COVID-19 Scientific Advisory Group Rapid Response Report

Key Research Question: Antimicrobial utilization in COVID-19 patients for suspected coinfection or superinfection:

- 1. What is the evidence for the use of antibacterial therapy upon admission for patients with respiratory symptoms who have suspected or confirmed COVID-19?
- 2. What is the incidence and etiology of bacterial or fungal superinfection later in the course of COVID-19?

Context

- Multiple jurisdictions are creating COVID-19 care pathways for patients in various care settings, many of which involve antibacterial therapy.
- This review was requested to assess current data on the incidence of co-infections at presentation or bacterial or fungal superinfection that may influence guideline creation.
- Literature on hospitalized patients with other viral respiratory tract infections suggests high rates of antimicrobial use without obvious benefit.

Key Messages from the Evidence Summary

- Infections with bacterial or fungal co-pathogens associated with SARS-CoV-2 infection (COVID-19) are not well described, with existing data mostly found in case series with both incomplete reporting, and a lack of microbiologic testing in COVID-19 patients. Co-pathogens have been described in approximately 8% of patients with COVID-19, more commonly in those who are severely ill and in those who die. Most co-pathogens isolated appear to be related to superinfection events in the later stages of illness rather than initial co-infection, as a small autopsy series of critically ill SARS-CoV-2 patients suggested superimposed bacterial bronchopneumonia was not uncommon.
- There is significant and widespread antibiotic use in hospitalized patients with COVID-19 reported in the literature despite the lack of reported evidence of initial co-infections and superinfections.
- There are no "signal" bacterial co-pathogens identified in COVID-19 infection thus far, with a wide range of bacterial isolates reported. There is a preliminary signal of possible fungal superinfection risk with Aspergillus species isolated usually in the setting of critically ill ARDS patients at later stage of illness.
- Antibiotic use in patients with COVID-19 has not been proven to improve clinical outcomes, but unnecessary antibiotic use in the stewardship literature has been proven to be associated with an increased risk of:
 - o Clostridioides difficile colitis.
 - o Adverse drug events such as kidney injury, allergy, neutropenia, and long QT
 - Resistant hospital-acquired bacterial and fungal infections.
- Antimicrobial stewardship programs can play a key role in guiding the appropriate use of antimicrobials in patients with COVID-19.

Committee Discussion

The committee noted the apparent underutilization of microbiologic testing in the literature (mostly case series) when broad spectrum antibiotic use was given to the majority of COVID19 patients, and supported the recommendations to acquire specimens prior to antibiotic therapy where possible. There was a desire to provide clinical guidance to support initial antibiotic therapy where there was a reasonable suspicion of coinfection but to



also support stopping (or not starting) antibiotics if there was a confirmed and classic COVID19 viral pneumonia picture.

Pragmatic Recommendations

Given the absence of data to support a meaningful benefit of antibiotics use in COVID-19 patients without proven bacterial or fungal co-infection or superinfection, the following pragmatic recommendations is partly derived from evidence surrounding other viral pneumonias:

- In patients hospitalized with suspect or confirmed COVID-19, empiric antibiotic therapy is generally not required for a classic viral pneumonia presentation unless the differential diagnosis includes community acquired pneumonia (CAP), or initial co-infection is strongly suspected based on a thorough clinical assessment.
 - a. Procurement of microbiologic specimens (sputum or endotracheal suction cultures in intubated patients as BAL is not recommended for diagnostic purposes alone), blood cultures, and urine cultures as clinically appropriate) upon hospital admission should be prioritized to allow for the assessment of co-pathogens and to guide subsequent antimicrobial therapy decisions, especially in those who are severely ill or critically ill.
- 2. In hospitalized patients with suspect or confirmed COVID-19 and where secondary bacterial infection is suspected based on thorough clinical assessment, empiric therapy for hospital acquired pneumonia (HAP) or ventilator associated pneumonia (VAP) can be considered after procurement of lower respiratory specimens for bacterial and fungal investigations.
- 3. Empiric antimicrobial therapy recommendations, based on the clinical syndrome suspected (CAP, HAP, sepsis, etc), can be found in AHS Bugs & Drugs (http://www.bugsanddrugs.org) and SpectrumMD.
- 4. Empiric antimicrobial therapy in either scenario should be re-assessed at day 3 and then with evolution of laboratory and culture results and the patient's clinical status, for opportunities to discontinue, de-escalate, or transition to targeted antimicrobial therapy. Confirmed SARS-CoV-2 infection and lack of co-pathogen isolation would often support discontinuation of antibiotics.
- 5. If there is evidence of bacterial CAP or HAP where cultures cannot be procured or culture results are felt to be unreliable, guideline supported duration of therapy includes a 5 day course of antibiotics for CAP and a 7 day course for HAP.

Summary of Evidence

Limitations of this review

Much of the available evidence informing this rapid review was extracted from descriptive case reports, case series and some cohort studies - however none reported primarily on antimicrobial therapy or the microbiology of bacterial or fungal co-infections. Furthermore, many studies reviewed were in pre-print status, which are limited by a lack of peer review and some were excluded. Limitations of the review include the short turnaround time from the conception of the scientific question to the review and summary of evidence and recommendations, broad scope of the question, breadth of search, and language limitations.

Evidence from the grey literature

Numerous reputable sources have published clinical practice guidelines for the management of patients with COVID-19 that specifically address the management of bacterial co-infections.

Interim guidance for the clinical management of patients with moderate to severe COVID-19 published by the Public Health Agency of Canada and endorsed by the Canadian Critical Care Society and Association of Medical Microbiology and Infectious Disease Canada have been published (https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents.html). These guidelines

recommend collection of appropriate cultures prior to the initiation of empiric antimicrobial therapy whenever possible. Regarding the treatment of co-infections, these guidelines recommend to give empiric antimicrobials to treat all likely pathogens causing severe acute respiratory infection and sepsis as soon as possible and within 1 hour of identification of sepsis. The choice of empiric antibiotic agent(s) is based on the clinical diagnosis (community-acquired pneumonia, hospital-acquired pneumonia, or sepsis). Finally, these guidelines recommend to de-escalate empiric therapy on the basis of microbiology results and clinical judgement.

The Canadian Pediatric Society clinical practice guideline on the acute management of paediatric coronavirus disease 2019 (COVID-19) indicate that antibiotics are not recommended to treat cases of COVID-19 without clinical suspicion of bacterial co-infection (https://www.cps.ca/en/documents/position/the-acute-management-of-paediatric-coronavirus-disease-2019covid-19). However, when there is evidence of a secondary infection, appropriate antibiotics should be administered pre-emptively, without waiting for confirmatory test results. A recent update reaffirms this approach (https://www.cps.ca/en/documents/position/update-on-covid-19-epidemiology-and-impact-on-medical-care-in-children-april-2020).

Similar guidance is available from the Infectious Disease Society of America (Bhimraj et al., 2020), Surviving Sepsis Campaign (Alhazzani et al., 2020), and from the World Health Organization (https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected).

Evidence from the primary literature

Research Question 1: What is the evidence for the use of antibacterial therapy upon admission for patients with respiratory symptoms who have suspected or confirmed COVID-19?

Co-infection and Superinfection Rates

Amongst hundreds of articles published with clinical COVID-19 data, relatively few have reported the rate of bacterial co-infections and superinfections.

Two studies specifically report that patients did not have co-infection upon admission. One retrospective study reported on 201 hospitalized patients in Wuhan, China and found that of the 148 (73.6%) patients who underwent sputum cultures upon admission, none had bacterial or fungal co-infection (Wu et al., 2020). A second study of patients admitted to two hospitals in Wuhan, China explicitly indicate that none of their 191 patients had bacterial co-infection diagnosed upon hospital admission (F. Zhou et al., 2020).

However, 15% of that same cohort were diagnosed with hospital-acquired co-infection, as defined by clinical symptoms or signs of pneumonia or bacteremia and a positive culture of a new pathogen obtained from lower respiratory tract specimens (qualified sputum, endotracheal aspirate, or bronchoalveolar lavage) or blood samples after admission, or as ventilator associated pneumonia according to IDSA guidelines (F. Zhou et al., 2020). In this cohort, 27/54 (50%) non-survivors versus only 1/137 (1%) of survivors developed secondary infection. Yang et al reported 6/52 (11.5%) patients developed hospital acquired pneumonia in their cohort (Yang et al., 2020). Feng et al reported secondary bacterial infection in 35/410 (8.5%) although the syndrome and microbiology were not identified (Feng et al., 2020). Huang et al reported secondary bacterial infection in 4 patients (10%) in their cohort, where all 4 were ICU patients again highlighting that severe or critically-ill patients are associated with secondary bacterial infections (C. Huang et al., 2020).

This retrospective study of 221 admitted adult patients in Wuhan, China, 17 (7.7%) were reported to have bacterial co-infection and 7 (3.2%) fungal co-infection, including 9 patients with multidrug resistant organisms, but further details on the specifics of these infections were not reported (G. Zhang et al., 2020). On the contrary,

Young et al report that of 18 patients admitted to hospital in Singapore, no bacterial co-infections were identified (Young et al., 2020).

It is important to note that while pulmonary bacterial co-infection is the focus of many reports, secondary bacterial infections of other body systems such as bacteremia or urinary tract infections have been reported (Arentz et al., 2020; Yang et al., 2020). Goyal et al reported bacteremia during hospital stay in 19 of 338 patients (5.6%) with the majority occurring in patients requiring invasive mechanical ventilation (Goyal et al., 2020).

While some studies aimed to report secondary bacterial pneumonia as a clinical outcome, it is apparent that not all patients had systematic bacteriologic or fungal cultures upon presentation and data generation was clinically driven (Guan et al., 2020).

In one autopsy study of 21 COVID-19 patients hospitalized in Switzerland, the primary cause of death was felt to be respiratory failure with exudative diffuse alveolar damage with capillary congestion. However histologic evidence of bronchopneumonia (assumed to be bacterial) was found in just under half (48%) of these cases highlighting what was felt to also be an important contributor to mortality.

Bacterial Pathogens

Similar to the rates of bacterial co-infection, the literature detailing the microbiology of these was limited. The major limitation was of inconsistent definitions of co-infection, secondary infection, versus colonization in the literature.

Methicillin-susceptible *Staphylococcus aureus* (Duployez et al., 2020; Easom et al., 2020), Group A Streptococcus (Khaddour, Sikora, Tahir, Nepomuceno, & Huang, 2020), and *Streptococcus pneumoniae* have all been reported to co-isolated with COVID-19. The latter was identified by respiratory pathogen real-time PCR detection panel on nasopharyngeal and oropharyngeal swab specimens in a case report from the Philippines (Edrada et al., 2020). Despite aggressive and effective treatment with ceftriaxone and azithromycin escalating to meropenem and vancomycin, the patient developed a cardiac arrest event and subsequently died raising the suspicion that *S. pneumoniae* may represent colonization.

A Spanish series of critically-ill patients identified co-infection in 6 of 48 patients: 3 (6%) *Pseudomonas aeruginosa*, 1 (2%) *Enterococcus faecium*, 1 (2%) *Haemophilus influenzae*, and 1 (2%) MRSA (Barrasa et al., 2020). The median time to ICU admission was 7 days, suggesting that these may represent late secondary infection.

Gram negative organisms have been commonly reported. Nosocomially acquired carbapenem-resistant *Klebsiella pneumoniae*, ESBL-positive *Klebsiella pneumoniae*, ESBL-positive *Pseudomonas aeruginosa*, ESBL-negative *Serratia marcescens, Escherichia coli, Haemophilus influenzae, Enterobacter cloacae*, and *Acinetobacter baumannii* have all been reported (N. Chen et al., 2020; Easom et al., 2020; Lescure et al., 2020; Liew, Lim, Liew, & Poh, 2020; Wang, Yang, Li, Wen, & Zhang, 2020; Yang et al., 2020). Zhang et al report that 5 (55.6%) patients who died in ICU were co-infected with carbapenem-resistant *A. baumannii* versus 4 (17.4%) patients who were successfully transferred to the ward (G. Zhang et al., 2020).

Polymicrobial infections have also been reported. Dong et al reported a case of secondary pneumonia with gram positive cocci and gram negative bacilli who received broad-spectrum antibiotics and caspofungin (Dong et al., 2020). Unfortunately, no further details regarding the microbiologic finding was available.

A case of *Mycoplasma pneumoniae* co-infection diagnosed by antibody titre of 1:160 with complicating cold agglutinin disease has been reported (Fan et al., 2020). However, in another report, *M. pneumoniae* was not detected in 116 SARS-CoV-2 positive patients on nasopharyngeal swabs using a real-time reverse transcriptase—polymerase chain reaction multiplex panel (Kim, Quinn, Pinsky, Shah, & Brown, 2020). During that same 3 week period, 6/1101 specimens negative for SARS-CoV-2 tested positive for *M. pneumoniae*.

Calls for more detailed reporting of bacterial co-infections and secondary infections have been made (Cox, Loman, Bogaert, & O'Grady, 2020; P. Zhou et al., 2020).

Use of Antibiotics

Reports indicate that up to 100% of patients with COVID-19 receive antibacterials (J. Cao et al., 2020; C. Huang et al., 2020; Z. Wang et al., 2020). Most cohorts reported antimicrobial use in 40-70% of patients (N. Chen et al., 2020; Feng et al., 2020; Wan et al., 2020; Z. Wang et al., 2020; Zhao et al., 2020).

Antibiotics prescribed were often broad-spectrum. A case series of 48 consecutive critically-ill adult patients with COVID-19 from Spain reported that 87% received antibiotics: 46% received levofloxacin, 35% received a beta-lactam plus linezolid, 31% linezolid, 21% ceftriaxone, and 18% azithromycin (Barrasa et al., 2020). Wang et al reported that out of 138 patients, 64.4% received moxifloxacin, 24.6% received ceftriaxone, and 18.1% received azithromycin (D. Wang et al., 2020). Zhao et al found that fluoroquinolones were used in 92.3% of patients, cephalosporins in 29.7%, and carbapenems only in 2.2% of patients in this study of 91 patients (Zhao et al., 2020). In a Chinese retrospective case series of 85 patients, 45.9% received a carbapenem (44.7% meropenem), 51.8% received a fluoroquinolone (47.1% moxifloxacin), 21.2% received linezolid, 10.6% received piperacillin/tazobactam, 8.3% received a 3rd generation cephalosporin with or without a beta-lactamase inhibitor, and 4.8% received a glycopeptide (2.4% vancomycin) (Du et al., 2020). The authors observed that administration of multiple antibiotics did not seem to change the disease outcome and recommended rational use of antibiotics although the study was not designed to answer this clinical question.

Feng et al report that in 476 patients, 67% received antibiotics (92.9% in the critically ill group, 83.3% in the severe group, and 59.4% in the moderate group), but identified bacterial co-infection in only 35/410 (8.5%) through BAL, bronchial aspirates, or sputum specimens (Feng et al., 2020). The diagnostics are further limited by the microbiologic technique and the subsequent interpretation of results. Additionally, it should be noted that moderately or severely ill patients who received antibiotics had longer lengths of hospital stay than patients who did not receive antibiotics (Feng et al., 2020).

Guan et al described similar findings in that more patients with severe disease received intravenous antibiotics than non-severe patients (80.3% vs 53.8%) (Guan et al., 2020). This was also a similar finding in other studies (Wan et al., 2020; G. Zhang et al., 2020). The authors also found that more patients who reached the composite primary end point (ICU admission, use of mechanical ventilation, or death) received IV antibiotics than those who did not reach the primary end point (89.6% vs 55.9%).

Therefore, there is a significant variance between the prevalence of proven bacterial co-infections and the rate of antibiotic utilization in these patients.

Select Immunocompromised Patients (Cancer, Transplant)

Zhang et al reported that 23/28 (82.1%) cancer patients admitted across 3 hospitals in Wuhan, China received antibiotics during their hospitalization without details of co-infection, secondary infection, microbiology, or types of antibiotics received (L. Zhang et al., 2020). Valentina et al reported 1 case of a patient with metastatic breast cancer receiving chemotherapy who received levofloxacin and piperacillin-tazobactam during her care for COVID-19 pneumonia and survived (Valentina, Alessio, & Hans-Ulrich, 2020). He et al reported that out of 13 hospitalized patients in Wuhan, China with COVID-19 and hematologic malignancy, 11 had bacterial co-infection (He et al., 2020). All 8 non-surviving patients versus 3/5 survivors had bacterial co-infection. The authors suggested that co-infections was a driver for higher mortality rates in patients with hematologic malignancy.

Solid organ transplant recipients with COVID-19 have been reported, but no published studies describe co-infections or secondary infections in detail. Not surprisingly, continuing broad-spectrum antibiotics despite negative cultures was common (Aigner, Dittmer, Kamler, Collaud, & Taube, 2020; Guillen et al., 2020). Huang et

al reported on one renal transplant and one bone marrow transplant recipient where both patients developed nosocomial bacterial infections but no further details were provided (J. Huang et al., 2020). A kidney transplant recipient admitted with COVID-19 was reported to do well without antibiotic therapy (Y. Kim et al., 2020).

Pregnant Patients

Although clinical characteristics of pregnant women with COVID-19 have been published, there is a paucity of data regarding bacterial co-infections in pregnant women (D. Cao et al., 2020; L. Chen et al., 2020; Ferrazzi et al., 2020). In a series of 116 pregnant women from 25 hospitals in China, 94% received broad-spectrum antibiotics (antibiotic regimens are described in 8 severe cases) (Yan et al., 2020). A systematic review of 4 studies describing 22 pregnancies reported similar findings (Di Mascio et al., 2020). However, only a single case series described co-infection microbiology in pregnant women (one case of Legionella co-infection in a series of 7 hospitalized pregnant women in Wuhan, China) (Yu et al., 2020).

An expert review published in the American Journal of Gynecology recommends to screen for bacterial coinfections and consider empiric antimicrobial therapy due to the risk for superimposed bacterial infections (Rasmussen, Smulian, Lednicky, Wen, & Jamieson, 2020).

Pediatric Patients

Xia et al report on 20 pediatric inpatients at Wuhan Children's Hospital and found that 4 (20%) had co-infection with *M. pneumoniae* (Xia et al., 2020).

Castagnoli R et al published a systematic review (Castagnoli et al., 2020) and found 2 case reports (F. Chen et al., 2020; Y. H. Zhang et al., 2020), neither in English, and a case series of 10 children (Cai et al., 2020) which reported on antibiotic use: one patient received ceftazidime and azithromycin, the second patient received meropenem and linezolid, and a few patients with pneumonia received "empiric antibiotic therapy" in the case series.

Numerous studies have been published with clinical data, but none have reported detailed rates of co-infection or secondary infections nor bacterial nor fungal pathogens (Ong, Tosoni, Kim, Kissoon, & Murthy, 2020; Qiu et al., 2020; Zimmermann & Curtis, 2020).

A pediatric series highlights excellent antimicrobial stewardship practices where two pediatric patients with COVID-19 required hospitalization for suspicion of invasive bacterial co-infections, had their empiric antibiotics discontinued when the septic workup results returned negative (36 – 48 hours) (Paret et al., 2020). Both patients were discharged in stable condition.

Elderly Patients

In a study examining 339 consecutive patients age ≥60 years with COVID-19 in Wuhan, 42.8% acquired bacterial infections during hospitalization (L. Wang et al., 2020). Similar to non-elderly patients, patients who died were more likely to have acquired secondary bacterial infection (49/65, 81.7%) versus those who survived (94/274, 34.4%). This study does not define secondary infection.

Few reports of elderly patients with COVID-19 have described the antibiotic therapies used (Borén et al., 2020).

Co-infection in Patients with Other Respiratory Viruses Infections

To inform the discussion, a brief sample of literature on hospitalized influenza is provided. In 322 patients admitted for influenza, cultures were ordered for 15.5%, and 22% had an abnormal CXR – but antibiotics were prescribed to 65.5% (211 patients), and continued in 34.5%. Patients receiving inappropriate antibiotic therapy had a longer length of stay and higher hospital costs (Ghazi et al., 2016). In a study of rapid diagnostics in 665 patients, identification of viral pathogens by rapid testing resulted in discontinuation of antibiotics in 34% and not starting antibiotics in 10%, but antibiotics are continued in a proportion of cases, particularly patients with COPD (OR 2.88), pneumonia (OR 18.8) and immunosuppression (OR 2.88) (Chavada, Clifford, & Weisback, 2020). The

influenza literature therefore suggests that patients with respiratory comorbidities and abnormal imaging (which are a risk factor for and an independent feature of COVID-19 infection respectively) tend to receive antibacterial therapy in spite of a known viral diagnosis.

Bacterial co-infection in patients with respiratory viral infections is common at approximately 4% (Jung et al., 2017). In influenza pneumonia specifically, bacterial co-infection ranges from 2 to 65% with the most common pathogens being *Streptococcus pneumoniae, Staphylococcus aureus*, *Haemophilus influenzae*, and gram negative bacilli (Klein et al., 2016). A myriad of co-infections has also been described for Severe Acute Respiratory Syndrome and Middle Eastern Respiratory Virus Syndrome (Rawson et al., 2020).

Antimicrobial Associated Complications

The widespread use of broad-spectrum antibiotic therapy accelerates the development antibiotic resistance (Holmes et al., 2016). De Natale et al suggested one possible explanation for the high mortality in patients with COVID-19 in Italy was possibly related to pre-existing high rates of death related to antimicrobial resistance (De Natale et al., 2020). Furthermore, *C. difficile* outbreaks has been described to be related to inappropriate antimicrobial therapy for community acquired pneumonia (Polgreen et al., 2007). Finally, antimicrobials can be associated with adverse drug events such as allergy, acute kidney injury, or ventricular arrhythmias related to long QT syndrome (Sapp et al., 2020).

Many have raised these concerns in patients with COVID-19 given the widespread use of antibiotics reported in descriptive series and have highlighted the crucial role of formal antimicrobial stewardship programs in combating antimicrobial resistance and antimicrobial complications (Clancy & Nguyen, 2020; Rawson et al., 2020; Stevens, Patel, & Nori, 2020).

Research Question 2:

What is the incidence and etiology of bacterial or fungal superinfection later in the course of COVID-19?

In a series of 52 critically ill patients with COVID-19, Yang et al identified *Aspergillus flavus* (2%) and *A. fumigatus* (2%) from respiratory tract specimens, and *Candida albicans* from urine culture of 1 patient (2%) (Yang et al., 2020). Chen et al reported fungal co-infection in 4/99 (4%) of their patients with COVID-19 including 3 isolates of *Candida albicans*, and 1 each of *A. flavus* and *C. glabrata* (N. Chen et al., 2020).

In a German retrospective review of 19 consecutive critically-ill patients with moderate to severe acute respiratory distress syndrome and COVID-19, 5 were found to have invasive pulmonary aspergillosis (Koehler et al., 2020); 2 were diagnosed based on serum galactomannan and 3 were based on lower respiratory tract culture. None were classifiable by EORTC/MSG criteria given the lack of host criterion, however all were either modified putative or putative according to the modified aspICU algorithm. Furthermore, nodules were seen on CT imaging in all 5 patients. Four were treated with voriconazole and 1 with isavuconazole however outcome data are not available.

Furthermore, Lescure et al reported a case of co-infection with both a bacterial and fungal pathogen (drug-susceptible *Acinetobacter baumannii* and *Aspergillus flavus*) from the first 5 cases in Europe (Lescure et al., 2020). The patient received antibacterials and isavuconazole as definitive therapy but ultimately died.

Others report routine fungal examinations being performed, but do not report the results (C. Huang et al., 2020). This may lead to underreporting especially when reports of CT halo signs without clinical correlation are being published (Li, Zeng, Liu, & Yu, 2020). Interestingly, 20 (50%) patients in a pediatric series that included 20 pediatric patients had a CT halo sign without microbiologic correlation (Xia et al., 2020)

Antifungals were used in up to 15% of patients (N. Chen et al., 2020; Du et al., 2020; Feng et al., 2020; Guan et al., 2020; G. Zhang et al., 2020).

Similar to the findings that patients with severe illness were more likely to receive antibiotics, 7.5% of patients with severe disease received antifungals vs 1.9% with non-severe disease (Guan et al., 2020). Others report similar findings (G. Zhang et al., 2020). Guan et al reported that 11.9% of patients who reached the primary end-point (ICU admission, use of mechanical ventilation, or death) received antifungal medications versus 2.2% of patients who did not reach the primary end-point (Guan et al., 2020).

He et al reported that out of 13 patients with COVID-19 and hematologic malignancy, 9 had fungal co-infection. Six of 8 non-surviving patients versus 3/5 survivors had fungal co-infection (He et al., 2020). No microbiologic findings were described.

Du et al found that 9.4% received voriconazole and 3.5% received fluconazole in their series of 85 fatal cases of COVID-19 infection. (Du et al., 2020).

Similarly, calls for detailed reporting of fungal co-infections and secondary infections have also been made (Cox et al., 2020; Gangneux, Bougnoux, Dannaoui, Cornet, & Zahar, 2020; P. Zhou et al., 2020).

Evolving Evidence

There is increasing recognition that the risk to benefit ratio of using antimicrobial and antifungal drugs in patients with COVID-19 is unclear, and attention from the Antimicrobial Stewardship community. This topic will need to be reviewed as it is anticipated that studies of early de-escalation and cessation of antimicrobials versus "standard care" may be undertaken.

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Date of first assessment: May 6, 2020

(If applicable) Date of re-assessment: (If applicable) Date of re-assessment:

Authorship and Committee Members

This review was written by Justin Chen and scientifically reviewed by Lynora Saxinger (co-chair), Kristen Brown (external reviewer), Deana Sabuda (external reviewer), and Susan Fryters (external reviewer). The full Scientific Advisory Group was involved in discussion and revision of the document: Braden Manns (co-chair), John Conly, Alexander Doroshenko, Shelley Duggan, Nelson Lee, Elizabeth Mackay, Andrew McRae, Jeremy Slobodan, James Talbot, Brandie Walker, and Nathan Zelyas.

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Appendix

List of Abbreviations

AHS: Alberta Health Services

COVID-19: Coronavirus Disease-2019

SAG: Scientific Advisory Group

KRS: Knowledge Resource Services

Literature Search Details

A literature search was conducted by Rachel Zhao from Knowledge Resources Services (KRS) within the Knowledge Management Department of Alberta Health Services. KRS searched databases for articles published from 2019 and 2020, and included: OVID MEDLINE, LitCovid, PubMed, TRIP PRO, WHO COVID-19 Database, BMJ Best practice, Centre for Evidence Based Medicine (CEBM), National Collaborating Centre for Methods and Tools, European Centre for Disease Prevention and Control (ECDC), CADTH, Cambridge Coronavirus Free Access Collection, Cochrane, National Institute for Health and Care Excellence, medRxiv and bioRxiv, Google and Google Scholar. The citation tracking method was also applied in Google Scholar. There were no articles found primarily reporting on coinfection, superinfection, or antimicrobial use. Data extracted in this review was primarily found in clinical reports of cases, series, and observational cohorts. As such, critical appraisal of the studies was not undertaken. The detailed search terms and strategies are outlined below.

Search #1

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 22, 2020

Searches Results

- exp Coronavirus/ or exp Coronavirus Infections/ or coronaviru*.mp. or "corona virus*".mp. or ncov*.mp. or ncov*.mp. or "covination".mp. or covination or covination or covination or covination or covination or covination.

 SARS-COV-2.mp. or SARSCOV-2.mp. or SARSCOV-2.mp. or SARSCOV-2.mp. or Sars-Cov-19.mp. or Sars-Cov-19.mp. or Sars-Cov-2019.mp. or severe acute respiratory syndrome cov 2".mp. or "2019 ncov".mp. or "2019 ncov".mp. or "2019 ncov".mp.
- 2 exp Anti-Bacterial Agents/ 721274
- (anti-bacterial agents or acetic acid or alamethicin or amdinocillin or amdinocillin pivoxil or amikacin or amoxicillin-potassium clavulanate combination or amphotericin b or ampicillin or anisomycin or antimycin a or aurodox or azithromycin or azlocillin or aztreonam or bacitracin or bacteriocins or bambermycins or bongkrekic acid or brefeldin a or butirosin sulfate or calcimycin or candicidin or capreomycin or carbenicillin or cafecillin or cefaclor or cefadroxil or cefamandole or cefatrizine or cefazolin or cefdinir or cefepime or cefixime or cefmenoxime or cefmetazole or cefonicid or cefoperazone or cefotaxime or cefotetan or cefotiam or cefoxitin or cefsulodin or ceftazidime or ceftibuten or ceftizoxime or ceftriaxone or cefuroxime or cephacetrile or cephalexin or cephaloglycin or cephaloridine or cephalosporins or cephalothin or cephamycins or cephapirin or cephradine or chloramphenicol or chlortetracycline or cilastatin, imipenem drug combination or ciprofloxacin or citrinin or clarithromycin or clavulanic acids or clindamycin or cloxacillin or colistin or cyclacillin or dactinomycin or daptomycin or demeclocycline or dibekacin or dicloxacillin or dihydrostreptomycin sulfate or diketopiperazines or distamycins or doripenem or doxycycline or echinomycin or edeine or enoxacin or enrofloxacin or enviomycin or ertapenem or erythromycin or erythromycin estolate or erythromycin ethylsuccinate or fidaxomicin or filipin or floxacillin or fluoroquinolones or fosfomycin or framycetin or fusidic acid or gatifloxacin or gemifloxacin or

gentamicins or gramicidin or hygromycin b or imipenem or josamycin or kanamycin or kitasamycin or lactams or lasalocid or leucomycins or levofloxacin or lincomycin or lincosamides or linezolid or lucensomycin or lymecycline or mafenide or mepartricin or meropenem or methacycline or methicillin or metronidazole or mezlocillin or mikamycin or minocycline or miocamycin or moxalactam or moxifloxacin or mupirocin or mycobacillin or nafcillin or nalidixic acid or natamycin or nebramycin or neomycin or netilmicin or netropsin or nigericin or nisin or nitrofurantoin or norfloxacin or novobiocin or nystatin or ofloxacin or oleandomycin or oligomycins or oxacillin or penicillin g benzathine or penicillin g procaine or penicillin v or penicillins or pipemidic acid or piperacillin or piperacillin, tazobactam drug combination or pivampicillin or polymyxin b or polymyxins or pristinamycin or prodigiosin or ribostamycin or rifabutin or rifamycins or rifaximin or ristocetin or rolitetracycline or roxarsone or roxithromycin or rutamycin or sirolimus or sisomicin or spectinomycin or spiramycin or streptogramin a or streptogramin group a or streptogramin group b or streptogramins or streptomycin or streptovaricin or sulbactam or sulbenicillin or sulfacetamide or sulfadiazine or sulfamerazine or sulfamethoxypyridazine or sulfanilamide or talampicillin or tazobactam or teicoplanin or tetracycline or thiamphenicol or thienamycins or thiostrepton or ticarcillin or tigecycline or tinidazole or tobramycin or tobramycin, dexamethasone drug combination or trimethoprim, sulfamethoxazole drug combination or troleandomycin or tunicamycin or tylosin or tyrocidine or tyrothricin or valinomycin or vancomycin or vernamycin b or viomycin or virginiamycin or beta-lactams or antitreponemal agents or arsphenamine or antitubercular agents or antibiotics, antitubercular or cycloserine or mycophenolic acid or rifampin or beta-lactamase inhibitors or clavulanic acid or leprostatic agents or acedapsone or clofazimine or dapsone or sulfameter or thalidomide).mp 888016

- 4 2 or 3 899800
- 5 1 and 4 335
- 6 limit 5 to yr="2019 -Current" 44
- 7 remove duplicates from 6 42

LitCovid

antibacteri* or anti-bacteri*

TRIP PRO

(antibacteri* or "anti-bacteri*") AND (coronaviru* OR "corona virus" OR ncov* OR n-cov* OR COVID-19 OR COVID-19 OR COVID-2019 OR COVID-2019 OR SARS-COV-2 OR SARSCOV-2 OR SARSCOV2 OR SARSCOV2 OR SARSCOV-19 OR SARS-COV-19 OR SARS-COV-2019 OR SARS-COV-2019 OR SARS-COV-2019 OR SARS-COV-2019 OR SARS-COV-2019 OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2019

PubMed

(("anti-bacterial agents" [MeSH Terms]) OR (anti-bacterial agents or acetic acid or alamethicin or amdinocillin or amdinocillin pivoxil or amikacin or amoxicillin or amoxicillin-potassium clavulanate combination or amphotericin b or ampicillin or anisomycin or antimycin a or aurodox or azithromycin or azlocillin or aztreonam or bacitracin or bacteriocins or bambermycins or bongkrekic acid or brefeldin a or butirosin sulfate or calcimycin or candicidin or capreomycin or carbenicillin or carfecillin or cefaclor or cefadroxil or cefamandole or cefatrizine or cefazolin or cefdinir or cefepime or cefixime or cefmenoxime or cefmetazole or cefonicid or cefoperazone or cefotaxime or cefotetan or cefotiam or cefoxitin or cefsulodin or ceftazidime or ceftibuten or ceftizoxime or ceftriaxone or cefuroxime or cephalostrile or cephalostrile

or cyclacillin or dactinomycin or daptomycin or demeclocycline or dibekacin or dicloxacillin or dihydrostreptomycin sulfate or diketopiperazines or distamycins or doripenem or doxycycline or echinomycin or edeine or enoxacin or enrofloxacin or enviomycin or ertapenem or erythromycin or erythromycin estolate or erythromycin ethylsuccinate or fidaxomicin or filipin or floxacillin or fluoroquinolones or fosfomycin or framycetin or fusidic acid or gatifloxacin or gemifloxacin or gentamicins or gramicidin or hygromycin b or imipenem or josamycin or kanamycin or kitasamycin or lactams or lasalocid or leucomycins or levofloxacin or lincomycin or lincosamides or linezolid or lucensomycin or lymecycline or mafenide or mepartricin or meropenem or methacycline or methicillin or metronidazole or mezlocillin or mikamycin or minocycline or miocamycin or moxalactam or moxifloxacin or mupirocin or mycobacillin or nafcillin or nalidixic acid or natamycin or nebramycin or neomycin or netilmicin or netropsin or nigericin or nisin or nitrofurantoin or norfloxacin or novobiocin or nystatin or ofloxacin or oleandomycin or oligomycins or oxacillin or oxolinic acid or oxytetracycline or paromomycin or pefloxacin or penicillanic acid or penicillic acid or penicillin g or penicillin g benzathine or penicillin g procaine or penicillin v or penicillins or pipemidic acid or piperacillin or piperacillin, tazobactam drug combination or pivampicillin or polymyxin b or polymyxins or pristinamycin or prodigiosin or ribostamycin or rifabutin or rifamycins or rifaximin or ristocetin or rolitetracycline or roxarsone or roxithromycin or rutamycin or sirolimus or sisomicin or spectinomycin or spiramycin or streptogramin a or streptogramin group a or streptogramin group b or streptogramins or streptomycin or streptovaricin or sulbactam or sulbenicillin or sulfacetamide or sulfadiazine or sulfamerazine or sulfamethoxypyridazine or sulfanilamide or talampicillin or tazobactam or teicoplanin or tetracycline or thiamphenical or thienamycins or thiostrepton or ticarcillin or tigecycline or tinidazole or tobramycin or tobramycin, dexamethasone drug combination or trimethoprim, sulfamethoxazole drug combination or troleandomycin or tunicamycin or tylosin or tyrocidine or tyrothricin or valinomycin or vancomycin or vernamycin b or viomycin or virginiamycin or beta-lactams or antitreponemal agents or arsphenamine or antitubercular agents or antibiotics, antitubercular or cycloserine or mycophenolic acid or rifampin or beta-lactamase inhibitors or clavulanic acid or leprostatic agents or acedapsone or clofazimine or dapsone or sulfameter or thalidomide)) AND (((wuhan[tw] AND (coronavirus[tw] OR corona virus[tw])) OR coronavirus*[ti] OR COVID*[tw] OR nCov[tw] OR 2019 ncov[tw] OR novel coronavirus[tw] OR novel corona virus[tw] OR covid-19[tw] OR SARS-COV-2[tw] OR Severe Acute Respiratory Syndrome Coronavirus 2[tw] OR coronavirus disease 2019[tw] OR corona virus disease 2019[tw] OR new coronavirus[tw] OR new corona virus[tw] OR new coronaviruses[all] OR novel coronaviruses[all] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[nm] OR 2019 ncov[tw] OR nCov 2019[tw] OR SARS Coronavirus 2[all]) AND (2019/12[dp]:2020[dp]))

WHO COVID-19 Database

anti-bacteri* or antibacter*

Google / Google Scholar

antibacterial AND COVID-19

Search #2

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 22, 2020

Searches Results

exp Coronavirus/ or exp Coronavirus Infections/ or coronaviru*.mp. or "corona virus*".mp. or ncov*.mp. or ncov*.mp. or "cov*.mp. or COVID-19.mp. or COVID-19.mp. or COVID-2019.mp. or COVID-2019.mp. or COVID-2019.mp. or SARS-COV-2.mp. or SARSCOV-2.mp. or SARSCOV-2.mp. or SARSCOV-2.mp. or SARSCOV-2019.mp. or Sars-Cov-19.mp. or Sars-Cov-2019.mp. or "severe acute respiratory syndrome cov 2".mp. or "2019 ncov".mp. or "2019ncov".mp. 25112

- 2 exp Bacteria/ 1352121
- 3 exp Bacterial Infections/880844
- 4 exp Healthcare-Associated Pneumonia/ 3522

(bacteria* or acidobacteria or agricultural inoculants or I forms or spheroplasts or bacteroidetes or bacteroidaceae or bacteroides or porphyromonas or prevotella or cytophagaceae or cytophaga or flexibacter or flavobacteriaceae or capnocytophaga or chryseobacterium or flavobacterium or ornithobacterium or riemerella or tenacibaculum or pedobacter or rhodothermus or sphingobacterium or tannerella forsythia or chlorobi or chlorobium or chloroflexi or chloroflexus or cyanobacteria or anabaena or aphanizomenon or cyanothece or cylindrospermopsis or microcystis or nodularia or nostoc or oscillatoria or plectonema or spirulina or synechococcus or synechocystis or trichodesmium or firmicutes or acidaminococcus or bacillales or alicyclobacillus or bacillaceae or anoxybacillus or bacillus or geobacillus or halobacillus or brevibacillus or brochothrix or gemella or listeria or paenibacillus or pasteuria or planococcaceae or sporosarcina or staphylococcaceae or staphylococcus or thermoactinomyces or clostridiales or butyrivibrio or clostridiaceae or clostridium or sarcina or eubacterium or faecalibacterium or peptococcaceae or desulfitobacterium or desulfotomaculum or peptococcus or peptostreptococcus or ruminococcus or erysipelothrix or lactobacillales or aerococcaceae or abiotrophia or aerococcus or carnobacteriaceae or carnobacterium or enterococcaceae or enterococcus or vancomycin-resistant enterococci or lactobacillaceae or lactobacillus or pediococcus or leuconostocaceae or leuconostoc or oenococcus or weissella or streptococcaceae or lactococcus or streptococcus or moorella or thermoanaerobacter or thermoanaerobacterium or veillonellaceae or fusobacteria or fusobacterium or leptotrichia or propionigenium or streptobacillus or arcobacter or bartonellaceae or bartonella or brachyspira or buchnera or campylobacter or chlamydiales or chlamydiaceae or chlamydia or chlamydophila or fibrobacteres or fibrobacter or caulobacter or "gram-negative aerobic rods and cocci" or acetobacteraceae or gram-negative anaerobic bacteria or gram-negative facultatively anaerobic rods or methylosinus or oceanospirillaceae or piscirickettsiaceae or planctomycetales or rhodobacter or rhodomicrobium or rhodovulum or rickettsiales or roseobacter or spirillaceae or tenericutes or verrucomicrobia or actinobacteria or actinomycetales or bifidobacterium or gardnerella or gram-positive cocci or gram-positive rods or gram-positive asporogenous rods or gram-positive endospore-forming rods or proteobacteria or alphaproteobacteria or bartonella bacilliformis or bartonella henselae or bartonella quintana or beijerinckiaceae or bradyrhizobiaceae or brucellaceae or caulobacteraceae or holosporaceae or hyphomicrobiaceae or methylobacteriaceae or methylocystaceae or phyllobacteriaceae or rhizobiaceae or rhodobacteraceae or rhodospirillales or anaplasmataceae or rickettsiaceae or rickettsieae or orientia tsutsugamushi or rickettsia or sphingomonadaceae or sphingomonas or zymomonas or betaproteobacteria or burkholderiales or alcaligenaceae or achromobacter or alcaligenes or bordetella or taylorella or burkholderiaceae or burkholderia or cupriavidus or ralstonia or comamonadaceae or comamonas or delftia or sphaerotilus or oxalobacteraceae or herbaspirillum or oxalobacter formigenes or gallionellaceae or hydrogenophilaceae or thiobacillus or methylophilaceae or methylobacillus or methylophilus or neisseriaceae or chromobacterium or eikenella or kingella or neisseria or neisseria meningitidis or neisseria mucosa or neisseria sicca or vitreoscilla or nitrosomonadaceae or nitrosomonas or rhodocyclaceae or azoarcus or thauera or zoogloea or spirillum or deltaproteobacteria or bdellovibrio or desulfovibrionales or desulfovibrionaceae or bilophila or desulfovibrio or desulfuromonas or geobacter or myxococcales or myxococcus or stigmatella or epsilonproteobacteria or campylobacterales or campylobacteraceae or helicobacteraceae or helicobacter or wolinella or gammaproteobacteria or acidithiobacillus or aeromonadales or aeromonadaceae or succinivibrionaceae or anaerobiospirillum or alcanivoraceae or alteromonadaceae or alteromonas or marinobacter or moritella or pseudoalteromonas or shewanella or cardiobacteriaceae or cardiobacterium or dichelobacter nodosus or chromatiaceae or chromatium or halothiobacillus or thiocapsa or thiocapsa roseopersicina or coxiellaceae or coxiella or ectothiorhodospiraceae or ectothiorhodospira or halorhodospira halophila or enterobacteriaceae or calymmatobacterium or carbapenem-resistant enterobacteriaceae or citrobacter or cronobacter or edwardsiella or enterobacter or erwinia or escherichia or escherichia coli or

enteropathogenic escherichia coli or enterotoxigenic escherichia coli or escherichia coli k12 or extraintestinal pathogenic escherichia coli or uropathogenic escherichia coli or shiga-toxigenic escherichia coli or enterohemorrhagic escherichia coli or escherichia coli o104 or escherichia coli o157 or hafnia or klebsiella or kluyvera or morganella or pantoea or pectobacterium or photorhabdus or plesiomonas or proteus or providencia or rahnella or salmonella enterica or salmonella enteritidis or salmonella paratyphi a or salmonella paratyphi b or salmonella paratyphi c or salmonella typhi or salmonella typhimurium or serratia or shigella or wigglesworthia or xenorhabdus or yersinia or francisella or halomonadaceae or chromohalobacter or halomonas or legionellaceae or legionella or methylococcaceae or methylococcus or methylomonas or moraxellaceae or acinetobacter or moraxella or psychrobacter or marinomonas or pasteurellaceae or actinobacillus or aggregatibacter or haemophilus or mannheimia or pasteurella or piscirickettsia or pseudomonadaceae or azotobacter or cellvibrio or pseudomonas or thiotrichaceae or beggiatoa or thiothrix or vibrionaceae or aliivibrio or listonella or photobacterium or vibrio or xanthomonadaceae or lysobacter or stenotrophomonas or xanthomonas or xylella or spirochaetales or leptospiraceae or leptospira or spirochaetaceae or borrelia or spirochaeta or Treponema).mp. 1972677

- 6 (bacteremia or hemorrhagic septicemia or lyme neuroborreliosis or neurosyphilis or tabes dorsalis or hordeolum or uveitis, suppurative or fournier gangrene or chlamydial pneumonia or chancroid or chlamydia infections or lymphogranuloma venereum or gonorrhea or granuloma inguinale or syphilis or actinomycosis, cervicofacial or angiomatosis, bacillary or digital dermatitis or ecthyma or erysipelas or erythema chronicum migrans or erythrasma or hidradenitis suppurativa or mycetoma or pinta or rhinoscleroma or staphylococcal skin infections or furunculosis or carbuncle or impetigo or staphylococcal scalded skin syndrome or erythema induratum or lupus vulgaris or yaws or tuberculosis or keratoconjunctivitis or uveitis or meningitis or tuberculoma).mp. 459524
- 7 (healthcare-associated pneumonia or ventilator-associated pneumonia or hospital-acquired pneumonia or nosocomial pneumonia).mp. 8467
- 8 or/2-7 2467917
- 9 1 and 8 1799
- 10 limit 9 to yr="2019 -Current" 177
- 11 remove duplicates from 10 173

LitCovid

bacter* or healthcare-associated pneumonia or ventilator-associated pneumonia or hospital-acquired pneumonia or nosocomial pneumonia

TRIP PRO

Search string 1: bacteri* AND (infect* or superinfect* or super-infect*) AND (coronaviru* OR "corona virus" OR ncov* OR n-cov* OR COVID-19 OR COVID19 OR COVID-2019 OR COVID2019 OR SARS-COV-2 OR SARS-COV-2 OR SARS-COV-19 OR SARS-COV-19 OR SARS-COV-19 OR SARS-COV-2019 OR SARS-COV-2019 OR "severe acute respiratory syndrome cov 2" OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2019

Search string 2: (healthcare-associated pneumonia or ventilator-associated pneumonia or hospital-acquired pneumonia or nosocomial pneumonia) AND (coronaviru* OR "corona virus" OR ncov* OR n-cov* OR COVID-19 OR COVID-2019 OR COVID-2019 OR SARS-COV-2 OR SARSCOV-2 OR SARSCOV-2 OR SARSCOV-19 OR SARS-COV-19 OR SARSCOV-19 OR SARS-COV-2019 OR SARS-COV-2019 OR SARSCOV-2019 OR SARSCOV-201

2019 OR "severe acute respiratory syndrome cov 2" OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2019

PubMed

(((("bacteria"[MeSH Terms]) AND ("bacterial infections"[MeSH Terms])) OR ("healthcare-associated pneumonia"[MeSH Terms])) OR (bacteria* or acidobacteria or agricultural inoculants or I forms or spheroplasts or bacteroidetes or bacteroidaceae or bacteroides or porphyromonas or prevotella or cytophagaceae or cytophaga or flexibacter or flavobacteriaceae or capnocytophaga or chryseobacterium or flavobacterium or ornithobacterium or riemerella or tenacibaculum or pedobacter or rhodothermus or sphingobacterium or tannerella forsythia or chlorobi or chlorobium or chloroflexi or chloroflexus or cyanobacteria or anabaena or aphanizomenon or cyanothece or cylindrospermopsis or microcystis or nodularia or nostoc or oscillatoria or plectonema or spirulina or synechococcus or synechocystis or trichodesmium or firmicutes or acidaminococcus or bacillales or alicyclobacillus or bacillaceae or anoxybacillus or bacillus or geobacillus or halobacillus or brevibacillus or brochothrix or gemella or listeria or paenibacillus or pasteuria or planococcaceae or sporosarcina or staphylococcaceae or staphylococcus or thermoactinomyces or clostridiales or butyriyibrio or clostridiaceae or clostridium or sarcina or eubacterium or faecalibacterium or peptococcaceae or desulfitobacterium or desulfotomaculum or peptococcus or peptostreptococcus or ruminococcus or erysipelothrix or lactobacillales or aerococcaceae or abiotrophia or aerococcus or carnobacteriaceae or carnobacterium or enterococcaceae or enterococcus or vancomycin-resistant enterococci or lactobacillaceae or lactobacillus or pediococcus or leuconostocaceae or leuconostoc or oenococcus or weissella or streptococcaceae or lactococcus or streptococcus or moorella or thermoanaerobacter or thermoanaerobacterium or veillonellaceae or fusobacteria or fusobacterium or leptotrichia or propionigenium or streptobacillus or arcobacter or bartonellaceae or bartonella or brachyspira or buchnera or campylobacter or chlamydiales or chlamydiaceae or chlamydia or chlamydophila or fibrobacteres or fibrobacter or caulobacter or "gram-negative aerobic rods and cocci" or acetobacteraceae or gram-negative anaerobic bacteria or gram-negative facultatively anaerobic rods or methylosinus or oceanospirillaceae or piscirickettsiaceae or planctomycetales or rhodobacter or rhodomicrobium or rhodovulum or rickettsiales or roseobacter or spirillaceae or tenericutes or verrucomicrobia or actinobacteria or actinomycetales or bifidobacterium or gardnerella or gram-positive cocci or gram-positive rods or gram-positive asporogenous rods or gram-positive endospore-forming rods or proteobacteria or alphaproteobacteria or bartonella bacilliformis or bartonella henselae or bartonella quintana or beijerinckiaceae or bradyrhizobiaceae or brucellaceae or caulobacteraceae or holosporaceae or hyphomicrobiaceae or methylobacteriaceae or methylocystaceae or phyllobacteriaceae or rhizobiaceae or rhodobacteraceae or rhodospirillales or anaplasmataceae or rickettsiaceae or rickettsieae or orientia tsutsugamushi or rickettsia or sphingomonadaceae or sphingomonas or zymomonas or betaproteobacteria or burkholderiales or alcaligenaceae or achromobacter or alcaligenes or bordetella or taylorella or burkholderiaceae or burkholderia or cupriavidus or ralstonia or comamonadaceae or comamonas or delftia or sphaerotilus or oxalobacteraceae or herbaspirillum or oxalobacter formigenes or gallionellaceae or hydrogenophilaceae or thiobacillus or methylophilaceae or methylobacillus or methylophilus or neisseriaceae or chromobacterium or eikenella or kingella or neisseria or neisseria meningitidis or neisseria mucosa or neisseria sicca or vitreoscilla or nitrosomonadaceae or nitrosomonas or rhodocyclaceae or azoarcus or thauera or zoogloea or spirillum or deltaproteobacteria or bdellovibrio or desulfovibrionales or desulfovibrionaceae or bilophila or desulfovibrio or desulfuromonas or geobacter or myxococcales or myxococcus or stigmatella or epsilonproteobacteria or campylobacterales or campylobacteraceae or helicobacteraceae or helicobacter or wolinella or gammaproteobacteria or acidithiobacillus or aeromonadales or aeromonadaceae or succinivibrionaceae or anaerobiospirillum or alcanivoraceae or alteromonadaceae or alteromonas or marinobacter or moritella or pseudoalteromonas or shewanella or cardiobacteriaceae or cardiobacterium or dichelobacter nodosus or chromatiaceae or chromatium or halothiobacillus or thiocapsa or thiocapsa roseopersicina or coxiellaceae or coxiella or ectothiorhodospiraceae or ectothiorhodospira or halorhodospira halophila or enterobacteriaceae or calymmatobacterium or carbapenem-resistant enterobacteriaceae or citrobacter or cronobacter or edwardsiella or enterobacter or erwinia or escherichia or escherichia coli or

enteropathogenic escherichia coli or enterotoxigenic escherichia coli or escherichia coli k12 or extraintestinal pathogenic escherichia coli or uropathogenic escherichia coli or shiga-toxigenic escherichia coli or enterohemorrhagic escherichia coli or escherichia coli o104 or escherichia coli o157 or hafnia or klebsiella or kluyvera or morganella or pantoea or pectobacterium or photorhabdus or plesiomonas or proteus or providencia or rahnella or salmonella or salmonella enterica or salmonella enteritidis or salmonella paratyphi a or salmonella paratyphi b or salmonella paratyphi c or salmonella typhi or salmonella typhimurium or serratia or shiqella or wigglesworthia or xenorhabdus or yersinia or francisella or halomonadaceae or chromohalobacter or halomonas or legionellaceae or legionella or methylococcaceae or methylococcus or methylomonas or moraxellaceae or acinetobacter or moraxella or psychrobacter or marinomonas or pasteurellaceae or actinobacillus or aggregatibacter or haemophilus or mannheimia or pasteurella or piscirickettsia or pseudomonadaceae or azotobacter or cellvibrio or pseudomonas or thiotrichaceae or beggiatoa or thiothrix or vibrionaceae or aliivibrio or listonella or photobacterium or vibrio or xanthomonadaceae or lysobacter or stenotrophomonas or xanthomonas or xylella or spirochaetales or leptospiraceae or leptospira or spirochaetaceae or borrelia or spirochaeta or Treponema)) OR (bacteremia or hemorrhagic septicemia or lyme neuroborreliosis or neurosyphilis or tabes dorsalis or hordeolum or uveitis, suppurative or fournier gangrene or chlamydial pneumonia or chancroid or chlamydia infections or lymphogranuloma venereum or gonorrhea or granuloma inguinale or syphilis or actinomycosis, cervicofacial or angiomatosis, bacillary or digital dermatitis or ecthyma or erysipelas or erythema chronicum migrans or erythrasma or hidradenitis suppurativa or mycetoma or pinta or rhinoscleroma or staphylococcal skin infections or furunculosis or carbuncle or impetigo or staphylococcal scalded skin syndrome or erythema induratum or lupus vulgaris or yaws or tuberculosis or keratoconjunctivitis or uveitis or meningitis or tuberculoma)) AND (((wuhan[tw] AND (coronavirus[tw] OR corona virus[tw])) OR coronavirus*[ti] OR COVID*[tw] OR nCov[tw] OR 2019 ncov[tw] OR novel coronavirus[tw] OR novel corona virus[tw] OR covid-19[tw] OR SARS-COV-2[tw] OR Severe Acute Respiratory Syndrome Coronavirus 2[tw] OR coronavirus disease 2019[tw] OR corona virus disease 2019[tw] OR new coronavirus[tw] OR new corona virus[tw] OR new coronaviruses[all] OR novel coronaviruses[all] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[nm] OR 2019 ncov[tw] OR nCov 2019[tw] OR SARS Coronavirus 2[all]) AND (2019/12[dp]:2020[dp]))

WHO COVID-19 Database

bacteri* OR healthcare-associated pneumonia or ventilator-associated pneumonia or hospital-acquired pneumonia or nosocomial pneumonia

Google / Google Scholar

Covid-19 and bacteri* or healthcare-associated pneumonia or ventilator-associated pneumonia or hospital-acquired pneumonia or nosocomial pneumonia

Search #3

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 22, 2020

Searches Results

exp Coronavirus/ or exp Coronavirus Infections/ or coronaviru*.mp. or "corona virus*".mp. or ncov*.mp. or ncov*.mp. or "novel cov".mp. or COVID-19.mp. or COVID19.mp. or COVID-2019.mp. or COVID2019.mp. or SARS-COV-2.mp. or SARS-COV-2.mp. or SARS-COV-2.mp. or SARS-COV-2.mp. or SARS-COV-2.mp. or Sars-Cov-19.mp. or Sars-Cov-2019.mp. or "severe acute respiratory syndrome cov 2".mp. or "2019 ncov".mp. or "2019ncov".mp. 25112

2 exp Fungi/ 384350

- 3 exp Mycoses/ 125647
- 4 (fungus or fungi or agricultural inoculants or ascomycota or eurotiales or byssochlamys or emericella or eupenicillium or eurotium or monascus or neosartorya or talaromyces or thermoascus or hypocreales or claviceps or cordyceps or epichloe or gibberella or hypocrea or nectria or magnaporthe or onygenales or arthrodermataceae or ophiostomatales or ophiostoma or parmeliaceae or usnea or phyllachorales or pneumocystis or pseudallescheria or saccharomycetales or candida or basidiomycota or blastocladiomycota or allomyces or blastocladiella or coelomomyces or chytridiomycota or entomophthorales or conidiobolus or entomophthora or mucorales or absidia or cunninghamella or mortierella or mucor or phycomyces or rhizomucor or rhizopus or glomeromycota or lichens or microsporidia or microsporea or microsporida or apansporoblastina or encephalitozoon or enterocytozoon or nosema or vittaforma or pansporablastina or amblyospora or glugea or loma or pleistophora or thelohania or acremonium or alternaria or aspergillus or beauveria or blastomyces or botrytis or brettanomyces or chrysosporium or cladosporium or coccidioides or colletotrichum or cryptococcus or duddingtonia or epidermophyton or exophiala or fusarium or geotrichum or gliocladium or helminthosporium or histoplasma or kloeckera or lacazia or madurella or malassezia or metarhizium or microsporum or neotyphodium or paecilomyces or paracoccidioides or penicillium or phialophora or pyricularia grisea or rhizoctonia or rhodotorula or scedosporium or scopulariopsis or sporothrix or stachybotrys or trichoderma or trichophyton or trichosporon or verticillium or mycorrhizae or neocallimastigomycota or neocallimastigales or neocallimastix or piromyces or yeasts or debaromyces or dekkera or dipodascus or endomyces or eremothecium or hanseniaspora or kluyveromyces or lipomyces or metschnikowia or pichia or saccharomyces or saccharomycopsis or schizosaccharomyces or torulaspora or williopsis or yarrowia).mp.
- (fungal infection* or mycoses or candidiasis or coccidioidomycosis or cryptococcosis or dermatomycoses or blastomycosis or chromoblastomycosis or hyalohyphomycosis or alternariosis or cerebral phaeohyphomycosis or fusariosis or lobomycosis or mycetoma or sporotrichosis or tinea or onychomycosis or panophthalmitis or geotrichosis or histoplasmosis or candidemia or fungemia or neuroaspergillosis or pulmonary aspergillosis or microsporidiosis or encephalitozoonosis or otomycosis or paracoccidioidomycosis or phaeohyphomycosis or piedra or pneumocystis infections or pneumonia, pneumocystis or trichosporonosis or zygomycosis or mucormycosis or fungal infection* or fungal lung disease* or Pneumocystis Pneumonia or Suppurative Uveitis or Cryptococcal Meningitis).mp. 136456

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LitCovid

fungi or fungus or fungal or mycoses

TRIP PRO

(fungi or fungus or fungal or mycoses) AND (coronaviru* OR "corona virus" OR ncov* OR n-cov* OR COVID-19 OR COVID19 OR COVID-2019 OR SARS-COV-2 OR SARSCOV-2 OR SARSCOV-2 OR SARSCOV-2 OR SARSCOV-19 OR SARSCOV-19 OR SARSCOV-19 OR SARSCOV-2019 OR SARSCOV-2019 OR SARSCOV-2019 OR "severe acute respiratory syndrome cov 2" OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2019

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(((fungi[MeSH Terms]) OR (mycoses[MeSH Terms])) OR (fungus or fungi or agricultural inoculants or ascomycota or eurotiales or byssochlamys or emericella or eupenicillium or eurotium or monascus or neosartorya or

talaromyces or thermoascus or hypocreales or claviceps or cordyceps or epichloe or gibberella or hypocrea or nectria or magnaporthe or onygenales or arthrodermataceae or ophiostomatales or ophiostoma or parmeliaceae or usnea or phyllachorales or pneumocystis or pseudallescheria or saccharomycetales or candida or basidiomycota or blastocladiomycota or allomyces or blastocladiella or coelomomyces or chytridiomycota or entomophthorales or conidiobolus or entomophthora or mucorales or absidia or cunninghamella or mortierella or mucor or phycomyces or rhizomucor or rhizopus or glomeromycota or lichens or microsporidia or microsporea or microsporida or apansporoblastina or encephalitozoon or enterocytozoon or nosema or vittaforma or pansporablastina or amblyospora or glugea or loma or pleistophora or thelohania or acremonium or alternaria or aspergillus or beauveria or blastomyces or botrytis or brettanomyces or chrysosporium or cladosporium or coccidioides or colletotrichum or cryptococcus or duddingtonia or epidermophyton or exophiala or fusarium or geotrichum or gliocladium or helminthosporium or histoplasma or kloeckera or lacazia or madurella or malassezia or metarhizium or microsporum or neotyphodium or paecilomyces or paracoccidioides or penicillium or phialophora or pyricularia grisea or rhizoctonia or rhodotorula or scedosporium or scopulariopsis or sporothrix or stachybotrys or trichoderma or trichophyton or trichosporon or verticillium or mycorrhizae or neocallimastigomycota or neocallimastigales or neocallimastix or piromyces or yeasts or debaromyces or dekkera or dipodascus or endomyces or eremothecium or hanseniaspora or kluyveromyces or lipomyces or metschnikowia or pichia or saccharomyces or saccharomycopsis or schizosaccharomyces or torulaspora or williopsis or yarrowia or ungal infection* or mycoses or candidiasis or coccidioidomycosis or cryptococcosis or dermatomycoses or blastomycosis or chromoblastomycosis or hyalohyphomycosis or alternariosis or cerebral phaeohyphomycosis or fusariosis or lobomycosis or mycetoma or sporotrichosis or tinea or onychomycosis or panophthalmitis or geotrichosis or histoplasmosis or candidemia or fungemia or neuroaspergillosis or pulmonary aspergillosis or microsporidiosis or encephalitozoonosis or otomycosis or paracoccidioidomycosis or phaeohyphomycosis or piedra or pneumocystis infections or pneumonia, pneumocystis or trichosporonosis or zygomycosis or mucormycosis or fungal infection* or fungal lung disease* or Pneumocystis Pneumonia or Suppurative Uveitis or Cryptococcal Meningitis)) AND (((wuhan[tw] AND (coronavirus[tw] OR corona virus[tw])) OR coronavirus*[ti] OR COVID*[tw] OR nCov[tw] OR 2019 ncov[tw] OR novel coronavirus[tw] OR novel corona virus[tw] OR covid-19[tw] OR SARS-COV-2[tw] OR Severe Acute Respiratory Syndrome Coronavirus 2[tw] OR coronavirus disease 2019[tw] OR corona virus disease 2019[tw] OR new coronavirus[tw] OR new corona virus[tw] OR new coronaviruses[all] OR novel coronaviruses[all] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[nm] OR 2019 ncov[tw] OR nCov 2019[tw] OR SARS Coronavirus 2[all]) AND (2019/12[dp]:2020[dp]))

WHO COVID-19 Database

fungi or fungus or fungal or mycoses

Google / Google Scholar

Covid-19 AND (fungi or fungus or fungal or mycoses)

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