Bacterial co-infection in COVID-19: a call to stay vigilant

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Abstract

Co-infection with diverse bacteria is commonly encountered in patients infected with the novel coronavirus, SARS-CoV-2. This type of co-infection significantly impacts the occurrence and development of the novel coronavirus infection. Bacterial co-pathogens are typically identified in the respiratory system and in blood culture, which complicate diagnosis, treatment, and prognosis of COVID-19, and even exacerbate the severity of the disease symptoms and increase mortality rates. However, the status and impact of bacterial co-infections during the COVID-19 pandemic have not been properly studied. Recently, the amount of literature on the co-infection of SARS-CoV-2 and bacteria has gradually increased, enabling a comprehensive discussion on this type of co-infection. In the present review, we focus on bacterial infections in the respiratory system and blood of patients with COVID-19, because these infection types significantly affect the severity and mortality of COVID-19. Furthermore, the development of COVID-19 has significantly increased the drug-resistance rates of bacteria. Understanding the drug-resistance rates of various bacteria is fundamental for the optimal utilization and management of antibiotics.

Keywords: COVID-19; SARS-CoV-2; Co-infection; Antimicrobial resistance; Ventilator-associated pneumonia; bloodstream infection

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Introduction

Since December 8, 2019, several cases of pneumonia of unknown etiology have been reported in Wuhan, Hubei province, China*(Huang et al., 2020; Lu et al., 2020)*. The disease, identified as being caused by a novel coronavirus strain, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was named coronavirus disease 2019 (COVID-19)*(WHO, 11 february 2020)*. On Jan 30, 2020, the World Health Organization (WHO) declared the COVID-19 outbreak as a Public Health Emergency of International Concern (PHEIC)*(WHO, 30 January 2020)*. In May 2023, WHO announced that COVID-19 was no longer a public health emergency*(WHO, 5 may 2023)*. However, although isolated COVID-19 infections will no longer pose a serious threat to human life, this perspective should be re-assessed in the presence of bacterial co-infections.

A bacterial co-infection is a common complication of many respiratory viral infections, which leads to a significant increase in the incidence and mortality rates*(Bakaletz, 2017; Westblade et al., 2021)*. During the 1918 influenza pandemic, bacterial co-infection was an important cause of most influenza-related deaths. Common upper respiratory tract bacteria, such as *Streptococcus pneumoniae*, *β-Hemolytic Streptococcus*, *Haemophilus influenzae*, and *Staphylococcus aureus*, were the most common pathogens*(Morens et al., 2008; Chien et al., 2009)*. During the 2009 influenza pandemic, 18-30% of all intensive care unit (ICU) patients with this disease developed bacterial co-infections *(MacIntyre et al., 2018)*. Other respiratory viruses, such as seasonal/pandemic influenza, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and SARS-CoV-1, also exhibit varying levels of bacterial/fungal mixed infections*(Zahariadis et al., 2006; Assiri et al., 2013; Joseph*

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et al., 2013). In comparison, the infection and mortality rates of COVID-19 have far exceeded any other common influenza pandemics*(Li et al., 2020)*.

The co-infection with the novel coronavirus and other microorganisms is a critical factor in the pathogenesis of COVID-19. Clinical trials and metagenomic studies show that, in patients with COVID-19, other viruses, bacteria, and fungi, coexist with the novel coronavirus*(Chen et al., 2020; Shen et al., 2020; Hoque et al., 2021)*, About 50% of all patients who died of COVID-19 suffered from secondary bacterial infections*(Chen et al., 2020; Zhou et al., 2020)*. Therefore, a bacterial co-infection may have additive effects on the pathophysiological progress of COVID-19. These additive effects may result in more difficult diagnosis and treatment, increased risk of shock and respiratory failure, prolonged hospitalization in an ICU, and even increased mortality rates*(Ruuskanen et al., 2011; Li et al., 2020; Zhou et al., 2020; Hoque et al., 2021)*. In addition, evidence shows that, due to COVID-19, an increased number of hospitalized patients have received an empirical antimicrobial treatment, potentially increasing the number of drug-resistant infections worldwide*(Chen et al., 2020; Zhou et al., 2020)*. A recent special report from the US Centers for Disease Control and Prevention found a 15% increase in drug-resistant microorganisms associated with the epidemic*(CDC,2022)*. Therefore, co-infection of drug-resistant bacteria not only brings difficulties to the treatment of COVID-19, but also challenges the management of antibiotics. However, and unfortunately, during the pandemic, these issues did not receive proper research and discussion.

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In the present review, we collect and discuss the research on bacterial co-infections published since the outbreak of COVID-19. We focus on bacterial co-infections of the respiratory system and bloodstream, because they greatly aggravate the development of COVID-19, increasing the rates of incidence and mortality of patients. In addition,

we also discuss drug resistance of related bacteria. The purpose of this review is to emphasize that microbial co-infection is a factor that cannot be ignored in COVID-19. Furthermore, we provide valuable references for clinicians, concerning the diagnosis or treatment of patients with COVID-19 and a bacterial co-infection.

Survey methodology

The search engines we employed included PubMed (https://pubmed.ncbi.nlm.nih.gov/), ScienceDirect (https://www.sciencedirect.com/), Scopus (http://www.scopus.com/), and Google Scholar (https://scholar.google.com/). We conducted keyword searches that centered around, but were not limited to, the terms **COVID-19**, **SARS-CoV-2**, **bacterial co-infection and COVID-19**, **risk factors for bacterial co-infection**, **pulmonary function and COVID-19**, **ventilator-associated pneumonia and COVID-19**, **bloodstream infections and COVID-19**, and **antibiotic resistance during COVID-19**.

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To address potential bias or low-quality articles, we applied a rigorous screening process. First, we conducted a title and abstract review to identify articles that were clearly irrelevant or did not meet our research criteria. Next, we undertook a full-text review to assess the methodological quality and scientific validity of the remaining articles. Articles were only included if they provided credible and unbiased evidence on the topic, had low risk of bias, and were of high quality according to our pre-specified criteria. If articles were found to have significant bias or low quality, they were excluded from the review. Additionally, we performed sensitivity analyses to account for any potential bias introduced by including or excluding individual studies.

Early evidence on COVID-19 and bacterial infections

Although there are limited data on bacterial infections in COVID-19 patients in the early stages of the outbreak, potential links between the two infection types have been investigated. Guan and colleagues evaluated the medical records of 1099 adult patients with laboratory-confirmed COVID-19, which were reported between December 11, 2019 and January 29, 2020. Many of these patients were admitted without sputum bacteriological or fungal assessments, possibly due to the overwhelmed state of many hospital resources at the time of the outbreak *(Guan et al., 2020)*.

With a large number of studies, reports of COVID-19 and bacterial infections have increased, and potential links have been discovered. Zhou and colleagues analyzed 191 adult COVID-19 hospitalized patients in Wuhan and found that sepsis was the most prevalent complication, both among non-survivors and survivors.*(Zhou et al., 2020)*. However, whether sepsis was caused by viral or bacterial infections in those patients still needs further studies. A study conducted at Zhongnan Hospital in Wuhan revealed that among the 221 adult COVID-19 patients, the incidence of mixed bacterial infections was significantly higher in severe cases, such as those requiring ICU and mechanical ventilation, compared to non-severe cases (25.5% vs. 1.8%; $p < 0.001$)*(Zhang et al., 2020)*. This difference suggests that bacterial infections may play a less relevant role in the early, non-severe stages of COVID-19. In fact, a UK study involving 836 patients with the novel coronavirus infection reported a relatively low frequency of bacterial co-infection during the early hospitalization for COVID-19 (3.2%, 0-5 days after admission)*(Hughes et al., 2020)*. Similarly, Rawson *et al*. analyzed a survey from China and the United States and reported that 8% of 806 COVID-19 patients had a mixed bacterial or fungal infection*(Rawson et al., 2020)*. Among 712 hospitalized adult COVID-19 patients at the Valladolid football Club in

Spain, 16% were reported to have a bacterial/fungal infection or co-infection*(Nebreda-Mayoral et al., 2022)*. Another study reported that the rates of co-infection and secondary infection in patients with COVID-19 ranged from as low as 0.6% to as high as 45%*(Lai et al., 2020)*.

Together, these early reports suggest that bacterial infections are present in COVID-19 patients. Given the limited medical resources available in many hospitals in the early stages of the outbreak, information on the microbial causes and effects on COVID-19 patients has been limited. This limitation reinforces the need to further study the effects of bacterial infections on COVID-19 patients, which we will focus of the following sections.

Main bacterial species associated with co-infection in COVID-19 patients

The global leading culprits in the cause of a hospital-acquired infection (HAI) or a community-acquired pneumonia (CAP) are the so-called ESKAPE pathogens: *E. faecium*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa* and *Enterobacter species(Rice, 2008)*. A recent microbiological study on patients with COVID-19 showed that, in the COVID-19 infected patients, specific genera including *Staphylococcus*, *Nostoc*, *Anabaena*, *Mycobacterium*, *Cyanothece*, *Bradyrhizobium*, *Actinomyces*, *Pseudomonas*, *Propionibacterium*, *Corynebacterium*, *Rhodopseudomonas*, *Nodularia*, *Burkholderia*, *Micrococcus*, *Acinetobacter*, *Methylobacterium*, *Streptomyces*, *Rhodococcus*, and *Rhodobacter* had higher relative abundances, in comparison with the non-COVID samples*(Hoque et al., 2021)*. Specifically, among the bacterial species reported to co-infect with COVID-19, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Acinetobacter baumannii*, *Legionella pneumophila* and *Clamydia pneumoniae* appear to be the most

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common*(Khatiwada & Subedi, 2020; Peddu et al., 2020; Hoque et al., 2021)*. The research by Sang *et al*. showed that, when patients with COVID-19 stayed in the ICU for more than 72 hours, a secondary infection became very common (86.6%). The most common bacteria involved in these secondary infections were *Klebsiella pneumoniae* (24.5%)*, Acinetobacter baumannii* (21.8%), *Stenotrophomonas maltophilia* (9.9%), *Candida albicans* (6.8%), and *Pseudomonas spp.* (4.8%)*(Sang et al., 2021).* In a retrospective, single-center study held by Chen *et al.*, among the 99 cases of 2019 novel coronavirus pneumonia in Wuhan, the co-infected bacterial species included *Acinetobacter baumannii* and *Klebsiella pneumoniae(Chen et al., 2020).* In another retrospective cohort study, Garcia-Vidal *et al*. studied the community-acquired infection and HAI of patients with COVID-19*(Garcia-Vidal et al., 2021)*. In these community-acquired co-infections, thirty community-acquired bacterial co-infections were documented in 25 patients (2.5%). *S. pneumoniae* and *S. aureus* were the most common bacteria in this scenario. For HAI, a total of 51 hospital-acquired infections were recorded among the 43 patients. Of these, 44 were bacterial and diagnosed in 38 patients (3.8%). The most commonly isolated microorganisms were *P. aeruginosa* (n = 8), *E. coli* (n = 6), *Klebsiella spp*. (n = 5), and *S. aureus* (n = 5)*(Garcia-Vidal et al., 2021)*. In another study on the lung microbiome of 20 deceased COVID-19 patients by post-mortem biopsies, the most common bacterial genera identified were *Acinetobacter*, *Chryseobacterium*, *Burkholderia*, *Brevundimonas*, *Sphingobium*, and *Enterobacteriaceae(Fan et al., 2020)*.

Concerning fungal infections, *Aspergillus flavus*, *Candida glabrata*, and *Candida albicans* were the most common co-infecting fungi*(Bassetti et al., 2020; Sang et al., 2021)*. In patients with COVID-19, Zuo *et al.* observed remarkable enrichments of

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opportunistic fungal pathogens, specifically belonging to the *Candida* and *Aspergillus* lineages, during the course of the disease. Among them, *C. albicans* was represented excessively in COVID-19 patients*(Zuo et al., 2020)*. In addition, a descriptive study by Chen *et al*. showed that *Aspergillus flavus*, *Candida glabrata*, and *Candida albicans* were the most common coinfecting fungi*(Chen et al., 2020)*. Similarly, Salehi *et al.* analyzed 53 hospitalized COVID-19 patients with oropharyngeal candidiasis (OPC). These researchers found that *C. albicans* was the most prevalent pathogen, accounting for 70.7% of all infections, followed by *C. glabrata* (10.7%), *C. dubliniensis* (9.2%), *C. parapsilosis sensu stricto* (4.6%), *C. tropicalis* (3%), and *C. krusei* (1.5%)*(Salehi et al., 2020)*.

In conclusion, there is a growing number of reports of bacterial infections in patients with COVID-19. Although the main types of bacterial infection in different regions of the world are different, it is clear that the rate of SARS-CoV-2 co-infection is in direct proportion to the severity of the disease*(Denina et al., 2020)*. It is also clear that co-infection increases COVID-19 mortality rates*(Bengoechea & Bamford, 2020)*. Therefore, carefully monitoring whether COVID-19 patients also have bacterial infections will help prevent and treat these patients.

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Impact of the combination of COVID-19 with bacterial infections on lung function

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In recent years, a large body of evidence has indicated that the lungs are the organs most severely affected by COVID-19, undergoing a series of pathophysiological events including diffuse alveolar epithelium destruction, hyaline membrane formation, capillary damage and bleeding, alveolar septal fibrous proliferation, and pulmonary consolidation*(Mo et al., 2020; Shi et al., 2020; Torres-Castro et al., 2021; Steinbeis et al., 2022)*. An important characteristic of COVID-19 is the extensive

injury of alveolar epithelial cells and endothelial cells with secondary fibroproliferation*(Venkataraman & Frieman, 2017; Wendisch et al., 2021)*. This type of injury indicates a potential for chronic vascular and alveolar remodeling, which can lead to lung fibrosis and/or pulmonary hypertension*(Frija-Masson et al., 2020; Wendisch et al., 2021)*. These changes in the lungs directly lead to the degradation of their function. According to statistics, 15-20% of ICU inpatients affected by COVID-19 received ventilation support*(Karagiannidis et al., 2020; Grasselli et al., 2021; Strålin et al., 2021)*. However, whether bacterial infection in COVID-19 played an important role in this process has not been discussed.

COVID-19 and ventilator-associated lower respiratory tract infections

Ventilator-associated pneumonia (VAP) is an important factor affecting the lung respiratory function. VAP that complicates COVID-19 infections has often occurred in late stages of mechanical ventilation*(Luyt et al., 2020; Blonz et al., 2021; Maes et al., 2021)*. Some studies have proved that the respiratory dysfunction of patients with COVID-19 has an important connection with bacterial ventilator-associated lower respiratory tract infections (VA-LRTIs)*(Luyt et al., 2020; Blonz et al., 2021; COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators, 2021; Rouzé et al., 2021; Razazi et al., 2023)*. Previous studies have found an increased risk of VAP and VA-LRTI in critically ill patients with COVID-19, with incidence rates ranging from 29% to 86%*(Razazi et al., 2020; Blonz et al., 2021; Giacobbe et al., 2021; Maes et al., 2021)*. In a retrospective study involving 91 patients with COVID-19 respiratory failure (81 on a ventilator for > 48 h), Maes *et al*. reported a hazard ratio of 2.1, compared to non-COVID-19 patients, and an incidence of VAP of 79%*(Maes et al., 2021)*. In another study of 568 COVID-19 patients, 29% had VAP, with a higher incidence than that observed in influenza pneumonia or non-viral

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pneumonia*(Giacobbe et al., 2021)*. Additionally, Hedberg *et al.* compared the VA-LRTIs of the first and second waves of the epidemic. They reported that the duration of mechanical ventilation was shorter during the second wave (8 days; interquartile range [IQR]: 5–16 days) compared with the first wave (11 days; IQR: 6–19 days). The mortality rate within 24 hours after extubation in the second wave (32%, 30/93) was significantly higher than that in the first wave (20%, 76/381) *(Hedberg et al., 2022)*. Bacteriology analysis of alveolar lavage fluid from VAP patients revealed that, at the ICU admission moment, the incidence of VA-LRTI was significantly higher in patients with COVID-19 pneumonia, than in patients with influenza pneumonia or no viral infection. Gram-negative bacilli, primarily *P. aeruginosa*, *Enterobacter spp*., and *Klebsiella spp*., were the causative agents in the majority of the first VA-LRTI episodes, while gram-positive bacteria were mainly *Staphylococcus aureus(Giacobbe et al., 2021; Grasselli et al., 2021; Rouzé et al., 2021; Wicky et al., 2021; Hedberg et al., 2022)*. Additionally, a considerably higher rate of Extended-spectrum Beta-lactamase-producing *Enterobacterales* (ESBL-PE) has been reported, compared to historical non-COVID-19 controls (72% vs 47%). *Aspergillus* appeared to be more common in COVID-19 respiratory failure patients than in other populations*(Razazi et al., 2020)*.

Taken together, existing evidence suggests that COVID-19 is associated with exceptionally long durations of mechanical ventilation treatment and high VA-LRTI occurrence proportions. Compared to patients with influenza-induced pneumonia or those hospitalized in ICUs without viral infections, individuals infected with SARS-CoV-2 are significantly more likely to develop VA-LRTI. Therefore, understanding the pathophysiology of VA-LRTI in patients with COVID-19 infection is very important for epidemic prevention, as well as for the control and treatment of the

disease.

Tuberculosis and COVID-19 co-infection: a double blow to lung function

In addition to the above-mentioned bacteria, *Mycobacterium tuberculosis* combined with COVID-19 infection also has an important impact on lung function. On the one hand, the lung is the main infection site of both COVID-19 and *M. tuberculosis*. As such, *M. tuberculosis* can also affect lung function during COVID-19 infection. On the other hand, lung damage caused by severe COVID-19 and the subsequent vulnerability to tuberculosis (TB) is also a significant concern*(Mousquer et al., 2021)*. The first cohort evaluating the association between TB and COVID-19 consisted of international cooperation, grouping 49 cases of co-infection, from 8 different countries. This study identified a higher mortality rate among elderly people (12.3%) with a previous history of TB*(Tadolini et al., 2020)*. Another study conducted in the Philippines has provided further clarity on the detrimental impact of TB on COVID-19, establishing a correlation between co-infection and a heightened risk of increased incidence and mortality*(Sy et al., 2020)*. Furthermore, a meta-analysis of co-infection with SARS-CoV-2 and *M. tuberculosis* has shown a two-fold increase in mortality among co-infected patients, and multiple case-control studies have confirmed the changes in disease pathology associated with co-infection*(Sarkar et al., 2021)*.

M. tuberculosis seriously interferes with the pulmonary microenvironment. During a latent tuberculosis infection, the persistent presence of mycobacteria can induce chronic pro-inflammatory reactions in the lung parenchyma, leading to lung injury*(Mousquer et al., 2021; Shah et al., 2022)*. The results from previous studies showed that a large proportion of patients with COVID-19 further complicated by tuberculosis branch infection needed ventilation (18%, of which 7.4% needed

intubation). 32% of these patients needed supplemental oxygen, and the hospital stay was significantly prolonged. In addition to the time required for tuberculosis healing, 61.7% of the patients needed an average of 14 days of hospital stay due to COVID-19*(Motta et al., 2020; Tadolini et al., 2020; Migliori et al., 2021; Visca et al., 2021)*. In a comprehensive view, the pulmonary cavitation caused by TB fundamentally alters the architecture of the lungs. The necrotic, thin-walled tissue is replaced by fibrous epithelial tissue, diminishing the available surface for gas exchange. Moreover, the bronchiectasis and bronchostenosis that were formed restrained the airflow, while obstructed capillaries compromised the lung fluid drainage*(Dheda et al., 2005; Kılıç et al., 2022; Shah et al., 2022)*. Imaging findings reported in TB patients with COVID-19 revealed the development of a multiple and bilateral ground glass opacity, and consolidations with the air bronchogram*(Lal et al., 2020; Motta et al., 2020; Tadolini et al., 2020; TB/COVID-19 Global Study Group, 2022)*. Unilateral pulmonary infiltrates were seen in 33% of patients with TB and COVID-19, while bilateral infiltrates were reported in 19% of the patients. Chest CT images suggesting the diagnosis of pulmonary TB have been obtained in cavitating lung lesions. Among TB patients, bilateral cavitary lesions have been reported more often (27%) than unilateral cavitary lesions (21%)*(Motta et al., 2020; Tadolini et al., 2020; TB/COVID-19 Global Study Group, 2022)*.

In general, the macro-structural changes caused by TB have damaged the function and defense capacity of the lower respiratory tract. Its consequences made the lungs more prone to severe complications, such as pneumonia and respiratory failure. In addition, *M. tuberculosis* infection is an inducer of the development of severe COVID-19. The lung injury caused by severe COVID-19, and the subsequent susceptibility to TB, is also a matter of concern. Understanding how pathogens affect lung function in the

lung microenvironment, and clarifying the mechanisms of susceptibility and prognosis of the two infections, will be the basis for developing new strategies to prevent and treat the tuberculosis/COVID-19 dual infection.

COVID-19 complications in the presence of bloodstream co-infection

A bloodstream infection (BSI) refers to the presence of viable microorganisms in the bloodstream*(Laupland & Church, 2014)*. BSI may lead to sepsis, defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection*(Singer et al., 2016)*. In patients receiving hemodialysis, BSI is an important cause of hospitalization, morbidity, and mortality. In all hospitalized patients, the BSI incidence rate is about 6%, and the associated mortality rate is about 15%, which affects 10-20% of all intensive care patients, and causes a three-fold increase in the mortality rate of this patient population*(Rhee et al., 2017; Pijl et al., 2021)*. Although it has been observed that some COVID-19 patients have BSI*(Giacobbe et al., 2020; He et al., 2020; Kokkoris et al., 2021; Patton et al., 2023)*, its co-occurrence has rarely been systematically discussed since the COVID-19 outbreak.

Incidence of BSI and pathogens

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Current research has shown that BSI is one of the main types of acquired infection in ICU patients with COVID-19, and has a high mortality rate*(Giacobbe et al., 2020; He et al., 2020; Grasselli et al., 2021; Kokkoris et al., 2021)*. In a recent meta-analysis, BSI occurred in 7.3% of all hospitalized patients with COVID-19, and in 29.6% of those admitted to the ICU*(Ippolito et al., 2021)*. It should be noted that the incidence rates of BSI vary among different regions, exceeding 30% in some research reports*(Giacobbe et al., 2020; Grasselli et al., 2021; Kokkoris et al., 2021)*. This variability may be related to the severity of the epidemic, the timing of data statistics,

and the local medical conditions*(Goyal et al., 2020; Langford et al., 2020; Kokkoris et al., 2021; Soriano et al., 2021)*. During the early phases of the pandemic, a study by Giacobbe *et al.* involving 78 critically ill COVID-19 patients, concluded that 45 ICU-acquired BSI episodes were recorded in 31 patients, with an incidence of 47 episodes per 1000 risky patients, per day. This incidence rate is significantly higher than that of 5-19 episodes per 1000 patient-days registered in other heterogeneous, non-COVID-19 ICU patient populations*(Giacobbe et al., 2020)*. Similarly, Grasselli *et al*. observed that, out of the 774 patients included, 359 patients (46%) experienced 759 hospital infections, with BSIs accounting for 44% (including catheter-related BSIs)*(Grasselli et al., 2021)*. This BSI rate was significantly higher than that reported in the largest study published so far in the general population of ICU patients. It was even higher than that observed in patients undergoing extracorporeal membrane oxygenation for refractory respiratory failure*(Vincent et al., 2009; Grasselli et al., 2017)*. Additionally, different types of COVID-19 may have different effects on the incidence of BSI; however, relevant literature is still limited in this field. Kang *et al.* reported that, during the surge of the Omicron variant, the incidence of central venous catheter-related BSI increased, which might be due to the increased workload of the attending nurses*(Kang et al., 2023)*. Regarding the mortality rates of BSI, they greatly varied among COVID-19 patients in ICUs, with BSI rates from 39% to 100%, in different studies*(Buetti et al., 2021; Grasselli et al., 2021; Kokkoris et al., 2021; Massart et al., 2021; Kurt et al., 2022; Torrecillas et al., 2022; Strelkova et al., 2023)*. These relatively high mortality rates may be due to a larger median age of the patients (in most studies, patients were 60-73 years old)*(Buetti et al., 2021; Grasselli et al., 2021; Kokkoris et al., 2021; Massart et al., 2021; Kurt et al., 2022; Torrecillas et al., 2022; Strelkova et al., 2023)*. In addition, infection with multidrug-resistant bacteria may be

an important factor leading to high mortality rates in BSI patients. The study of Kurt *et al*. suggests that the high mortality rate of BSI (83%) may be related to the high comorbidity and incidence of multidrug-resistant *Acinetobacter baumannii* and carbapenem-resistant *Klebsiella pneumoniae* (60%)*(Kurt et al., 2022)*. Similar to the study by Palanisamy *et al.*, *Acinetobacter baumannii* and *Klebsiella pneumoniae* dominate, with a total mortality rate of 100%*(Palanisamy et al., 2021)*.

Regarding pathogens, most studies have shown that Gram-positive bacteria accounted for a large proportion, mainly *Enterococcus faecalis*, coagulase-negative *staphylococci*, *Staphylococcus aureus*, and *Candida spp.(Giacobbe et al., 2020; He et al., 2020; Bonazzetti et al., 2021; Grasselli et al., 2021; Kokkoris et al., 2021; Buetti et al., 2022; Gago et al., 2022; Mormeneo Bayo et al., 2022; Bonazzetti et al., 2023)*. *Enterococci* were more frequently isolated in BSI of COVID-19 patients, ranging from 10% to 50% of all cases*(Giacobbe et al., 2020; Bonazzetti et al., 2021; Grasselli et al., 2021; Kokkoris et al., 2021; Buetti et al., 2022; Gago et al., 2022; Bonazzetti et al., 2023)*, which may be related to the imbalance of the intestinal microbiota and bacterial translocations into the blood during COVID-19*(Prasad et al., 2022; Venzon et al., 2022)*. It should be noted that, although coagulase-negative Staphylococcus also accounts for a reasonable proportion of these infections, it needs to be ruled out when the infection is caused by blood culture contamination*(Hughes et al., 2020; Mormeneo Bayo et al., 2022)*. Other studies have also shown that the main pathogens were Gram-negative bacteria*(Kokkoris et al., 2021; Buetti et al., 2022; Andrianopoulos et al., 2023; Aslan et al., 2023; Strelkova et al., 2023)*, including *Acinetobacter spp*., *Klebsiella spp*., *Escherichia coli* and *Pseudomonas spp.* which may be related to the use of immunosuppressants and bacterial resistance. It is worth noting that, although most studies have shown that Gram-negative bacteria were not

the main isolates, they could lead to high mortality rates in ICU patients, which could be related to their elevated drug resistance*(Palanisamy et al., 2021; Gago et al., 2022; Kurt et al., 2022; Aslan et al., 2023; Strelkova et al., 2023)*.

Risk factors of BSI

The number of studies on the risk factors of BSI in COVID-19 patients is limited, but growing. According to existing reports, the incidence of BSI is mainly related to specific factors, such as the use of immunosuppressants (mainly corticosteroids and tocilizumab)*(Kurt et al., 2022; Nakagawara et al., 2023)* and antibiotics*(Massart et al., 2021; Gago et al., 2022)*, invasive interventions (including mechanical ventilation, central venous catheter placement, extracorporeal membrane oxygenation, and others)*(Gragueb-Chatti et al., 2021; Palanisamy et al., 2021; Kurt et al., 2022)*, comorbidities (such as hypertension, type 2 diabetes, chronic kidney disease, malignancy, and other conditions)*(Bonazzetti et al., 2023; Strelkova et al., 2023)*, the length of the ICU stay*(Grasselli et al., 2021; Khatri et al., 2021)*, and any anti-inflammatory effects*(Giacobbe et al., 2020; Kurt et al., 2022)*. However, there are some controversies on the risk factors of BSI in COVID-19 patients, especially concerning immunosuppressive agents. Some studies have shown that corticosteroids and interleukin inhibitors (mainly tocilizumab and anakinra) were associated with an increased probability of BSI development*(Giacobbe et al., 2020; Buetti et al., 2021; Cona et al., 2021; Meynaar et al., 2022; Nakagawara et al., 2023)*, while others described that this increase only occurred in patients receiving combination therapy*(Giacobbe et al., 2020; Khatri et al., 2021; Kurt et al., 2022; Meynaar et al., 2022)*. Moreover, several researchers found no connection between immunosuppressive therapy and BSI occurrence*(Abelenda-Alonso et al., 2021; Kuwahara et al., 2022; Bonazzetti et al., 2023)*. In the study by Strelkova *et al*, an

414 immunosuppressive therapy during a previous hospitalization and a higher total dose
415 of dexamethasone before transfer to the ICU were both risk factors for BSI. The
416 patients included in this study received higher daily doses of dexamethasone, which
417 were administered for longer time periods, being the use of interleukin inhibitors also
418 very common*(Strelkova et al., 2023)*. This finding indicates that the accumulation of
419 high-dose corticosteroids with tocilizumab may lead to immune suppression and
420 promote the occurrence of BSI *(Kurt et al., 2022; Strelkova et al., 2023)*. Additionally,
421 the presence of comorbidities also brings additional uncertainty factors to the
422 therapeutic effects of immunosuppressants*(Bonazzetti et al., 2023)*. On the one hand,
423 the different comorbidities may result in different immune environments in different
424 patients, which may lead to different therapeutic effects of the
425 immunosuppressants*(Palanisamy et al., 2021; Kurt et al., 2022; Bonazzetti et al.,*
426 *2023)*. On the other hand, the severity of the disease in different patients may require
427 different invasive interventions, which further increase the complexity of the interplay
428 between immunosuppressants and BSIs*(Grasselli et al., 2021; Kurt et al., 2022)*.

429 There are additional controversial aspects in this field. For example, most studies
430 showed that the risk of BSI increased with the duration of hospitalization*(Giacobbe et*
431 *al., 2020; Kokkoris et al., 2021)*, however, other studies showed that a prolonged ICU
432 hospitalization was an independent protective factor*(Kurt et al., 2022)* or had a
433 negative correlation with the occurrence of SBI*(Gago et al., 2022)*. In another study,
434 Strelkova *et al*. found that stronger respiratory support during the first 48 hours of
435 ICU had a protective effect on BSIs *(Strelkova et al., 2023)*. On the other hand, Cona
436 *et al*. reported that both non-invasive mechanical ventilation (NIMV) and invasive
437 mechanical ventilation (IMV) were independent risk factors for BSI*(Cona et al.,*
438 *2021)*. The reasons for these differences could be related to the timing of BSI

occurrence, antibiotic use, underlying diseases, and the types of invasive interventions.

Taken together, the risk factors of BSI are diverse and complex. The prevalence of the local COVID-19 epidemic, medical conditions, health measures, and the comorbidities of the patients are factors that pose challenges to the co-infection assessment. Moreover, for the assessment of risk factors, more details may need to be considered, including the immortal time bias and the classification of the comorbidities*(Abelenda-Alonso et al., 2021; Vail et al., 2021)*. These issues still require more extensive research for a systematic elucidation.

Antimicrobial resistance associated with COVID-19 infection

Growing evidence shows that antimicrobial resistance (AMR) may be increased in patients with COVID-19 under excessive use of antibiotics*(Bengoechea & Bamford, 2020; Council of Canadian Academies, 2021; WHO, 20 September 2021)*. The overuse of antibiotics can lead to antibiotic-resistant microorganisms that have a negative impact on humans. AMR is known as one of the top ten threats to the global public health. The frequent use of antibiotics in patients with COVID-19 may aggravate antibiotic resistance. A systematic analysis published in 2022 shows that between 900,000 and 1.7 million deaths in 2019 can be attributed to bacterial resistance, making it one of the main causes of global mortality*(Antimicrobial Resistance Collaborators, 2022)*. Additionally, according to the previous analysis of COVID-19, it is estimated that, in the next 30 years, AMR will cause about 10 million deaths worldwide, which is higher than the predicted number of deaths caused by cancer (8.2 million), diabetes (1.5 million), and other conditions*(Rizvi & Ahammad, 2022)*. Later, the outbreak of COVID-19 has led to changes in the global antibiotic

consumption patterns, and the number of people who die from AMR is expected to reach higher numbers in the future.

Recent evidence suggests that, due to the COVID-19 pandemic, an increasing number of hospitalized patients have been receiving empirical antimicrobial treatments, potentially increasing the worldwide number of AMR infections*(Nori et al., 2021; Rawson et al., 2021; Kariyawasam et al., 2022)*. Noteworthy data from a study shows that, even without overlapping bacterial infections, the broad-spectrum antibiotic administration rates of patients with severe COVID-19 infections are of about 71.8%*(Rawson et al., 2020; Goncalves Mendes Neto et al., 2021)*. A systematic review of 24 studies and 3506 patients showed that 71.8% (95% confidence interval [CI]: 56.1%-87.7%) of patients received antibiotic treatment at hospital admission*(Langford et al., 2020)*. In Wuhan, China, Zhou *et al*. reported observations of 191 hospitalized patients and found that even 95% of those patients received antibiotics*(Zhou et al., 2020)*. Overall, more than one half of COVID-19 patients received antibiotic treatment. Among the antibiotics used, the most common drugs were fluoroquinolones, cephalosporins, carbapenems, azithromycin, vancomycin, and linezolid*(Langford et al., 2021; Antimicrobial Resistance Collaborators, 2022; Wu et al., 2022)*.

Of note, compared with pneumonia caused by other respiratory pathogens, pneumonia caused by SARS-CoV-2 usually leads to a longer course of the disease*(Budinger et al., 2021)*. Patients with bacterial infections have longer hospital stays*(Cheng et al., 2020; Baskaran et al., 2021)*. Therefore, long-term hospitalized patients have an increased risk of hospital-acquired AMR bacterial infections. As an aggravating factor, the widespread use of antibiotics during the epidemic has led to an increase in the prevalence of multidrug-resistant (MDR) bacteria*(Hsu, 2020; Lai et al., 2021)*. A

recent special report from the US Centers for Disease Control and Prevention demonstrates that the COVID-19 epidemic has led to an increase in the incidence of AMR. Moreover, the drug-resistant microorganisms associated with the COVID-19 epidemic have increased by 15%*(CDC,2022)*. Therefore, this cascade amplification effect must attract and deserve our attention.

The data from two recent systematic reviews showed that, among patients with COVID-19 complicated with bacterial infections, the proportion of drug-resistant strains accounted for 29% and 37.5% respectively*(Kariyawasam et al., 2022; Langford et al., 2023)*. The proportion of patients infected with drug-resistant bacteria was as high as 60%*(Langford et al., 2023)*. Most studies have shown that, among drug-resistant bacteria, the most common resistant Gram-negative bacteria were *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa(Li et al., 2020; Tiri et al., 2020; Clancy et al., 2021; Gomez-Simmonds et al., 2021; Gysin et al., 2021; Kariyawasam et al., 2022; Pourajam et al., 2022; Wu et al., 2022)*. Among them, *Acinetobacter baumannii* and *Klebsiella pneumoniae* were one of the most common drug-resistant bacteria. Research has concluded that *Acinetobacter baumannii* had high resistance to carbapenems and quinolones, ranging from 90% to 100%, with carbapenem-resistant *A. baumannii* accounting for 91.7%*(Li et al., 2020; Rawson et al., 2020; Sharifipour et al., 2020; Bazaid et al., 2022; Sulayyim et al., 2022)*. Additionally, one study reported the highly increased resistance rates of *A. baumannii* to all tested antibiotics, except colistin*(Sharifipour et al., 2020)*. Overall, according to current evidence, *Acinetobacter baumannii* exhibits high resistance rates to amikacin, cefepime, ceftazidime, gentamicin, meropenem, imipenem, ciprofloxacin, and piperacillin/tazobactam*(Li et al., 2020; Rawson et al., 2020; Sharifipour et al., 2020; Bazaid et al., 2022)*. Among drug-resistant bacteria,

the proportion of carbapenem-resistant *Klebsiella pneumoniae* remains high, exceeding 70%*(Li et al., 2020; Tiri et al., 2020; Sang et al., 2021; Kariyawasam et al., 2022; Sulayyim et al., 2022)*. A systematic review by Sulayyim *et al*. showed that the resistance rates of *Klebsiella pneumoniae* to ampicillin, cefazolin, and ceftazidime were M 100% (IQR: 90.5-100%), M 93% (IQR: 78-95.5%), and M 93.5% (IQR: 83.7-97.9%), respectively*(Sulayyim et al., 2022)*, which are much higher than their corresponding values from studies published in 2019 and previous years*(Azimi et al., 2019; Effah et al., 2020)*. It is worth noting that colistin, as an important antibiotic for various types of Gram-negative bacteria, has also been observed in several studies to significantly increase the resistance of *Klebsiella pneumoniae*, with its resistance rate increasing from 5% to 50%*(Gaspar et al., 2021; de Carvalho Hessel Dias et al., 2022; Sulayyim et al., 2022)*.

Compared with *Acinetobacter baumannii* and *Klebsiella pneumoniae*, although *Pseudomonas aeruginosa* is not the most detected drug-resistant bacterium, its drug resistance rate is still higher than before the COVID-19 epidemic*(Subedi et al., 2018; Kariyawasam et al., 2022; Wu et al., 2022; Langford et al., 2023)*. The research report by Sulayyim *et al*. shows that their resistance to imipenem and ciprofloxacin has twice increased*(Sulayyim et al., 2022)*. In addition, the resistance rate of ESBL-producing *Escherichia coli* has also increased, in comparison with the time period before the epidemic, currently accounting for 75%*(Azimi et al., 2019; Despotovic et al., 2021; Wardoyo et al., 2021; Kariyawasam et al., 2022)*. It shows high resistance to ampicillin, amoxicillin. clavulanic acid, levofloxacin, ceftriaxone, ciprofloxacin, and cefuroxime*(Wardoyo et al., 2021; Sulayyim et al., 2022)*.

For Gram-positive bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA), coagulase-negative *Staphylococcus*, and vancomycin-resistant *Enterococcus genus* are

the most common resistant bacteria in current reports*(Li et al., 2020; Tiri et al., 2020; Caruso et al., 2021; Gysin et al., 2021; Saini et al., 2021; Jamnani et al., 2022; Pourajam et al., 2022)*. A study by Li *et al.* found that 100% *Staphylococcus aureus* and coagulase-negative *Staphylococcus* had methicillin resistance; however, no vancomycin resistance was detected*(Li et al., 2020)*. This observation indicates that, if a secondary infection occurs, vancomycin can be used as an empirical choice for Gram-positive bacteria. In addition, *Staphylococcus aureus* also has high resistance rates to oxacillin and clindamycin*(Li et al., 2020; Sulayyim et al., 2022)*. *Enterococcus* mainly includes *Enterococcus faecalis* and *Enterococcus faecium*, which are mainly resistant to ampicillin, erythromycin, ciprofloxacin, vancomycin, and tetracycline*(Li et al., 2020; Gisselø et al., 2022; Kariyawasam et al., 2022; Sulayyim et al., 2022)*. In addition, there are few reports on fungal resistance. In a systematic review by Kariyawasam *et al*., three types of fungal resistance were described, including resistant *Candida auricula*, *Candida albicans*, and an unidentified *Candida spp.(Kariyawasam et al., 2022)*.

Collectively, the evidence shows that AMR is common and has significantly increased during the COVID-19 epidemic, which is related to the use of a large number of antibiotics. In current reports, the most commonly found drug resistance appears in *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and MRSA. It is worth noting that there is a significant heterogeneity among different research reports, concerning the type of pressure-resistant bacteria or the resistance rates. On the one hand, this heterogeneity is related to the local medical conditions and health management measures in different countries or regions. On the other hand, there are inherent difficulties in the statistical analysis of data, mainly due to the lack of relatively comprehensive implementation guidelines. From the literature we currently review,

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less than 40% of all studies have used clear explanatory standards and guidelines, such as the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or the Clinical and Laboratory Standards Institute (CLSI). In addition, there is currently a lack of risk factor assessment for AMR, with only a few studies evaluating its risk factors, which include self-antibiotic medication, antibiotic prescription by general practitioners, and empirical antibiotic treatment before admission to the ICU*(Caruso et al., 2021; Temperoni et al., 2021; Pourajam et al., 2022)*. Therefore, more scientific research guidelines and more comprehensive antibiotic management plans are crucial, in order to reduce the incidence of AMR.

Concluding remarks

Mixed infection with various microorganisms is often found in patients infected with the novel coronavirus, SARS-CoV-2. Here, we focused on infections in the respiratory system and in the bloodstream, because they significantly affect the severity and mortality rates of COVID-19. However, our understanding of the co-infected microorganisms, as well as their interactions with other microorganisms and with the host, is limited. Existing evidence shows that bacterial infections are common in patients with COVID-19, especially in ICU patients. *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* are the most common pathogens in mixed infections. Moreover, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* account for a large proportion of drug-resistant bacteria. In addition, *Staphylococcus aureus* and *Enterococcus* are the main Gram-positive bacteria that cause bloodstream infections.

It is worth noting that there is significant heterogeneity among multiple studies,

especially in the meta-analysis of bacterial mixed infections, which did not consider the age groups, the eternal time bias, and environmental factors. This unexplained heterogeneity may be due to the disease severity, patient comorbidities, treatment differences (such as corticosteroid administration and other procedures), differences between studies using antibiotics before and during hospitalization, and other unknown covariates. Therefore, further research should focus on the epidemiological, clinical, and laboratory characteristics of co-infected pathogens in different COVID-19 patient groups, from different geographical and environmental areas. It is also necessary to evaluate the impact of co-infected microorganisms on the treatment and prognosis of COVID-19 patients. In addition, as discussed above, there is still the lack of more scientific or comprehensive guidelines as a reference, including data statistics, health management, and antibiotic use guidelines. Notably, careful antibiotic management is highly recommended. Optimizing the management of antibiotics is very important for the antibacterial treatment of COVID-19 patients and for minimizing the increase in the risk of antibiotic resistance.

It is also worth noting that most of the current data refers to the first wave of the epidemic. Concerning the second wave, there are still relatively scarce data statistics. In addition, most of the included studies refer to the α and δ variats. The Omicron variant was first discovered in November 2021*(Viana et al., 2022)*. Up to now, no research has focused on the epidemiology of Omicron variants co-infected with bacteria associated with COVID-19, for which further research is needed. We believe that, in the subsequent epidemic wave, the evaluation of bacterial co-infections is also crucial, especially considering that the treatment procedure of these patients has changed, due to factors, such as the routine use of corticosteroids and the emergence of new novel coronavirus variants.

Finally, we would like to emphasize that, although COVID-19 is no longer a public health emergency, according to the data from the World Health Organization, since May 2023, more than 300,000 people around the world are still being infected with COVID-19, every week*(World Health Organization: https://covid19.who.int/)*. Importantly, the co-infection of COVID-19 and bacteria is still common. Therefore, we should not underestimate the serious threat of the COVID-19 infection to human health and its associated global burden.

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Declaration of competing interest

The authors confirm that there are no conflicts of interest.

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REFERENCES

Abelenda-Alonso G, Rombauts A, Gudiol C, Oriol I, Simonetti A, Coloma A, Rodríguez-Molinero A, Izquierdo E, Díaz-Brito V, Sanmartí M, Padullés A, Grau I, Ras M, Bergas A, Guillem L, Blanco-Arévalo A, Alvarez-Pouso C, Pallarés N, Videla S, Tebé C, Carratalà J. 2021. Immunomodulatory therapy, risk factors and outcomes of hospital-acquired bloodstream infection in patients with severe COVID-19 pneumonia: a Spanish case-control matched multicentre study (BACTCOVID). *Clinical microbiology and*

infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases **27(11)**:1685-1692 DOI 10.1016/j.cmi.2021.06.041.

Andrianopoulos I, Maniatopoulou T, Lagos N, Kazakos N, Papathanasiou A, Papathanakos G, Koulenti D, Kittas C, Koulouras V. **2023**. Acinetobacter baumannii Bloodstream Infections in the COVID-19 Era: A Comparative Analysis between COVID-19 and Non-COVID-19 Critically Ill Patients. *Microorganisms* **11(7)**DOI 10.3390/microorganisms11071811.

Aslan AT, Tabah A, Köylü B, Kalem AK, Aksoy F, Erol Ç, Karaali R, Tunay B, Guzeldağ S, Batirel A, Dindar EK, Akdoğan Ö, Bilir Y, Ersöz G, Öztürk B, Selçuk M, Yilmaz M, Akyol A, Akbaş T, Sungurtekin H, Timuroğlu A, Gürbüz Y, Çolak O, Bayindir Y, Eroğlu A, Ferlicolak L, Çeşme U, Dağ O, Buetti N, Barbier F, Ruckly S, Staiquly Q, Timsit JF, Akova M. **2023**. Epidemiology and risk factors of 28-day mortality of hospital-acquired bloodstream infection in Turkish intensive care units: a prospective observational cohort study. *The Journal of antimicrobial chemotherapy* **78(7)**:1757-1768 DOI 10.1093/jac/dkad167.

Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, Flemban H, Al-Nassir WN, Balkhy HH, Al-Hakeem RF, Makhdoom HQ, Zumla AI, Memish ZA. **2013**. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *The Lancet. Infectious diseases* **13(9)**:752-761 DOI 10.1016/S1473-3099(13)70204-4.

Azimi T, Maham S, Fallah F, Azimi L, Gholinejad Z. **2019**. Evaluating the antimicrobial resistance patterns among major bacterial pathogens isolated from clinical specimens taken from patients in Mofid Children's Hospital, Tehran, Iran: 2013-2018. *Infection and drug resistance* **12**:2089-2102 DOI 10.2147/IDR.S215329.

Bakaletz LO. **2017**. Viral-bacterial co-infections in the respiratory tract. *Current opinion in microbiology* **35**:30-35 DOI 10.1016/j.mib.2016.11.003.

Baskaran V, Lawrence H, Lansbury LE, Webb K, Safavi S, Zainuddin NI, Huq T, Eggleston C, Ellis J, Thakker C, Charles B, Boyd S, Williams T, Phillips C, Redmore E, Platt S, Hamilton E, Barr A, Venyo L, Wilson P, Bewick T, Daniel P, Dark P, Jeans AR,

McCanny J, Edgeworth JD, Llewelyn MJ, Schmid ML, McKeever TM, Beed M, Lim WS. **2021**. Co-infection in critically ill patients with COVID-19: an observational cohort study from England. *Journal of medical microbiology* **70(4)**DOI 10.1099/jmm.0.001350.

Bassetti M, Kollef MH, Timsit JF. **2020**. Bacterial and fungal superinfections in critically ill patients with COVID-19. *Intensive care medicine* **46(11)**:2071-2074 DOI 10.1007/s00134-020-06219-8.

Bazaid AS, Barnawi H, Qanash H, Alsaif G, Aldarhami A, Gattan H, Alharbi B, Alrashidi A, Al-Soud WA, Moussa S, Alfouzan F. **2022**. Bacterial Coinfection and Antibiotic Resistance Profiles among Hospitalised COVID-19 Patients. *Microorganisms* **10(3)**DOI 10.3390/microorganisms10030495.

Bengoechea JA, Bamford CG. **2020**. SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19. *EMBO molecular medicine* **12(7)**:e12560 DOI 10.15252/emmm.202012560.

Blonz G, Kouatchet A, Chudeau N, Pontis E, Lorber J, Lemeur A, Planche L, Lascarrou JB, Colin G. **2021**. Epidemiology and microbiology of ventilator-associated pneumonia in COVID-19 patients: a multicenter retrospective study in 188 patients in an un-inundated French region. *Critical care : the official journal of the Critical Care Forum* **25(1)**:72 DOI 10.1186/s13054-021-03493-w.

Bonazzetti C, Morena V, Giacomelli A, Oreni L, Casalini G, Galimberti LR, Bolis M, Rimoldi M, Ballone E, Colombo R, Ridolfo AL, Antinori S. **2021**. Unexpectedly High Frequency of Enterococcal Bloodstream Infections in Coronavirus Disease 2019 Patients Admitted to an Italian ICU: An Observational Study. *CRITICAL CARE MEDICINE* **49(1)**:e31-31e40 DOI 10.1097/CCM.0000000000004748.

Bonazzetti C, Rinaldi M, Giacomelli A, Colombo R, Ottolina D, Rimoldi SG, Pagani C, Morena V, Ridolfo AL, Vatamanu O, Giacomini ME, Campoli C, Oreni L, Rizzardini G, Viale P, Antinori S, Giannella M. **2023**. Risk factors associated with bacteremia in COVID-19 patients admitted to intensive care unit: a retrospective multicenter cohort study. *INFECTION* **51(1)**:129-136 DOI 10.1007/s15010-022-01853-4.

Budinger G, Misharin AV, Ridge KM, Singer BD, Wunderink RG. **2021**. Distinctive features of severe SARS-CoV-2 pneumonia. *The Journal of clinical investigation* **131(14)**DOI

10.1172/JCI149412.

Buetti N, Ruckly S, de Montmollin E, Reignier J, Terzi N, Cohen Y, Siami S, Dupuis C, Timsit JF. **2021**. COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network. *Intensive care medicine* **47(2)**:180-187 DOI 10.1007/s00134-021-06346-w.

Buetti N, Tabah A, Loiodice A, Ruckly S, Aslan AT, Montrucchio G, Cortegiani A, Saltoglu N, Kayaaslan B, Aksoy F, Murat A, Akdoğan Ö, Saracoglu KT, Erdogan C, Leone M, Ferrer R, Paiva JA, Hayashi Y, Ramanan M, Conway Morris A, Barbier F, Timsit JF, Eurobact 2 study group. **2022**. Different epidemiology of bloodstream infections in COVID-19 compared to non-COVID-19 critically ill patients: a descriptive analysis of the Eurobact II study. *Critical care : the official journal of the Critical Care Forum* **26(1)**:319 DOI 10.1186/s13054-022-04166-y.

Caruso P, Maiorino MI, Macera M, Signoriello G, Castellano L, Scappaticcio L, Longo M, Gicchino M, Campitiello F, Bellastella G, Coppola N, Esposito K. **2021**. Antibiotic resistance in diabetic foot infection: how it changed with COVID-19 pandemic in a tertiary care center. *Diabetes research and clinical practice* **175**:108797 DOI 10.1016/j.diabres.2021.108797.

Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. **2020**. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* **395(10223)**:507-513 DOI 10.1016/S0140-6736(20)30211-7.

Cheng K, He M, Shu Q, Wu M, Chen C, Xue Y. **2020**. Analysis of the Risk Factors for Nosocomial Bacterial Infection in Patients with COVID-19 in a Tertiary Hospital. *Risk management and healthcare policy* **13**:2593-2599 DOI 10.2147/RMHP.S277963.

Chien YW, Klugman KP, Morens DM. **2009**. Bacterial pathogens and death during the 1918 influenza pandemic. *The New England journal of medicine* **361(26)**:2582-2583 DOI 10.1056/NEJMc0908216.

Clancy CJ, Schwartz IS, Kula B, Nguyen MH. **2021**. Bacterial Superinfections Among Persons With Coronavirus Disease 2019: A Comprehensive Review of Data From Postmortem Studies. *Open forum infectious diseases* **8(3)**:ofab065 DOI 10.1093/ofid/ofab065.

Council of Canadian Academies. 2021. When antibiotics fail: The expert panel on the potential socio-economic impacts of antimicrobial resistance in Canada. http://www.deslibris.ca/ID/10102747 Accessed 20 September, 2021.

Antimicrobial Resistance Collaborators. **2022**. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* **399(10325)**:629-655 DOI 10.1016/S0140-6736(21)02724-0.

COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators. **2021**. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. *Intensive care medicine* **47(1)**:60-73 DOI 10.1007/s00134-020-06294-x.

TB/COVID-19 Global Study Group. **2022**. Tuberculosis and COVID-19 co-infection: description of the global cohort. *The European respiratory journal* **59(3)**DOI 10.1183/13993003.02538-2021.

Cona A, Tavelli A, Renzelli A, Varisco B, Bai F, Tesoro D, Za A, Biassoni C, Battaglioli L, Allegrini M, Viganò O, Gazzola L, Bini T, Marchetti GC, d'Arminio Monforte A. **2021**. Incidence, Risk Factors and Impact on Clinical Outcomes of Bloodstream Infections in Patients Hospitalised with COVID-19: A Prospective Cohort Study. *Antibiotics* **10(9)**DOI 10.3390/antibiotics10091031.

de Carvalho Hessel Dias VM, Tuon F, de Jesus Capelo P, Telles JP, Fortaleza C, Pellegrino Baena C. **2022**. Trend analysis of carbapenem-resistant Gram-negative bacteria and antimicrobial consumption in the post-COVID-19 era: an extra challenge for healthcare institutions. *The Journal of hospital infection* **120**:43-47 DOI 10.1016/j.jhin.2021.11.011.

Denina M, Pellegrino F, Morotti F, Coppo P, Bonsignori IM, Garazzino S, Ravanini P, Avolio M, Cavallo R, Bertolotti L, Felici E, Acucella G, Montin D, Rabbone I, Licciardi F. **2020**. All that glisters is not COVID: Low prevalence of seroconversion against SARS-CoV-2 in a pediatric cohort of patients with chilblain-like lesions. *Journal of the American Academy of Dermatology* **83(6)**:1751-1753 DOI 10.1016/j.jaad.2020.08.021.

Despotovic A, Milosevic B, Cirkovic A, Vujovic A, Cucanic K, Cucanic T, Stevanovic G. **2021**. The Impact of COVID-19 on the Profile of Hospital-Acquired Infections in Adult Intensive Care Units. *Antibiotics* **10(10)**DOI 10.3390/antibiotics10101146.

Dheda K, Booth H, Huggett JF, Johnson MA, Zumla A, Rook GA. **2005**. Lung remodeling in pulmonary tuberculosis. *The Journal of infectious diseases* **192(7)**:1201-1209 DOI 10.1086/444545.

Effah CY, Sun T, Liu S, Wu Y. **2020**. Klebsiella pneumoniae: an increasing threat to public health. *Annals of clinical microbiology and antimicrobials* **19(1)**:1 DOI 10.1186/s12941-019-0343-8.

Fan J, Li X, Gao Y, Zhou J, Wang S, Huang B, Wu J, Cao Q, Chen Y, Wang Z, Luo D, Zhou T, Li R, Shang Y, Nie X. **2020**. The lung tissue microbiota features of 20 deceased patients with COVID-19. *The Journal of infection* **81(3)**:e64-64e67 DOI 10.1016/j.jinf.2020.06.047.

Frija-Masson J, Debray MP, Gilbert M, Lescure FX, Travert F, Borie R, Khalil A, Crestani B, d'Ortho MP, Bancal C. **2020**. Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post-infection. *The European respiratory journal* **56(2)**DOI 10.1183/13993003.01754-2020.

Gago J, Filardo TD, Conderino S, Magaziner SJ, Dubrovskaya Y, Inglima K, Iturrate E, Pironti A, Schluter J, Cadwell K, Hochman S, Li H, Torres VJ, Thorpe LE, Shopsin B. **2022**. Pathogen Species Is Associated With Mortality in Nosocomial Bloodstream Infection in Patients With COVID-19. *Open forum infectious diseases* **9(6)**:ofac083 DOI 10.1093/ofid/ofac083.

Garcia-Vidal C, Sanjuan G, Moreno-García E, Puerta-Alcalde P, Garcia-Pouton N, Chumbita M, Fernandez-Pittol M, Pitart C, Inciarte A, Bodro M, Morata L, Ambrosioni J, Grafia I, Meira F, Macaya I, Cardozo C, Casals C, Tellez A, Castro P, Marco F, García F, Mensa J, Martínez JA, Soriano A, COVID-19 Researchers Group. **2021**. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* **27(1)**:83-88 DOI 10.1016/j.cmi.2020.07.041.

Gaspar GG, Ferreira LR, Feliciano CS, Campos Júnior CP, Molina F, Vendruscolo A, Bradan G, Lopes N, Martinez R, Bollela VR. **2021**. Pre- and post-COVID-19 evaluation of antimicrobial susceptibility for healthcare-associated infections in the intensive care unit

of a tertiary hospital. *Revista da Sociedade Brasileira de Medicina Tropical* **54**:e00902021 DOI 10.1590/0037-8682-0090-2021.

Giacobbe DR, Battaglini D, Ball L, Brunetti I, Bruzzone B, Codda G, Crea F, De Maria A, Dentone C, Di Biagio A, Icardi G, Magnasco L, Marchese A, Mikulska M, Orsi A, Patroniti N, Robba C, Signori A, Taramasso L, Vena A, Pelosi P, Bassetti M. 2020. Bloodstream infections in critically ill patients with COVID-19. *European journal of clinical investigation* **50(10)**:e13319 DOI 10.1111/eci.13319.

Giacobbe DR, Battaglini D, Enrile EM, Dentone C, Vena A, Robba C, Ball L, Bartoletti M, Coloretti I, Di Bella S, Di Biagio A, Brunetti I, Mikulska M, Carannante N, De Maria A, Magnasco L, Maraolo AE, Mirabella M, Montrucchio G, Patroniti N, Taramasso L, Tiseo G, Fornaro G, Fraganza F, Monastra L, Roman-Pognuz E, Paluzzano G, Fiorentino G, Corcione A, Bussini L, Pascale R, Corcione S, Tonetti T, Rinaldi M, Falcone M, Biagioni E, Ranieri VM, Giannella M, De Rosa FG, Girardis M, Menichetti F, Viale P, Pelosi P, Bassetti M. 2021. Incidence and Prognosis of Ventilator-Associated Pneumonia in Critically Ill Patients with COVID-19: A Multicenter Study. *Journal of clinical medicine* **10(4)**DOI 10.3390/jcm10040555.

Gisselø KL, Rubin I, Knudsen MS, From-Hansen M, Stangerup M, Kavalaris CP, Pinholt M, Mollerup S, Westh H, Bartels MD, Petersen AM. 2022. Substantial Decrease in Vancomycin-Resistant Enterococcus faecium Outbreak Duration and Number of Patients During the Danish COVID-19 Lockdown: A Prospective Observational Study. *Microbial drug resistance : MDR : mechanisms, epidemiology, and disease* **28(1)**:73-80 DOI 10.1089/mdr.2021.0040.

Gomez-Simmonds A, Annavajhala MK, McConville TH, Dietz DE, Shoucri SM, Laracy JC, Rozenberg FD, Nelson B, Greendyke WG, Furuya EY, Whittier S, Uhlemann AC. 2021. Carbapenemase-producing Enterobacterales causing secondary infections during the COVID-19 crisis at a New York City hospital. *The Journal of antimicrobial chemotherapy* **76(2)**:380-384 DOI 10.1093/jac/dkaa466.

Goncalves Mendes Neto A, Lo KB, Wattoo A, Salacup G, Pelayo J, DeJoy R 3rd, Bhargav R, Gul F, Peterson E, Albano J, Patarroyo-Aponte G, Rangaswami J, Azmaiparashvili Z. 2021. Bacterial infections and patterns of antibiotic use in patients with COVID-19.

Journal of medical virology **93(3)**:1489-1495 DOI 10.1002/jmv.26441.

Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, Satlin MJ, Campion TR Jr, Nahid M, Ringel JB, Hoffman KL, Alshak MN, Li HA, Wehmeyer GT, Rajan M, Reshetnyak E, Hupert N, Horn EM, Martinez FJ, Gulick RM, Safford MM. **2020**. Clinical Characteristics of Covid-19 in New York City. *The New England journal of medicine* **382(24)**:2372-2374 DOI 10.1056/NEJMc2010419.

Gragueb-Chatti I, Lopez A, Hamidi D, Guervilly C, Loundou A, Daviet F, Cassir N, Papazian L, Forel JM, Leone M, Dellamonica J, Hraiech S. **2021**. Impact of dexamethasone on the incidence of ventilator-associated pneumonia and blood stream infections in COVID-19 patients requiring invasive mechanical ventilation: a multicenter retrospective study. *Annals of intensive care* **11(1)**:87 DOI 10.1186/s13613-021-00876-8.

Grasselli G, Cattaneo E, Florio G, Ippolito M, Zanella A, Cortegiani A, Huang J, Pesenti A, Einav S. **2021**. Mechanical ventilation parameters in critically ill COVID-19 patients: a scoping review. *Critical care : the official journal of the Critical Care Forum* **25(1)**:115 DOI 10.1186/s13054-021-03536-2.

Grasselli G, Scaravilli V, Di Bella S, Biffi S, Bombino M, Patroniti N, Bisi L, Peri AM, Pesenti A, Gori A, Alagna L. **2017**. Nosocomial Infections During Extracorporeal Membrane Oxygenation: Incidence, Etiology, and Impact on Patients' Outcome. *CRITICAL CARE MEDICINE* **45(10)**:1726-1733 DOI 10.1097/CCM.0000000000002652.

Grasselli G, Scaravilli V, Mangioni D, Scudeller L, Alagna L, Bartoletti M, Bellani G, Biagioni E, Bonfanti P, Bottino N, Coloretti I, Cutuli SL, De Pascale G, Ferlicca D, Fior G, Forastieri A, Franzetti M, Greco M, Guzzardella A, Linguadoca S, Meschiari M, Messina A, Monti G, Morelli P, Muscatello A, Redaelli S, Stefanini F, Tonetti T, Antonelli M, Cecconi M, Foti G, Fumagalli R, Girardis M, Ranieri M, Viale P, Raviglione M, Pesenti A, Gori A, Bandera A. **2021**. Hospital-Acquired Infections in Critically Ill Patients With COVID-19. *Chest* **160(2)**:454-465 DOI 10.1016/j.chest.2021.04.002.

Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui D, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li

G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS, China Medical Treatment Expert Group for Covid-19. **2020**. Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England journal of medicine* **382(18)**:1708-1720 DOI 10.1056/NEJMoa2002032.

Gysin M, Acevedo CT, Haldimann K, Bodendoerfer E, Imkamp F, Bulut K, Buehler PK, Brugger SD, Becker K, Hobbie SN. **2021**. Antimicrobial susceptibility patterns of respiratory Gram-negative bacterial isolates from COVID-19 patients in Switzerland. *Annals of clinical microbiology and antimicrobials* **20(1)**:64 DOI 10.1186/s12941-021-00468-1.

He Y, Li W, Wang Z, Chen H, Tian L, Liu D. **2020**. Nosocomial infection among patients with COVID-19: A retrospective data analysis of 918 cases from a single center in Wuhan, China. *Infection control and hospital epidemiology* **41(8)**:982-983 DOI 10.1017/ice.2020.126.

Hedberg P, Ternhag A, Giske CG, Strålin K, Özenci V, Johansson N, Spindler C, Hedlund J, Mårtensson J, Nauclér P. **2022**. Ventilator-Associated Lower Respiratory Tract Bacterial Infections in COVID-19 Compared With Non-COVID-19 Patients. *CRITICAL CARE MEDICINE* **50(5)**:825-836 DOI 10.1097/CCM.0000000000005462.

Hoque MN, Akter S, Mishu ID, Islam MR, Rahman MS, Akhter M, Islam I, Hasan MM, Rahaman MM, Sultana M, Islam T, Hossain MA. **2021**. Microbial co-infections in COVID-19: Associated microbiota and underlying mechanisms of pathogenesis. *Microbial pathogenesis* **156**:104941 DOI 10.1016/j.micpath.2021.104941.

Hoque MN, Rahman MS, Ahmed R, Hossain MS, Islam MS, Islam T, Hossain MA, Siddiki AZ. **2021**. Diversity and genomic determinants of the microbiomes associated with COVID-19 and non-COVID respiratory diseases. *Gene reports* **23**:101200 DOI 10.1016/j.genrep.2021.101200.

Hsu J. **2020**. How covid-19 is accelerating the threat of antimicrobial resistance. *BMJ : British medical journal* **369**:m1983 DOI 10.1136/bmj.m1983.

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. **2020**. Clinical features of patients infected

with 2019 novel coronavirus in Wuhan, China. *Lancet* **395(10223)**:497-506 DOI 10.1016/S0140-6736(20)30183-5.

Hughes S, Troise O, Donaldson H, Mughal N, Moore L. **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 : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* **26(10)**:1395-1399 DOI 10.1016/j.cmi.2020.06.025.

Ippolito M, Simone B, Filisina C, Catalanotto FR, Catalisano G, Marino C, Misseri G, Giarratano A, Cortegiani A. **2021**. Bloodstream Infections in Hospitalized Patients with COVID-19: A Systematic Review and Meta-Analysis. *Microorganisms* **9(10)**DOI 10.3390/microorganisms9102016.

Jamnani AN, Montazeri M, Mirzakhani M, Moosazadeh M, Haghighi M. **2022**. Evaluation of Bacterial Coinfection and Antibiotic Resistance in Patients with COVID-19 Under Mechanical Ventilation. *SN comprehensive clinical medicine* **4(1)**:19 DOI 10.1007/s42399-021-01114-9.

Joseph C, Togawa Y, Shindo N. **2013**. Bacterial and viral infections associated with influenza. *Influenza and other respiratory viruses* **7 Suppl 2(Suppl 2)**:105-113 DOI 10.1111/irv.12089.

Kang H, Stewart KO, Khan AN, Casale SC, Adams Barker CM, Kim JJ. **2023**. Investigating potential drivers of increased central line-associated bloodstream infections during the coronavirus disease 2019 (COVID-19) Omicron surge. *American journal of infection control* DOI 10.1016/j.ajic.2023.04.168.

Karagiannidis C, Mostert C, Hentschker C, Voshaar T, Malzahn J, Schillinger G, Klauber J, Janssens U, Marx G, Weber-Carstens S, Kluge S, Pfeifer M, Grabenhenrich L, Welte T, Busse R. **2020**. Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study. *The Lancet. Respiratory medicine* **8(9)**:853-862 DOI 10.1016/S2213-2600(20)30316-7.

Kariyawasam RM, Julien DA, Jelinski DC, Larose SL, Rennert-May E, Conly JM, Dingle TC, Chen JZ, Tyrrell GJ, Ronksley PE, Barkema HW. **2022**. Antimicrobial resistance (AMR) in COVID-19 patients: a systematic review and meta-analysis (November 2019-

June 2021). *Antimicrobial resistance and infection control* **11(1)**:45 DOI 10.1186/s13756-022-01085-z.

Khatiwada S, Subedi A. **2020**. Lung microbiome and coronavirus disease 2019 (COVID-19): Possible link and implications. *Human microbiome journal* **17**:100073 DOI 10.1016/j.humic.2020.100073.

Khatri A, Malhotra P, Izard S, Kim A, Oppenheim M, Gautam-Goyal P, Chen T, Doan TL, Berlinrut I, Niknam N, Flannery S, Hirschwerk D, Epstein M, Farber B. **2021**. Hospital-Acquired Bloodstream Infections in Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 Infection (Coronavirus Disease 2019): Association With Immunosuppressive Therapies. *Open forum infectious diseases* **8(7)**:ofab339 DOI 10.1093/ofid/ofab339.

Kokkoris S, Papachatzakis I, Gavrielatou E, Ntaidou T, Ischaki E, Malachias S, Vrettou C, Nichlos C, Kanavou A, Zervakis D, Perivolioti E, Ranellou K, Argyropoulou A, Zakynthinos S, Kotanidou A, Routsi C. **2021**. ICU-acquired bloodstream infections in critically ill patients with COVID-19. *The Journal of hospital infection* **107**:95-97 DOI 10.1016/j.jhin.2020.11.009.

Kurt AF, Mete B, Urkmez S, Demirkiran O, Dumanli GY, Bozbay S, Dilken O, Karaali R, Balkan II, Saltoğlu N, Dikmen Y, Tabak F, Aygun G. **2022**. Incidence, Risk Factors, and Prognosis of Bloodstream Infections in COVID-19 Patients in Intensive Care: A Single-Center Observational Study. *Journal of intensive care medicine* **37(10)**:1353-1362 DOI 10.1177/08850666221103495.

Kuwahara M, Kamigaito M, Nitta S, Hasegawa K, Murakami H, Kobayashi T, Shirai K, Kohama K, Hirata JI. **2022**. Effect of Tocilizumab Treatment on Patients with Coronavirus Disease 2019 and Bacteremia: A Retrospective Cohort Study. *Infectious diseases and therapy* **11(1)**:533-541 DOI 10.1007/s40121-022-00592-1.

Kılıç L, Altın S, Gönenç Ortaköylü M, Kanmaz ZD, Tutar T, Özkan GZ. **2022**. Co-infection of COVID-19 and Tuberculosis. *Turkish thoracic journal* **23(1)**:58-62 DOI 10.5152/TurkThoracJ.2022.21045.

Lai CC, Chen SY, Ko WC, Hsueh PR. **2021**. Increased antimicrobial resistance during the COVID-19 pandemic. *International journal of antimicrobial agents* **57(4)**:106324 DOI

10.1016/j.ijantimicag.2021.106324.

Lai CC, Wang CY, Hsueh PR. **2020**. Co-infections among patients with COVID-19: The need for combination therapy with non-anti-SARS-CoV-2 agents. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi* **53(4)**:505-512 DOI 10.1016/j.jmii.2020.05.013.

Lal A, Mishra AK, Sahu KK, Abraham GM. **2020**. The return of Koch's: Ineffective treatment or re-infection. *Enfermedades infecciosas y microbiologia clinica (English ed.)* **38(3)**:144-145 DOI 10.1016/j.eimc.2019.06.001.

Langford BJ, So M, Raybardhan S, Leung V, Soucy JR, Westwood D, Daneman N, MacFadden DR. **2021**. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* **27(4)**:520-531 DOI 10.1016/j.cmi.2020.12.018.

Langford BJ, So M, Raybardhan S, Leung V, Westwood D, MacFadden DR, Soucy JR, Daneman N. **2020**. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* **26(12)**:1622-1629 DOI 10.1016/j.cmi.2020.07.016.

Langford BJ, So M, Simeonova M, Leung V, Lo J, Kan T, Raybardhan S, Sapin ME, Mponponsuo K, Farrell A, Leung E, Soucy JR, Cassini A, MacFadden D, Daneman N, Bertagnolio S. **2023**. Antimicrobial resistance in patients with COVID-19: a systematic review and meta-analysis. *The Lancet. Microbe* **4(3)**:e179-179e191 DOI 10.1016/S2666-5247(22)00355-X.

Langford BJ, Soucy JR, Leung V, So M, Kwan A, Portnoff JS, Bertagnolio S, Raybardhan S, MacFadden DR, Daneman N. **2023**. Antibiotic resistance associated with the COVID-19 pandemic: a systematic review and meta-analysis. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* **29(3)**:302-309 DOI 10.1016/j.cmi.2022.12.006.

Laupland KB, Church DL. **2014**. Population-based epidemiology and microbiology of community-onset bloodstream infections. *Clinical microbiology reviews* **27(4)**:647-664

967 DOI 10.1128/CMR.00002-14.
968 **Li J, Wang J, Yang Y, Cai P, Cao J, Cai X, Zhang Y**. **2020**. Etiology and antimicrobial
969 resistance of secondary bacterial infections in patients hospitalized with COVID-19 in
970 Wuhan, China: a retrospective analysis. *Antimicrobial resistance and infection control*
971 **9(1)**:153 DOI 10.1186/s13756-020-00819-1.
972 **Li R, Pei S, Chen B, Song Y, Zhang T, Yang W, Shaman J**. **2020**. Substantial undocumented
973 infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). *Science*
974 **368(6490)**:489-493 DOI 10.1126/science.abb3221.
975 **Lu H, Stratton CW, Tang YW**. **2020**. Outbreak of pneumonia of unknown etiology in Wuhan,
976 China: The mystery and the miracle. *Journal of medical virology* **92(4)**:401-402 DOI
977 10.1002/jmv.25678.
978 **Luyt CE, Sahnoun T, Gautier M, Vidal P, Burrel S, Pineton de Chambrun M, Chommeloux**
979 **J, Desnos C, Arzoine J, Nieszkowska A, Bréchot N, Schmidt M, Hekimian G,**
980 **Boutolleau D, Robert J, Combes A, Chastre J**. **2020**. Ventilator-associated pneumonia in
981 patients with SARS-CoV-2-associated acute respiratory distress syndrome requiring
982 ECMO: a retrospective cohort study. *Annals of intensive care* **10(1)**:158 DOI
983 10.1186/s13613-020-00775-4.
984 **MacIntyre CR, Chughtai AA, Barnes M, Ridda I, Seale H, Toms R, Heywood A**. **2018**. The
985 role of pneumonia and secondary bacterial infection in fatal and serious outcomes of
986 pandemic influenza a(H1N1)pdm09. *BMC infectious diseases* **18(1)**:637 DOI
987 10.1186/s12879-018-3548-0.
988 **Maes M, Higginson E, Pereira-Dias J, Curran MD, Parmar S, Khokhar F, Cuchet-Lourenço**
989 **D, Lux J, Sharma-Hajela S, Ravenhill B, Hamed I, Heales L, Mahroof R, Soderholm**
990 **A, Forrest S, Sridhar S, Brown NM, Baker S, Navapurkar V, Dougan G, Bartholdson**
991 **Scott J, Conway Morris A**. **2021**. Ventilator-associated pneumonia in critically ill patients
992 with COVID-19. *Critical care : the official journal of the Critical Care Forum* **25(1)**:25
993 DOI 10.1186/s13054-021-03460-5.
994 **Massart N, Maxime V, Fillatre P, Razazi K, Ferré A, Moine P, Legay F, Voiriot G, Amara M,**
995 **Santi F, Nseir S, Marque-Juillet S, Bounab R, Barbarot N, Bruneel F, Luyt CE,**
996 **COVID ICU Bacteremia Study Group on behalf of the COVID-ICU Investigators**.

2021. Characteristics and prognosis of bloodstream infection in patients with COVID-19 admitted in the ICU: an ancillary study of the COVID-ICU study. *Annals of intensive care* **11(1)**:183 DOI 10.1186/s13613-021-00971-w.

Meynaar IA, van Rijn S, Ottens TH, van Burgel ND, van Nieuwkoop C. **2022**. Increased risk of central line-associated bloodstream infection in COVID-19 patients associated with dexamethasone but not with interleukin antagonists. *Intensive care medicine* **48(7)**:954-957 DOI 10.1007/s00134-022-06750-w.

Migliori GB, Visca D, van den Boom M, Tiberi S, Silva DR, Centis R, D'Ambrosio L, Thomas T, Pontali E, Saderi L, Schaaf HS, Sotgiu G, contributing members of the Global Tuberculosis Network. **2021**. Tuberculosis, COVID-19 and hospital admission: Consensus on pros and cons based on a review of the evidence. *Pulmonology* **27(3)**:248-256 DOI 10.1016/j.pulmoe.2020.12.016.

Mo X, Jian W, Su Z, Chen M, Peng H, Peng P, Lei C, Chen R, Zhong N, Li S. **2020**. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *The European respiratory journal* **55(6)**DOI 10.1183/13993003.01217-2020.

Morens DM, Taubenberger JK, Fauci AS. **2008**. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. *The Journal of infectious diseases* **198(7)**:962-970 DOI 10.1086/591708.

Mormeneo Bayo S, Palacián Ruíz MP, Moreno Hijazo M, Villuendas Usón MC. **2022**. Bacteremia during COVID-19 pandemic in a tertiary hospital in Spain. *Enfermedades infecciosas y microbiologia clinica (English ed.)* **40(4)**:183-186 DOI 10.1016/j.eimce.2021.01.007.

Motta I, Centis R, D'Ambrosio L, García-García JM, Goletti D, Gualano G, Lipani F, Palmieri F, Sánchez-Montalvá A, Pontali E, Sotgiu G, Spanevello A, Stochino C, Tabernero E, Tadolini M, van den Boom M, Villa S, Visca D, Migliori GB. **2020**. Tuberculosis, COVID-19 and migrants: Preliminary analysis of deaths occurring in 69 patients from two cohorts. *Pulmonology* **26(4)**:233-240 DOI 10.1016/j.pulmoe.2020.05.002.

Mousquer GT, Peres A, Fiegenbaum M. **2021**. Pathology of TB/COVID-19 Co-Infection: The phantom menace. *Tuberculosis* **126**:102020 DOI 10.1016/j.tube.2020.102020.

Nakagawara K, Kamata H, Chubachi S, Namkoong H, Tanaka H, Lee H, Otake S, Fukushima T, Kusumoto T, Morita A, Azekawa S, Watase M, Asakura T, Masaki K, Ishii M, Endo A, Koike R, Ishikura H, Takata T, Matsushita Y, Harada N, Kokutou H, Yoshiyama T, Kataoka K, Mutoh Y, Miyawaki M, Ueda S, Ono H, Ono T, Shoko T, Muranaka H, Kawamura K, Mori N, Mochimaru T, Fukui M, Chihara Y, Nagasaki Y, Okamoto M, Amishima M, Odani T, Tani M, Nishi K, Shirai Y, Edahiro R, Ando A, Hashimoto N, Ogura S, Kitagawa Y, Kita T, Kagaya T, Kimura Y, Miyazawa N, Tsuchida T, Fujitani S, Murakami K, Sano H, Sato Y, Tanino Y, Otsuki R, Mashimo S, Kuramochi M, Hosoda Y, Hasegawa Y, Ueda T, Takaku Y, Ishiguro T, Fujiwara A, Kuwahara N, Kitamura H, Hagiwara E, Nakamori Y, Saito F, Kono Y, Abe S, Ishii T, Ohba T, Kusaka Y, Watanabe H, Masuda M, Watanabe H, Kimizuka Y, Kawana A, Kasamatsu Y, Hashimoto S, Okada Y, Takano T, Katayama K, Ai M, Kumanogoh A, Sato T, Tokunaga K, Imoto S, Kitagawa Y, Kimura A, Miyano S, Hasegawa N, Ogawa S, Kanai T, Fukunaga K, Japan COVID-19 Task Force. 2023. Diagnostic significance of secondary bacteremia in patients with COVID-19. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy* **29(4)**:422-426 DOI 10.1016/j.jiac.2023.01.006.

Nebreda-Mayoral T, Miguel-Gómez MA, March-Rosselló GA, Puente-Fuertes L, Cantón-Benito E, Martínez-García AM, Muñoz-Martín AB, Orduña-Domingo A. 2022. Bacterial/fungal infection in hospitalized patients with COVID-19 in a tertiary hospital in the Community of Castilla y León, Spain. *Enfermedades infecciosas y microbiologia clinica (English ed.)* **40(4)**:158-165 DOI 10.1016/j.eimce.2022.02.002.

Nori P, Cowman K, Chen V, Bartash R, Szymczak W, Madaline T, Punjabi Katiyar C, Jain R, Aldrich M, Weston G, Gialanella P, Corpuz M, Gendlina I, Guo Y. 2021. Bacterial and fungal coinfections in COVID-19 patients hospitalized during the New York City pandemic surge. *Infection control and hospital epidemiology* **42(1)**:84-88 DOI 10.1017/ice.2020.368.

Palanisamy N, Vihari N, Meena DS, Kumar D, Midha N, Tak V, Sharma A, Bohra GK, Kothari N, Dutt N, Bhatia PK, Garg MK, Misra S. 2021. Clinical profile of bloodstream infections in COVID-19 patients: a retrospective cohort study. *BMC*

infectious diseases **21(1)**:933 DOI 10.1186/s12879-021-06647-x.

Patton MJ, Orihuela CJ, Harrod KS, Bhuiyan M, Dominic P, Kevil CG, Fort D, Liu VX, Farhat M, Koff JL, Lal CV, Gaggar A, Richter RP, Erdmann N, Might M, Gaggar A. **2023**. COVID-19 bacteremic co-infection is a major risk factor for mortality, ICU admission, and mechanical ventilation. *Critical care : the official journal of the Critical Care Forum* **27(1)**:34 DOI 10.1186/s13054-023-04312-0.

Peddu V, Shean RC, Xie H, Shrestha L, Perchetti GA, Minot SS, Roychoudhury P, Huang ML, Nalla A, Reddy SB, Phung Q, Reinhardt A, Jerome KR, Greninger AL. **2020**. Metagenomic Analysis Reveals Clinical SARS-CoV-2 Infection and Bacterial or Viral Superinfection and Colonization. *Clinical chemistry* **66(7)**:966-972 DOI 10.1093/clinchem/hvaa106.

Pijl JP, Londema M, Kwee TC, Nijsten M, Slart R, Dierckx R, van der Voort P, Glaudemans A, Pillay J. **2021**. FDG-PET/CT in intensive care patients with bloodstream infection. *Critical care : the official journal of the Critical Care Forum* **25(1)**:133 DOI 10.1186/s13054-021-03557-x.

Pourajam S, Kalantari E, Talebzadeh H, Mellali H, Sami R, Soltaninejad F, Amra B, Sajadi M, Alenaseri M, Kalantari F, Solgi H. **2022**. Secondary Bacterial Infection and Clinical Characteristics in Patients With COVID-19 Admitted to Two Intensive Care Units of an Academic Hospital in Iran During the First Wave of the Pandemic. *Frontiers in cellular and infection microbiology* **12**:784130 DOI 10.3389/fcimb.2022.784130.

Prasad R, Patton MJ, Floyd JL, Fortmann S, DuPont M, Harbour A, Wright J, Lamendella R, Stevens BR, Oudit GY, Grant MB. **2022**. Plasma Microbiome in COVID-19 Subjects: An Indicator of Gut Barrier Defects and Dysbiosis. *International journal of molecular sciences* **23(16)**DOI 10.3390/ijms23169141.

Rawson TM, Moore L, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, Satta G, Cooke G, Holmes A. **2020**. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* **71(9)**:2459-2468 DOI 10.1093/cid/ciaa530.

Rawson TM, Wilson RC, Holmes A. **2021**. Understanding the role of bacterial and fungal

infection in COVID-19. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* **27(1)**:9-11 DOI 10.1016/j.cmi.2020.09.025.

Razazi K, Arrestier R, Haudebourg AF, Benelli B, Carteaux G, Decousser JW, Fourati S, Woerther PL, Schlemmer F, Charles-Nelson A, Botterel F, de Prost N, Mekontso Dessap A. **2020**. Risks of ventilator-associated pneumonia and invasive pulmonary aspergillosis in patients with viral acute respiratory distress syndrome related or not to Coronavirus 19 disease. *Critical care : the official journal of the Critical Care Forum* **24(1)**:699 DOI 10.1186/s13054-020-03417-0.

Razazi K, Martins Bexiga A, Arrestier R, Peiffer B, Voiriot G, Luyt CE, Urbina T, Mayaux J, Pham T, Roux D, Bellaiche R, AIt Hamou Z, Gaudry S, Azoulay E, Mekontso Dessap A, Rodriguez C, Pawlotsky JM, Fourati S, de Prost N. **2023**. SARS-CoV-2 variants and mutational patterns: relationship with risk of ventilator-associated pneumonia in critically ill COVID-19 patients in the era of dexamethasone. *Scientific reports* **13(1)**:6658 DOI 10.1038/s41598-023-33639-5.

Rhee C, Dantes R, Epstein L, Murphy DJ, Seymour CW, Iwashyna TJ, Kadri SS, Angus DC, Danner RL, Fiore AE, Jernigan JA, Martin GS, Septimus E, Warren DK, Karcz A, Chan C, Menchaca JT, Wang R, Gruber S, Klompas M, CDC Prevention Epicenter Program. **2017**. Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014. *JAMA* **318(13)**:1241-1249 DOI 10.1001/jama.2017.13836.

Rice LB. **2008**. Federal funding for the study of antimicrobial resistance in nosocomial pathogens: no ESKAPE. *The Journal of infectious diseases* **197(8)**:1079-1081 DOI 10.1086/533452.

Rizvi SG, Ahammad SZ. **2022**. COVID-19 and antimicrobial resistance: A cross-study. *The Science of the total environment* **807(Pt 2)**:150873 DOI 10.1016/j.scitotenv.2021.150873.

Rouzé A, Martin-Loeches I, Povoa P, Makris D, Artigas A, Bouchereau M, Lambiotte F, Metzelard M, Cuchet P, Boulle Geronimi C, Labruyere M, Tamion F, Nyunga M, Luyt CE, Labreuche J, Pouly O, Bardin J, Saade A, Asfar P, Baudel JL, Beurton A, Garot D, Ioannidou I, Kreitmann L, Llitjos JF, Magira E, Mégarbane B, Meguerditchian D, Moglia E, Mekontso-Dessap A, Reignier J, Turpin M, Pierre A, Plantefeve G, Vinsonneau C, Floch PE, Weiss N, Ceccato A, Torres A, Duhamel A,

Nseir S, coVAPid study Group. **2021**. Relationship between SARS-CoV-2 infection and the incidence of ventilator-associated lower respiratory tract infections: a European multicenter cohort study. *Intensive care medicine* **47(2)**:188-198 DOI 10.1007/s00134-020-06323-9.

Ruuskanen O, Lahti E, Jennings LC, Murdoch DR. **2011**. Viral pneumonia. *Lancet* **377(9773)**:1264-1275 DOI 10.1016/S0140-6736(10)61459-6.

Saini V, Jain C, Singh NP, Alsulimani A, Gupta C, Dar SA, Haque S, Das S. **2021**. Paradigm Shift in Antimicrobial Resistance Pattern of Bacterial Isolates during the COVID-19 Pandemic. *Antibiotics* **10(8)**DOI 10.3390/antibiotics10080954.

Salehi M, Ahmadikia K, Mahmoudi S, Kalantari S, Jamalimoghadamsiahkali S, Izadi A, Kord M, Dehghan Manshadi SA, Seifi A, Ghiasvand F, Khajavirad N, Ebrahimi S, Koohfar A, Boekhout T, Khodavaisy S. **2020**. Oropharyngeal candidiasis in hospitalised COVID-19 patients from Iran: Species identification and antifungal susceptibility pattern. *Mycoses* **63(8)**:771-778 DOI 10.1111/myc.13137.

Sang L, Xi Y, Lin Z, Pan Y, Song B, Li CA, Zheng X, Zhong M, Jiang L, Pan C, Zhang W, Lv Z, Xia J, Chen N, Wu W, Xu Y, Chen S, Liu D, Liang W, Liu X, Liu X, Li S, Zhong N, Ye D, Xu Y, Zhang N, Zhang D, Li Y. **2021**. Secondary infection in severe and critical COVID-19 patients in China: a multicenter retrospective study. *Annals of palliative medicine* **10(8)**:8557-8570 DOI 10.21037/apm-21-833.

Sarkar S, Khanna P, Singh AK. **2021**. Impact of COVID-19 in patients with concurrent co-infections: A systematic review and meta-analyses. *Journal of medical virology* **93(4)**:2385-2395 DOI 10.1002/jmv.26740.

Shah T, Shah Z, Yasmeen N, Baloch Z, Xia X. **2022**. Pathogenesis of SARS-CoV-2 and Mycobacterium tuberculosis Coinfection. *Frontiers in immunology* **13**:909011 DOI 10.3389/fimmu.2022.909011.

Sharifipour E, Shams S, Esmkhani M, Khodadadi J, Fotouhi-Ardakani R, Koohpaei A, Doosti Z, Ej Golzari S. **2020**. Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. *BMC infectious diseases* **20(1)**:646 DOI 10.1186/s12879-020-05374-z.

Shen Z, Xiao Y, Kang L, Ma W, Shi L, Zhang L, Zhou Z, Yang J, Zhong J, Yang D, Guo L,

Zhang G, Li H, Xu Y, Chen M, Gao Z, Wang J, Ren L, Li M. **2020**. Genomic Diversity of Severe Acute Respiratory Syndrome-Coronavirus 2 in Patients With Coronavirus Disease 2019. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* **71(15)**:713-720 DOI 10.1093/cid/ciaa203.

Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, Fan Y, Zheng C. **2020**. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *The Lancet. Infectious diseases* **20(4)**:425-434 DOI 10.1016/S1473-3099(20)30086-4.

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC. **2016**. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* **315(8)**:801-810 DOI 10.1001/jama.2016.0287.

Soriano MC, Vaquero C, Ortiz-Fernández A, Caballero A, Blandino-Ortiz A, de Pablo R. **2021**. Low incidence of co-infection, but high incidence of ICU-acquired infections in critically ill patients with COVID-19. *The Journal of infection* **82(2)**:e20-20e21 DOI 10.1016/j.jinf.2020.09.010.

Steinbeis F, Thibeault C, Doellinger F, Ring RM, Mittermaier M, Ruwwe-Glösenkamp C, Alius F, Knape P, Meyer HJ, Lippert LJ, Helbig ET, Grund D, Temmesfeld-Wollbrück B, Suttorp N, Sander LE, Kurth F, Penzkofer T, Witzenrath M, Zoller T. **2022**. Severity of respiratory failure and computed chest tomography in acute COVID-19 correlates with pulmonary function and respiratory symptoms after infection with SARS-CoV-2: An observational longitudinal study over 12 months. *Respiratory medicine* **191**:106709 DOI 10.1016/j.rmed.2021.106709.

Strelkova D, Rachina S, Fedina L, Vlasenko A, Tetevina M, Drogashevskaya D, Chesnokova M, Kuleshov V, Burmistrova E, Sychev I, Ananicheva N. **2023**. Identification of risk factors and development of a predictive model for bloodstream infection in intensive care unit COVID-19 patients. *The Journal of hospital infection* **139**:150-157 DOI 10.1016/j.jhin.2023.06.026.

Strålin K, Wahlström E, Walther S, Bennet-Bark AM, Heurgren M, Lindén T, Holm J, Hanberger H. **2021**. Mortality trends among hospitalised COVID-19 patients in Sweden:

A nationwide observational cohort study. *The Lancet regional health. Europe* **4**:100054 DOI 10.1016/j.lanepe.2021.100054.

Subedi D, Vijay AK, Willcox M. **2018**. Overview of mechanisms of antibiotic resistance in Pseudomonas aeruginosa: an ocular perspective. *Clinical & experimental optometry* **101(2)**:162-171 DOI 10.1111/cxo.12621.

Sulayyim H, Ismail R, Hamid AA, Ghafar NA. **2022**. Antibiotic Resistance during COVID-19: A Systematic Review. *International journal of environmental research and public health* **19(19)**DOI 10.3390/ijerph191911931.

Sy K, Haw N, Uy J. **2020**. Previous and active tuberculosis increases risk of death and prolongs recovery in patients with COVID-19. *Infectious diseases* **52(12)**:902-907 DOI 10.1080/23744235.2020.1806353.

Tadolini M, Codecasa LR, García-García JM, Blanc FX, Borisov S, Alffenaar JW, Andréjak C, Bachez P, Bart PA, Belilovski E, Cardoso-Landivar J, Centis R, D'Ambrosio L, Luiza De Souza-Galvão M, Dominguez-Castellano A, Dourmane S, Fréchet Jachym M, Froissart A, Giacomet V, Goletti D, Grard S, Gualano G, Izadifar A, Le Du D, Marín Royo M, Mazza-Stalder J, Motta I, Ong C, Palmieri F, Rivière F, Rodrigo T, Silva DR, Sánchez-Montalvá A, Saporiti M, Scarpellini P, Schlemmer F, Spanevello A, Sumarokova E, Tabernero E, Tambyah PA, Tiberi S, Torre A, Visca D, Zabaleta Murguiondo M, Sotgiu G, Migliori GB. **2020**. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *The European respiratory journal* **56(1)**DOI 10.1183/13993003.01398-2020.

Temperoni C, Caiazzo L, Barchiesi F. **2021**. High Prevalence of Antibiotic Resistance among Opportunistic Pathogens Isolated from Patients with COVID-19 under Mechanical Ventilation: Results of a Single-Center Study. *Antibiotics* **10(9)**DOI 10.3390/antibiotics10091080.

Tiri B, Sensi E, Marsiliani V, Cantarini M, Priante G, Vernelli C, Martella LA, Costantini M, Mariottini A, Andreani P, Bruzzone P, Suadoni F, Francucci M, Cirocchi R, Cappanera S. **2020**. Antimicrobial Stewardship Program, COVID-19, and Infection Control: Spread of Carbapenem-Resistant Klebsiella Pneumoniae Colonization in ICU COVID-19 Patients. What Did Not Work. *Journal of clinical medicine* **9(9)**DOI

10.3390/jcm9092744.

Torrecillas M, Gumucio VD, Padullés A, Tubau F, Marco D, Shaw E, Fernández-Huerta M, Maisterra K, Grau I, Petito MM, Berbel D, Puig-Asensio M, Pérez XL, Domínguez MÁ, Sabater J, Ardanuy C, Càmara J. 2022. Antimicrobial use and aetiology of bloodstream infections in critically ill patients during early stages of SARS-CoV-2 pandemic. *Infection prevention in practice* **4(4)**:100241 DOI 10.1016/j.infpip.2022.100241.

Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, Vilaró J. 2021. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. *Pulmonology* **27(4)**:328-337 DOI 10.1016/j.pulmoe.2020.10.013.

US Centers for Disease Control and Prevention. 2022. National Center for Emerging and Zoonotic Infectious Diseases; 2022. COVID-19: U.S. Impact on antimicrobial resistance, special report 2022https://stacks.cdc.gov/view/cdc/117915.

Vail EA, Gershengorn HB, Wunsch H, Walkey AJ. 2021. Attention to Immortal Time Bias in Critical Care Research. *American journal of respiratory and critical care medicine* **203(10)**:1222-1229 DOI 10.1164/rccm.202008-3238CP.

Venkataraman T, Frieman MB. 2017. The role of epidermal growth factor receptor (EGFR) signaling in SARS coronavirus-induced pulmonary fibrosis. *Antiviral research* **143**:142-150 DOI 10.1016/j.antiviral.2017.03.022.

Venzon M, Bernard-Raichon L, Klein J, Axelrad JE, Zhang C, Hussey GA, Sullivan AP, Casanovas-Massana A, Noval MG, Valero-Jimenez AM, Gago J, Putzel G, Pironti A, Wilder E, Yale IMPACT Research Team, Thorpe LE, Littman DR, Dittmann M, Stapleford KA, Shopsin B, Torres VJ, Ko AI, Iwasaki A, Cadwell K, Schluter J. 2022. Gut microbiome dysbiosis during COVID-19 is associated with increased risk for bacteremia and microbial translocation. *bioRxiv : the preprint server for biology* DOI 10.1101/2021.07.15.452246.

Viana R, Moyo S, Amoako DG, Tegally H, Scheepers C, Althaus CL, Anyaneji UJ, Bester PA, Boni MF, Chand M, Choga WT, Colquhoun R, Davids M, Deforche K, Doolabh D, du Plessis L, Engelbrecht S, Everatt J, Giandhari J, Giovanetti M, Hardie D, Hill

V, Hsiao NY, Iranzadeh A, Ismail A, Joseph C, Joseph R, Koopile L, Kosakovsky Pond SL, Kraemer M, Kuate-Lere L, Laguda-Akingba O, Lesetedi-Mafoko O, Lessells RJ, Lockman S, Lucaci AG, Maharaj A, Mahlangu B, Maponga T, Mahlakwane K, Makatini Z, Marais G, Maruapula D, Masupu K, Matshaba M, Mayaphi S, Mbhele N, Mbulawa MB, Mendes A, Mlisana K, Mnguni A, Mohale T, Moir M, Moruisi K, Mosepele M, Motsatsi G, Motswaledi MS, Mphoyakgosi T, Msomi N, Mwangi PN, Naidoo Y, Ntuli N, Nyaga M, Olubayo L, Pillay S, Radibe B, Ramphal Y, Ramphal U, San JE, Scott L, Shapiro R, Singh L, Smith-Lawrence P, Stevens W, Strydom A, Subramoney K, Tebeila N, Tshiabuila D, Tsui J, van Wyk S, Weaver S, Wibmer CK, Wilkinson E, Wolter N, Zarebski AE, Zuze B, Goedhals D, Preiser W, Treurnicht F, Venter M, Williamson C, Pybus OG, Bhiman J, Glass A, Martin DP, Rambaut A, Gaseitsiwe S, von Gottberg A, de Oliveira T. **2022**. Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. *Nature* **603(7902)**:679-686 DOI 10.1038/s41586-022-04411-y.

Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K, EPIC II Group of Investigators. **2009**. International study of the prevalence and outcomes of infection in intensive care units. *JAMA* **302(21)**:2323-2329 DOI 10.1001/jama.2009.1754.

Visca D, Ong C, Tiberi S, Centis R, D'Ambrosio L, Chen B, Mueller J, Mueller P, Duarte R, Dalcolmo M, Sotgiu G, Migliori GB, Goletti D. **2021**. Tuberculosis and COVID-19 interaction: A review of biological, clinical and public health effects. *Pulmonology* **27(2)**:151-165 DOI 10.1016/j.pulmoe.2020.12.012.

Wardoyo EH, Suardana IW, Yasa I, Sukrama I. **2021**. Antibiotics susceptibility of Escherichia coli isolates from clinical specimens before and during COVID-19 pandemic. *Iranian journal of microbiology* **13(2)**:156-160 DOI 10.18502/ijm.v13i2.5974.

Wendisch D, Dietrich O, Mari T, von Stillfried S, Ibarra IL, Mittermaier M, Mache C, Chua RL, Knoll R, Timm S, Brumhard S, Krammer T, Zauber H, Hiller AL, Pascual-Reguant A, Mothes R, Bülow RD, Schulze J, Leipold AM, Djudjaj S, Erhard F, Geffers R, Pott F, Kazmierski J, Radke J, Pergantis P, Baßler K, Conrad C, Aschenbrenner AC, Sawitzki B, Landthaler M, Wyler E, Horst D, Deutsche COVID-

19 OMICS Initiative (DeCOI), Hippenstiel S, Hocke A, Heppner FL, Uhrig A, Garcia C, Machleidt F, Herold S, Elezkurtaj S, Thibeault C, Witzenrath M, Cochain C, Suttorp N, Drosten C, Goffinet C, Kurth F, Schultze JL, Radbruch H, Ochs M, Eils R, Müller-Redetzky H, Hauser AE, Luecken MD, Theis FJ, Conrad C, Wolff T, Boor P, Selbach M, Saliba AE, Sander LE. **2021**. SARS-CoV-2 infection triggers profibrotic macrophage responses and lung fibrosis. *Cell* **184(26)**:6243-6261.e27 DOI 10.1016/j.cell.2021.11.033.

Westblade LF, Simon MS, Satlin MJ. **2021**. Bacterial Coinfections in Coronavirus Disease 2019. *Trends in microbiology* **29(10)**:930-941 DOI 10.1016/j.tim.2021.03.018.

World Health Organization. 2021. Antibiotic resistance. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance. Accessed 20 September, 2021.

World Health Organization. 2020. WHO's COVID-19 response. https://www.who.int/news/item/29-06-2020-covidtimeline.

World Health Organization. 2023. WHO Director-General's opening remarks at the media briefing – 5 May 2023; https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing---5-may-2023.

World Health Organization. 2020. WHO Director-General's statement on IHR Emergency Committee on Novel Coronavirus (2019-nCoV); https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-ihr-emergency-committee-on-novel-coronavirus-(2019-ncov).

Wicky PH, Niedermann MS, Timsit JF. **2021**. Ventilator-associated pneumonia in the era of COVID-19 pandemic: How common and what is the impact. *Critical care : the official journal of the Critical Care Forum* **25(1)**:153 DOI 10.1186/s13054-021-03571-z.

Wu HY, Chang PH, Chen KY, Lin IF, Hsih WH, Tsai WL, Chen JA, Lee SS, GREAT working group. **2022**. Coronavirus disease 2019 (COVID-19) associated bacterial coinfection: Incidence, diagnosis and treatment. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi* **55(6 Pt 1)**:985-992 DOI 10.1016/j.jmii.2022.09.006.

Zahariadis G, Gooley TA, Ryall P, Hutchinson C, Latchford MI, Fearon MA, Jamieson FB, Richardson S, Kuschak T, Mederski B. **2006**. Risk of ruling out severe acute respiratory

syndrome by ruling in another diagnosis: variable incidence of atypical bacteria coinfection based on diagnostic assays. *Canadian respiratory journal* **13(1)**:17-22 DOI 10.1155/2006/862797.

Zhang G, Hu C, Luo L, Fang F, Chen Y, Li J, Peng Z, Pan H. **2020**. Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China. *Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology* **127**:104364 DOI 10.1016/j.jcv.2020.104364.

Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. **2020**. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* **395(10229)**:1054-1062 DOI 10.1016/S0140-6736(20)30566-3.

Zuo T, Zhan H, Zhang F, Liu Q, Tso E, Lui G, Chen N, Li A, Lu W, Chan F, Chan P, Ng SC. **2020**. Alterations in Fecal Fungal Microbiome of Patients With COVID-19 During Time of Hospitalization until Discharge. *Gastroenterology* **159(4)**:1302-1310.e5 DOI 10.1053/j.gastro.2020.06.048.