris* in a COVID-19-specific healthcare setting.**
- **Evidence is currently inconclusive regarding the risk of healthcare facility acquired (nosocomial) infections in patients with COVID-19 and whether critical illness associated with COVID-19 creates a higher risk of nosocomial infections compared to other forms of critical illness.**
- **The literature does not support routine use of empiric antibiotics in the management of confirmed COVID-19 infection.**
- **Successfully implemented infection control practices in response to COVID-19 have been associated with a decrease in the incidence of hospital acquired *Clostridiodes difficile*.**
- **The COVID-19 pandemic has been associated with a remarkable decline in other respiratory viruses, most notably influenza.**

Outbreaks of Other Infections in Clinical Units Caring for Patients with COVID-19

At this time, outbreaks of fungal and bacterial infections in clinical units caring for patients with COVID-19 do not appear to be widespread; however ongoing surveillance is warranted to prevent such outbreaks in these settings. A cluster of infections with the yeast *Candida auris* was reported in a specialty care ward treating COVID-19 patients (Prestel*). Multiple studies have characterized changes in the frequency of infections with the common hospital-acquired bacterium *Clostridioides* (formerly *Clostridium*) *difficile* in the setting of COVID-19 care and have indicated that the incidence *C. difficile* has

decreased in many healthcare facilities during the COVID-19 pandemic, potentially due to the implementation of stronger infection control measures.

Candida auris

C. auris is an emerging multidrug-resistant yeast that can cause invasive infection. Prior to the COVID-19 pandemic, outbreaks of *C. auris* have occurred in healthcare settings due in part to asymptomatic carriage and its persistence on surfaces (CDC, Tsay). Prevention and control measures have included aggressive implementation of contact tracing and screening in response to the identification of new cases. During July-August 2020, a hospital in Florida experienced an outbreak of *C. auris* that involved three *C. auris* bloodstream infections and one urinary tract infection in patients with COVID-19 who were being treated in a dedicated COVID-19 ward (Prestel*). Upon identification of these cases, screening of 67 patients admitted to the COVID-19 unit found that 35 (52%) had positive test results. An investigation of the outbreak concluded that widespread *C. auris* transmission was likely aided by the use of multiple gown and glove layers by the healthcare providers in the COVID-19 unit, extended use of the underlayer of personal protective equipment (PPE), lapses in cleaning and disinfection of shared medical equipment, and lapses in adherence to hand hygiene (Prestel*). After the hospital put in place measures to address these concerns, no subsequent *C. auris* cases were detected in follow-up surveys. The authors state that "CDC does not recommend the use of more than one isolation gown or pair of gloves at a time when providing care to patients with suspected or confirmed SARS-CoV-2 infection. Such practices among HCP might be motivated by fear of becoming infected with SARS-CoV-2 but instead might increase risks for self-contamination when doffing and for transmission of other pathogens among patients and exacerbate PPE supply shortages."

Clostridioides* (previously *Clostridium*) *difficile

C. difficile is a common hospital acquired bacterial gastrointestinal infection with spores that are resistant to the alcohol-based sanitizers commonly used for hand hygiene in COVID-19 care. Hand hygiene procedures effective against *C. difficile* transmission include washing hands with soap and water. Antibiotic exposure is a risk factor for *C. difficile*. Several studies have characterized changes in *C. difficile* infection patterns in settings of COVID-19 clinical care. Luo et al found no significant difference in incidence of hospital-associated *C. difficile* episodes in a New York hospital despite a trend toward increased high-risk antibiotic exposures. A study from a hospital in Spain observed a 70% decrease in the incidence of hospital associated *C. difficile* during the COVID-19 pandemic compared to a pre-pandemic control period, despite no change in antibiotic use, which the authors attribute to the implementation of control measures to prevent nosocomial transmission by healthcare workers and asymptomatic colonized patients (Ponce-Alonso). Similar declines in hospital acquired *C. difficile* infections during the COVID-19 pandemic have been observed elsewhere (Bentivegna, Hazel).

Nosocomial Infections in Patients with COVID-19

Bacterial co-infections have been reported in hospital settings caring for patients with COVID-19, but the frequency of bacterial infections has been low. The Infectious Disease Society of America has concluded the following:

- Current data indicate that bacterial coinfections with SARS-CoV-2 infection are relatively infrequent (likely occurring in <10% of hospitalized COVID-19 patients).

- The literature does not support routine use of empiric antibiotics in the management of confirmed COVID-19 infection.
- Objective findings that increase the concern for bacterial superinfection include rise in leukocyte counts, lobar consolidation or evidence of necrotizing infection on chest imaging and recrudescence of fever after initial defervescence.
- Fungal superinfection (with *Aspergillus*) is also a concern, but the true incidence has not been defined. Risk factors for fungal superinfection include steroid use, invasive catheters and prolonged mechanical ventilation.
- Antimicrobial stewardship programs can help optimize antimicrobial use during the pandemic. Continued investigation into optimal antimicrobial stewardship program interventions to limit antibiotic overuse during the COVID-19 pandemic is warranted.

A multicenter analysis of the clinical microbiology usage in hospitalized patients in the US found patients with COVID-19 had similar rates of non-SARS-CoV-2 co-infections compared to patients without COVID-19, but that COVID-19 disease was associated with higher rates of hospital-onset infections, greater antimicrobial usage, and extended hospital and ICU length of stay (Puzniak). In a case series of patients with COVID-19 in the UK, bacterial co-infections were identified in 3% of patients 0-5 days after admission and in 6% of patients throughout hospital admission (Hughes). Comparable rates of bacterial co-infection were identified in a control group of patients with confirmed influenza infection. In one study of samples with a positive co-infection culture from patients hospitalized in New York City during the first COVID-19 surge, the most commonly isolated organisms in respiratory infections were *Staphylococcus aureus* (44%), *Pseudomonas aeruginosa* (16%), *Klebsiella spp* (10%), *Enterobacter spp* (8%), and *Escherichia coli* (4%) (Nori). The most commonly isolated organisms in bloodstream infections were *S. aureus* (30%), *Staphylococcus epidermidis* (12%), *Streptococcus spp* (10%), *Enterococcus spp* (7%), *E. coli* (7%), *P. aeruginosa* (6%), *Klebsiella spp* (3%), and *Enterobacter spp* (3%).

Invasive Pulmonary Aspergillosis

Several studies have raised concern that COVID-19 patients may be more susceptible to invasive fungal infections, particularly invasive pulmonary aspergillosis (IPA), through multiple mechanisms, including declines in lymphocyte counts and viral damage to airway tissues (Koehler). Several case series and observational cohort studies, most of which have involved relatively small numbers of patients, have found that 20-30% of patients with severe COVID-19, particularly those receiving mechanical ventilation, have invasive pulmonary aspergillosis, with a high case fatality (~65-75%) among these patients. However, the Infectious Disease Society of America has urged caution regarding these findings, outlining the limitations in interpreting these observational studies, and has concluded that currently, the true incidence of COVID-19 associated pulmonary aspergillosis is not known.

A literature review on the topic of IPA in patients with COVID-19 with severe or critical illness concluded that the incidence of IPA in patients with COVID-19 ranged from 20% to 33% (Lai). Most studies included in the literature review involved a relatively small number of patients (~30), although one study from Jiangsu Province, China from January 22 to February 2, 2020 found IPA in 60 (23%) out of 243 patients. The case fatality among patients with COVID-19 who were co-infected with IPA was high (65% among a cohort of 34 patients). In an Italian cohort of 108 patients with confirmed COVID-19 (4 ICUs from 3 hospitals) who were receiving mechanical ventilation, 28% were found to have pulmonary aspergillosis

and 18% were classified as having putative IPA (Bartoletti). The 30-day mortality was significantly higher among patients with pulmonary aspergillosis (44% vs 19%, P = 0.002) and IPA (74% vs 26%, P < .001) compared to patients without aspergillosis. A summary of reports of pulmonary aspergillosis and guidance on diagnosis is provided by Armstrong-James et al.

Other studies have not found pulmonary aspergillosis to be common in COVID-19 patients. An investigation in a single center in France of 54 patients with COVID-19 with moderate to severe acute respiratory distress syndrome (ARDS) found that two patients (3.7%) showed early putative IPA, neither of whom had prior immunosuppression or host risk factors (Versyck*). Immunosuppression was observed in two patients, neither of whom had IPA. The authors conclude that the frequency of IPA among patients with COVID-19 with ARDS was relatively low and was similar to what has been described in other populations with ARDS.

Nosocomial infections associated with immunomodulatory treatments

There are two primary immunomodulatory therapies currently in use for the treatment of severe COVID-19. These include corticosteroids (primarily dexamethasone) and IL-6 blockers (primarily tocilizumab). Since each of these medications target the immune system, it is biologically plausible that they would be associated with secondary infections.

Tocilizumab:

Studies have reported mixed results regarding the risk of secondary infections associated with tocilizumab. A systematic review found five studies have reported an increased prevalence of infection whereas twelve studies have reported either no association or reduced infections in patients treated with tocilizumab (Khan). The differences between these studies that lead to such wide discrepancies in results are unclear. It is worth noting that almost all studies followed patients for only 28 days, whereas the half-life of tocilizumab is long with the doses typically used for treatment in COVID-19 (8mg/kg intravenous), leading to a half-life of 18 days (Abdallah). One hypothesis for why some studies have found an elevated risk of infection in the placebo arm is that tocilizumab is very effective at suppressing fever, suggesting that there may be fewer investigations for infections performed (Strohbehn).

A randomized, double blind trial of severe COVID-19 determined that there were fewer "serious infections" in tocilizumab patients. Details regarding the nature of these infections are unclear (Stone). Industry-sponsored randomized trials have not found a difference in the risk of "serious" secondary infections when compared to placebo. These include COVACTA and EMPACTA (Salama, Rosas). In the former study, the majority of participants received glucocorticoids (~80%) whereas in the latter only 20-30% of participants received glucocorticoids. The RECOVERY Trial (a large multicenter public sector trial) did not find differences in "excess deaths from other infections" among patients who received tocilizumab. Another randomized trial in patients with moderate-to-severe COVID who were not intubated did not find a difference in secondary infections (Hermine). In India, the COVINTOC trial (open label) recently reported no differences in infections between treatment arm and standard of care (Soin).

Some observational studies of tocilizumab under real-work conditions have also found no increased risk of secondary infections (Ignatius, Campochino et al., Eur J Int Med 2020), while others have found a

substantially elevated risk of infection, including some autopsy proved bacterial infections (Kimmig, Guaraldi).

Corticosteroids:
We identified few investigations of the potential risk of secondary infections associated with short term corticosteroid use for the treatment COVID-19. The median duration of dexamethasone in the RECOVERY trial was seven days and no increases in other infections were reported (Horby*).

Indirect Effects of the COVID-19 Pandemic on Vaccination

Stay-at-home orders intended to reduce the transmission of SARS-CoV-2 and concerns about acquiring SARS-CoV-2 in health care settings had the indirect of effect of reducing the rate of administration of routine vaccinations, at least in the early phase of the pandemic (Lassi*). Vaccination rates for bacterial pneumonia, tetanus-diphtheria-pertussis, and shingles among Medicare beneficiaries over the age of 65 declined by 25% to 62% compared with the corresponding period in 2019, reaching a low point in mid-April 2020 and recovering slowly in between May and July 2020 (Hong*). While national vaccination coverage among US kindergarteners was high for the 2019-20 school year, despite most schools shifting to virtual learning in the spring due to the COVID-19 pandemic, the CDC authors caution that disruptions caused by the pandemic are likely to reduce vaccination coverage for the 2020-21 school year (Seither*).

Indirect Effects of the COVID-19 Pandemic on Other Respiratory Viruses

Widespread implementation of measures to prevent community transmission of SARS-CoV-2, including stay-at-home orders, physical distancing, use of facemasks, and other non-pharmaceutical interventions (NPI) appears to have had broad indirect effects on the transmission of other respiratory infections. Evidence from many settings has shown dramatically lower incidence of influenza, rhinovirus, enterovirus, and respiratory syncytial virus (RSV) infections following the implementation of NPIs to prevent SARS-CoV-2 compared to the same time period in years prior to the COVID-19 pandemic (Freeman*, Partridge*, Sherman*). An examination of temporal trends in the incidence of these infections indicates that they occurred at rates similar to previous years during the period immediately prior to the COVID-19 pandemic and declined rapidly following implementation of NPIs (Partridge*, Zhang*). Evidence from children's hospitals indicates that declines in influenza, RSV, and hospitalization for lower respiratory infections have also declined substantially in children (Trenholme*).

Annotated Bibliography

Abdallah et al. (Apr 1, 2017). Pharmacokinetic and Pharmacodynamic Analysis of Subcutaneous Tocilizumab in Patients With Rheumatoid Arthritis From 2 Randomized, Controlled Trials: SUMMACTA and BREVACTA. Journal of Clinical Pharmacology. https://doi.org/10.1002/jcph.826

Armstrong-James et al. (Oct 1, 2020). Confronting and Mitigating the Risk of COVID-19 Associated Pulmonary Aspergillosis. European Respiratory Journal. https://doi.org/10.1183/13993003.02554-2020

Bartoletti et al. (July 28, 2020). Epidemiology of Invasive Pulmonary Aspergillosis Among Intubated Patients With COVID-19: A Prospective Study. Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciaa1065

Bentivegna et al. (2020). Impact of COVID-19 Prevention Measures on Risk of Health Care-Associated Clostridium Difficile Infection. American Journal of Infection Control. https://doi.org/10.1016/j.ajic.2020.09.010

Campochiaro et al. (June 1, 2020). Efficacy and Safety of Tocilizumab in Severe COVID-19 Patients: A Single-Centre Retrospective Cohort Study. European Journal of Internal Medicine. https://doi.org/10.1016/j.ejim.2020.05.021

CDC. (2020). Candida Auris. https://www.cdc.gov/fungal/candida-auris/index.html

Freeman et al. (Jan 1, 2021). Effectiveness of Physical Distancing: Staying 6 Feet Over to Put Respiratory Viruses 6 Feet Under. Mayo Clinic Proceedings. https://doi.org/10.1016/j.mayocp.2020.10.040

- Results from an analysis of 13,324 nasopharyngeal swabs collected at a single hospital in Arizona between January 1, 2017, and July 31, 2020, found a significant reduction in the detection of respiratory viruses other than SARS-CoV-2, coinciding with the implementation of distancing and masking policies during the COVID-19 pandemic. The average monthly positivity rate for the months between April and July declined from 25% for 2017–2019 to 2% in the same period of 2020. However, it is not clear what proportions of the observed declines in testing and positivity were due to non-pharmaceutical interventions, since the COVID-19 pandemic may also be causing reluctance to seek medical care.

Guaraldi et al. (Aug 1, 2020). Tocilizumab in Patients with Severe COVID-19: A Retrospective Cohort Study. The Lancet Rheumatology. https://doi.org/10.1016/S2665-9913(20)30173-9

Hazel et al. (2021). The Other "C": Hospital-Acquired Clostridioides Difficile Infection during the COVID-19 Pandemic. Infection Control and Hospital Epidemiology. https://doi.org/10.1017/ice.2021.3

Hermine et al. (Jan 1, 2021). Effect of Tocilizumab vs Usual Care in Adults Hospitalized with COVID-19 and Moderate or Severe Pneumonia: A Randomized Clinical Trial. JAMA Internal Medicine. https://doi.org/10.1001/jamainternmed.2020.6820

Hong et al. (Feb 19, 2021). Decline in Receipt of Vaccines by Medicare Beneficiaries During the COVID-19 Pandemic - United States, 2020. MMWR. https://doi.org/10.15585/mmwr.mm7007a4

- During the first week after the national COVID-19 emergency declaration in March 2020, weekly vaccination rates for bacterial pneumonia, tetanus-diphtheria-pertussis, and shingles among Medicare beneficiaries over the age of 65 declined by 25% to 62% compared with the corresponding period in 2019. Vaccination rates among racial and ethnic minority adults were lower than were those among white adults. By mid-April 2020, vaccination rates reached low points of 70% to 89% below 2019 rates. Vaccination rates partially recovered gradually during the period between May and July 2020, when data collection ended.

Horby et al. (July 17, 2020). Dexamethasone in Hospitalized Patients with Covid-19. New England Journal of Medicine. https://doi.org/10.1056/NEJMoa2021436

- In patients hospitalized with COVID-19, the administration of 6 mg/day for ten days of the steroid dexamethasone resulted in statistically significantly lower 28-day mortality among those who were receiving either invasive mechanical ventilation (29% vs. 41%) or oxygen alone (23% vs. 26%) at randomization but not among those receiving no respiratory support (18% vs. 14%). Patients in the dexamethasone group also had a shorter duration of hospitalization than those in the usual care group (median, 12 days vs. 13 days).

Hughes et al. (Oct 1, 2020). Bacterial and Fungal Coinfection among Hospitalized Patients with COVID-19: A Retrospective Cohort Study in a UK Secondary-Care Setting. Clinical Microbiology and Infection. https://doi.org/10.1016/j.cmi.2020.06.025

Ignatius et al. (Jan 1, 2021). Tocilizumab for the Treatment of COVID-19 Among Hospitalized Patients: A Matched Retrospective Cohort Analysis. Open Forum Infectious Diseases. https://doi.org/10.1093/ofid/ofaa598

Khan et al. (Feb 12, 2021). Systematic Review and Meta-Analysis of Anakinra, Sarilumab, Siltuximab and Tocilizumab for COVID-19. Thorax. https://doi.org/10.1136/thoraxjnl-2020-215266

Kimmig et al. (Oct 28, 2020). IL-6 Inhibition in Critically Ill COVID-19 Patients Is Associated With Increased Secondary Infections. Frontiers in Medicine. https://doi.org/10.3389/fmed.2020.583897

Koehler et al. (2021). Defining and Managing COVID-19-Associated Pulmonary Aspergillosis: The 2020 ECMM/ISHAM Consensus Criteria for Research and Clinical Guidance. The Lancet Infectious Diseases. https://doi.org/10.1016/S1473-3099(20)30847-1

Lai and Yu. (Feb 1, 2020). COVID-19 Associated with Pulmonary Aspergillosis: A Literature Review. Journal of Microbiology, Immunology and Infection. https://doi.org/10.1016/j.jmii.2020.09.004

Lassi et al. (Jan 22, 2021). The Impact of the COVID-19 Pandemic on Immunization Campaigns and Programs: A Systematic Review. International Journal of Environmental Research and Public Health. https://doi.org/10.3390/ijerph18030988

- A systematic review of 17 studies examining the impact of the COVID-19 pandemic on existing global vaccination programs found a reduction in vaccination coverage and a decline in the total number of vaccines administered. Polio cases increased by about fourfold in polio endemic countries. Factors contributing to low vaccine coverage included fear of being exposed to the virus at health care facilities, restriction on city-wide movements, shortage of workers, and diversion of resources from

child health to address the pandemic. 10 of these studies focused on campaigns in high-income countries.

Luo et al. (2020). Hospital-Onset Clostridioides Difficile Infections during the COVID-19 Pandemic. Infection Control and Hospital Epidemiology. https://doi.org/10.1017/ice.2020.1223

Nori et al. (Jan 1, 2021). Bacterial and Fungal Coinfections in COVID-19 Patients Hospitalized during the New York City Pandemic Surge. Infection Control and Hospital Epidemiology. https://doi.org/10.1017/ice.2020.368

Partridge et al. (Jan 25, 2021). Evaluation of Seasonal Respiratory Virus Activity Before and After the Statewide COVID-19 Shelter-in-Place Order in Northern California. JAMA Network Open. https://doi.org/10.1001/jamanetworkopen.2020.35281

- Infection rates for influenza and rhinovirus or enterovirus were significantly lower during March 25 to July 31, 2020 compared to the same time period during the past 5 years, according to a cohort study in California that included over 45,000 tests for the viral respiratory infections. This significant drop in infection rates coincided with implementation of shelter-in-place orders on March 19, 2020. Influenza infection rates decreased by 93%, while rhinovirus or enterovirus infection rates decreased by 81%. In contrast, infection rates for the portions of the 2020 respiratory virus season prior to March 25th were similar to rates for the same period over the past 5 years (30.4 vs 33.7 positive results per 100 tests).

Ponce-Alonso et al. (2020). Impact of the COVID-19 Pandemic on Nosocomial Clostridioides Difficile Infection. Infection Control and Hospital Epidemiology. https://doi.org/10.1017/ice.2020.454

Prestel and Anderson. (Jan 15, 2021). Candida Auris Outbreak in a COVID-19 Specialty Care Unit — Florida, July–August 2020. MMWR. https://doi.org/10.15585/mmwr.mm7002e3

- A dedicated COVID-19 specialty care unit at an acute care hospital in Florida reported four fungal infections with *Candida auris,* which is often resistant to several anti-fungal medications, in July 2020. An additional 35 patients were found to be colonized with *C. auris* during testing between August 4 and 18. During that time, investigators observed lapses in hand hygiene and opportunities for contamination of the base layer of PPE during removal of PPE and through direct contact with the patient care environment or potentially contaminated surfaces. The authors note that the COVID-19 pandemic has prompted some facilities to implement PPE conservation strategies and to use PPE in non-routine ways, such as extended wear and reuse. They recommend that health care workers should continue to implement infection prevention practices intended to prevent transmission of other pathogens while caring for patients in a dedicated COVID-19 unit.

Puzniak et al. (Feb 27, 2021). A Multicenter Analysis of the Clinical Microbiology and Antimicrobial Usage in Hospitalized Patients in the US with or without COVID-19. BMC Infectious Diseases. https://doi.org/10.1186/s12879-021-05877-3

Rosas et al. (Feb 25, 2021). Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia. The New England Journal of Medicine. https://doi.org/10.1056/NEJMoa2028700

Salama et al. (Jan 7, 2021). Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. New England Journal of Medicine. https://doi.org/10.1056/nejmoa2030340

Sherman et al. (Nov 8, 2020). The Effect of SARS-CoV-2 Mitigation Strategies on Seasonal Respiratory Viruses: A Tale of Two Large Metropolitan Centers in the United States. Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciaa1704

- Public health measures implemented to reduce SARS-CoV-2 transmission may have reduced the transmission of other seasonal respiratory viruses. In a retrospective review of medical records from health systems in Atlanta and Boston, average reproductive number (R_t) was found to remain above 1 for much longer in the past 5 seasons for influenza A, influenza B, and respiratory syncytial virus (RSV) compared to the September 2019-May 2020 season, which coincided with the COVID-19 pandemic. Declines in R_t in both locations in 2020 seemed to coincide with implementation of non-pharmaceutical interventions.

Seither et al. (Jan 22, 2021). Vaccination Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2019–20 School Year. MMWR. https://doi.org/10.15585/mmwr.mm7003a2

- National vaccination coverage among US kindergarteners was high for the 2019-20 school year, despite most schools shifting to virtual learning in the spring due to the COVID-19 pandemic. Vaccination coverage for state-required number of doses of DTaP, MMR, and varicella (chickenpox) was 94.9%, 95.2%, and 94.8%, respectively. The exemption rate was 2.5%, and only 2.3% were not up-to-date for MMR and without vaccine exemptions. However, CDC authors caution that disruptions caused by the pandemic are likely to reduce vaccination coverage for the 2020-21 school year.

Soin et al. (Mar 4, 2021). Tocilizumab plus Standard Care versus Standard Care in Patients in India with Moderate to Severe COVID-19-Associated Cytokine Release Syndrome (COVINTOC): An Open-Label, Multicentre, Randomised, Controlled, Phase 3 Trial. The Lancet. Respiratory Medicine. https://doi.org/10.1016/S2213-2600(21)00081-3

Stone et al. (Dec 10, 2020). Efficacy of Tocilizumab in Patients Hospitalized with Covid-19. New England Journal of Medicine. https://doi.org/10.1056/nejmoa2028836

Trenholme et al. (Dec 2, 2021). COVID-19 and Infant Hospitalizations for Seasonal Respiratory Virus Infections, New Zealand, 2020. Emerging Infectious Diseases. https://doi.org/10.3201/eid2702.204041

- A pediatric hospital in South Auckland, New Zealand observed a dramatic decrease in cases of influenza and respiratory syncytial virus after COVID-19 lockdown measures were implemented in March 2020, compared to prior seasons. Additionally, case reductions were sustained after gradual reopening beginning in April 2020. While annual hospitalizations for lower respiratory tract infections ranged from 1,486 to 2,046 during 2015-2019, only 268 admissions were reported in 2020, despite similar rates of clinician-directed PCR tests.

Stone et al. (Dec 10, 2020). Efficacy of Tocilizumab in Patients Hospitalized with Covid-19. New England Journal of Medicine. https://doi.org/10.1056/nejmoa2028836

Strohbehn et al. (Mar 1, 2020). COVIDOSE: A Phase II Clinical Trial of Low-Dose Tocilizumab in the Treatment of Noncritical COVID-19 Pneumonia. Clinical Pharmacology and Therapeutics. https://doi.org/10.1002/cpt.2117

Tsay et al. (May 19, 2017). Notes from the Field: Ongoing Transmission of Candida Auris in Health Care Facilities — United States, June 2016–May 2017. MMWR. https://doi.org/10.15585/mmwr.mm6619a7

Versyck et al. (Feb 16, 2021). Invasive Pulmonary Aspergillosis in COVID-19 Critically Ill Patients: Results of a French Monocentric Cohort. Journal of Medical Mycology. https://doi.org/10.1016/j.mycmed.2021.101122

- The prevalence of invasive pulmonary aspergillosis (IPA) was not higher for mechanically ventilated COVID-19 patients compared to what has been described in other populations with acute respiratory distress syndrome (ARDS), according to a retrospective cohort study. The prevalence of IPA among non-immunocompromised patients in this cohort (n=52 patients) was 3.7%. Most (71%) of the patients were male, and their median age was 65.

Zhang et al. (Nov 30, 2020). Rapid Disappearance of Influenza Following the Implementation of COVID-19 Mitigation Measures in Hamilton Ontario. Pre-print downloaded Dec 1 from https://doi.org/10.1101/2020.11.27.20240036

- *[Pre-print, not peer reviewed]* Following population-wide implementation of COVID-19 interventions in Hamilton, Ontario, the proportion of samples that tested positive for influenza A and B dropped rapidly to 0% by the week of March 15-21. During the 2010-2019 influenza seasons, the proportion of positive tests reached 0% on a median of the week of May 30-June 6. Data were collected from all nasopharyngeal swab specimens (n=57,503) submitted for routine respiratory virus testing between January 2010 and June 2020.