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Review

The Management of Urinary Tract Infections during the COVID-19 Pandemic: What Do We Need to Know?

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Abstract: The landscape of management of urinary tract infections (UTI) is changing rapidly. The COVID-19 pandemic draws our attention to the SARS-CoV-2 management with a subsequent reduced attention on bacterial infections. The COVID-19 diffusion containing procedures, such as use of facemasks and handwashing, have reduced spreading of bacteria and bacterial lung infections. However, a brief analysis of UTI management during the COVID-19 pandemic reveals that the pandemic has changed our management of UTI in a way that violates the principles of antimicrobial stewardship. We therefore remind all urologists and other physicians who manage patients affected by UTI about the importance of continued adherence to antimicrobial stewardship principles during the COVID-19 pandemic.

Keywords: SARS-CoV-2; COVID-19; urinary tract infections; antimicrobial stewardship; antibiotic resistances

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1. Background and Aims

Since 2020, SARS-COV-2 infections have had a high impact on national and international healthcare systems and caused more than 5,100,000 deaths worldwide [1,2]. In the last 2 years, significant health resources have been used on development of medical drugs and vaccines in the war against SARS-COV2 disease (COVID-19). COVID-19 diffusion containing measures, such as facemasks and handwashing, reduced the spread of all viruses and bacteria, with a subsequent reduction of bacterial-related lung infections [3]. However, the prevalence of urinary tract infections was not reduced by these preventive measures, and it is still necessary to maintain high level of adherence to antimicrobial stewardship in everyday clinical practice. During the COVID-19 pandemic, it became important to reduce the number of hospitalizations to prevent the spread of SARS-CoV-2 infection. For this reason, antimicrobial treatment is now prescribed earlier, and broad-spectrum antibiotics has been more frequently used in patients with suspected UTI in order to avoid severe infections and hospitalizations. Recently, Bendala Estrada et al. demonstrated in a multicenter, retrospective study, that the overall percentage of bacterial co-infection among patients with COVID-19 was low, but the use of antibiotics was high [4]. Moreover, the

recent International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) report demonstrated that 62% of patients with COVID-19 had received antimicrobial therapy, even though the prevalence of bacterial infections in COVID-19 has been low [5]. This is the background for the present work and the reason for discussing the role of UTI management during the COVID-19 pandemic. The aim of this Editor's perspective is to give a brief narrative review of the management of UTIs during the COVID-19 pandemic, in order to provide the readers with some navigation points in everyday clinical practice.

2. Materials and Methods

Search of Evidence

Our objective is to give an update on UTI management during the COVID-19 pandemic, focusing on changes in practice that have an impact on antimicrobial stewardship. A literature search was performed in Embase, MEDLINE, Web of Science, and Google Scholar databases for relevant publications by using the following terms: "urinary tract infections" AND/OR "antimicrobial stewardship" AND ("SARS-CoV-2" OR "COVID-19"). Two authors (TC and CT) reviewed all selected articles independently. Any disagreements among reviewers were resolved through discussion and consensus. All references cited in relevant articles were also reviewed and analyzed. EndNote software was used to analyze all references (https://endnote.com/, accessed on 12 December 2021). The filters used included English language and humans. Even if this search was planned for a narrative review, our search was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) and the recommendations of the European Association of Urology Guidelines (EAU) office for conducting systematic reviews and meta-analyses [6,7]. Our search identified 320 articles of potential interest. After the first screening round, 23 articles were considered eligible for inclusion (Table 1). The detailed selection process of the included studies is displayed in Figure 1.

Table 1. The summary of all studies included in this narrative review. Abbreviations used: ARDS = Adult Respiratory Distress Syndrome; CAUTI = Catheter associated urinary tract infections; and PE = Pulmonary Embolism.

Author	Year	Setting	Type of Study	Aim of Study	Sample Size	Median Age (IQR)	Gender	Most Important Findings
Wang Z et al. [8]	2020	Hospital (China)	Retrospective	Clinical features of COVID19 infection	69	42 (35–62)	Male 46% Female 54%	COVID-19 symptoms: Fever (87%), cough (55%), fatigue (42%), Sp02 < 90% (20%)
Wu C et al. [9]	2020	Hospital (China)	Retrospective	Risk factors associated with ARDS and death	201	51 (43–60)	Male 63.7% Female 36.3%	Older age is associated with greater risk of ARDS (41.8%) and death (52.4%)
Wan S et al. [10]	2020	Hospital (China, North-east)-Chongqing	Retrospective	Clinical features of COVID-19 infection	135	47 (36–55)	Male: 53.3% Female: 46.7%	COVID-19 symptoms: Fever (88.9%), cough (76.5%), fatigue (32.5%)

Table 1. *Cont.*

Author	Year	Setting	Type of Study	Aim of Study	Sample Size	Median Age (IQR)	Gender	Most Important Findings
Lansbury L et al. [11]	2020	Hospital (China, Europe, USA)	Retrospective	Clinical features of COVID-19 infection	2590 (22 studies included)	47 (36–55)	Male 53.3% Female 46.7%	Bacterial co-infections: 7% Common pathogens: *Mycoplasma pneumonia*, *Pseudomonas aeruginosa*, *Haemophilus influenzae* Routine use of antibiotics should be avoided
Rawson TM et al. [12]	2020	China, USA, Saudi Arabia, Taiwan, South-Korea, Canada, Hong-Kong	Systematic review	Evaluation of patients with concomitant bacterial and fungal co-infection in patients with COVID 19	2010 patients (18 studies included) -806 COVID-19 -811 No COVID-19	-	-	COVID-19 positive: 8% No COVID-19: 11% 72% of the overall cohort received wide-spectrum antimicrobial therapy
Bardi T et al. [13]	2021	Single-centre; Case-control study (Spain, Europe)	Retrospective	Evaluation of ICU-acquired infections in COVID-19 patients	140	61 (57–67)	Male 77% Female 33%	HAUTI Incidence: 47%; Primary (31%); catheter-related (25%); pneumonia (23%); tracheobronchitis (10%); UTI (8%) with 60% of risk of septic shock
Karaba SM et al. [14]	2020	Hospitals, Multicen-tric (USA)	Retrospective	Incidence of bacterial respiratory and non-respiratory co-infections	1016	62 (48–74)	Male 54% Female 46%	Bacterial respiratory: 1.2%; Bacterial pneumonia: 1.1% UTI: 3%
Van Laethem J et al. [15]	2021	Hospital, single center (Belgium)	Retrospective	Quantitative/ Qualitative evaluation of UTI in COVID-19 ward	622	63	Male 58% Female 42%	UTI Incidence 13% 12% of UTI subgroup under antibiotic therapy 61% overdiagnosis rate (unnecessary therapy)
Langford BJ et al. [16]	2020	Hospitals, Multicen-tric (China, USA, Europe)	Systematic review and meta-analysis	Prevalence of bacterial co-infection (admission) and secondary infection (during hos-pitalization) in COVID-19 wards	3338 24 included studies	2–71	Male: 54.2% Female: 45.8%	Low incidence of bacterial co-infection in COVID-19 wards (6.9%) but 71.9% of patients received antimicrobial therapy

Table 1. *Cont.*

Author	Year	Setting	Type of Study	Aim of Study	Sample Size	Median Age (IQR)	Gender	Most Important Findings
Rawson TM et al. [17]	2020	Editorial comment (Point of debate)	Comment	Potential impacts of healthcare system adaption during COVID-19 pandemic on antimicrobial resistance	-	-	-	Reinforce antimicrobial stewardship independently of COVID-19 pandemic
Lai J et al. [18]	2020	Hospitals, multicentric (China)	Cross-sectional survey	Mental evaluation of health-care workers	1257 60.8% Nurses 39.2% Physicians	26–40	Male: 23.3% Female: 76.7%	High psychological burden. Depression, anxiety, distress more pronounced in nurse staff during the pandemic
Huttner BD et al. [19]	2020	Editorial comment	-	Antimicrobial stewardship principles in the COVID-19 pandemic era	-	-	-	Unmet needs: -National recommendations on antimicrobial stewardship in COVID-19 patients -Establish incidence of co-infections and super-infections -Assess relationship between antibiotic-resistance and COVID-19 infection
Borek AJ et al. [20]	2021	Survey report–Audio Structured-recorded Questionnaires (UK)	-	GPs experience and perception of COVID-19 pandemic	18	-	-	-Increased use of telemedicine in COVID-19 pandemic -No impact on antibiotic prescriptions -Increased workload due to COVID-19 pandemic
Han J et al. [21]	2020	Letter to the editor	-	The role of procalcitonin for identifying bacterial co-infection in COVID-19 patients	-	-	-	Procalcitonin may represent a negative prognostic factor (clinical deterioration) in patients admitted to COVID-19 wards
Muller et al. [22]	2000	Prospective multicentric study (Europe, USA)		Role of calcitonin precursors in predicting septic shock	101 ICU patients	59 (23–86)	Male: 60% Female: 40%	Calcitonin precursors are sensitive markers of sepsis compared to serum C-reactive and interleukins

Table 1. *Cont.*

Author	Year	Setting	Type of Study	Aim of Study	Sample Size	Median Age (IQR)	Gender	Most Important Findings
Suleyman G et al. [23]	2021	Hospitals, USA (Abstract)	Retrospective–cross sectional study (USA) (Abstract)	Impact of COVID-19 on catheter-associated urinary tract infections (CAUTIs)	877	-	-	COVID-19 pandemic did not significantly change CAUTI incidence
Van de Pol AC [24]	2021	JGPN (Julius General Practition-ers' Network) registry 2019–2020	Care-based observational cohort study	Evaluation of number of infectious disease episodes, complications, and antibiotic prescription rates	2019: 27.263 2020: 37.604 (consulta-tions)	-	2019: Res-piratory (21%); Urinary (54%); GI (3%); Skin (31%)–2020 Respira-tory (13%); Urinary (57%); GI (4%); Skin 34%	Decrease in number of infectious diseases treated with antibiotics due to lockdown restrictions
Reyes R et al. [25]	2020	Editorial comment	Editorial comment	The impact of urinary tract infection in the era of COVID-19	-	-	-	Careful clinical observation before antimicrobial treatment
Dasgupta M et al. [26]	2017	Hospital, Canada	Prospective cohort study	Determination of asymptomatic UTI treatment rate in older medically ill delirious patients	343	85.3 (range not reported)	Male: 29% Female: 71%	27% treated for a UTI. Treatment of UTI associated with poor functional recovery and consequently of questionable utility
Antonello VS et al. [27]	2021	Hospital, Brazil, Maternity Unit	Retrospective analysis	Consumption of personal protective equipment and products (PPEP) and frequency of surgical site infection among non-COVID 19 patients	Not reported	Not described	Not described	Increased safety of healthcare workers associated with reduction of SSI
Jue S et al. [28]	2020	Editorial comment	Editorial comment	Thrombo-prophylaxis guidelines in COVID-19 patients	-	-	-	COVID-19 caused a hyper-coagulability state with increased risk of DIC (Disseminated intravascular coagulation)
Manne BK et al. [29]	2020	Hospital, Single center (USA)	Retrospective series	Pathway analysis of COVID-19 infection on platelets	58 (Healthy donor s = 17) (non-ICU COVID-19 = 24) ICU COVID-19 (=17)	49.9	Male: 53% Female: 47%	COVID-19 increases platelet hyperreactivity

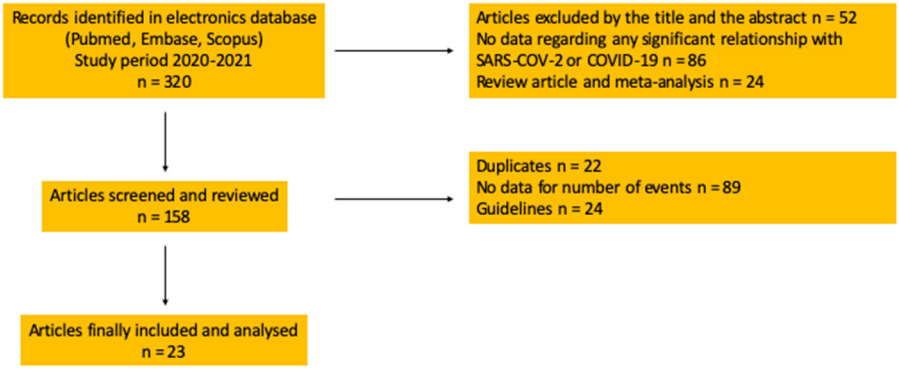

Figure 1. Study flow-chart.

The Figure 1 shows the flow-chart of the selection process of studies included in this narrative review.

3. Evidence and Recommendations

3.1. Evidence

3.1.1. The Prevalence of Bacterial Co-Infections in COVID-19

Several studies demonstrated empiric use of antibiotics in a majority of patients with COVID-19 in a hospital setting [8,9]. The high use of antibiotics in COVID-19 patients is probably due to increased levels of blood inflammatory markers of bacterial infection, such as raised procalcitonin and C-reactive protein, in patients with COVID-19. However, most of these patients did not have a microbiologically proven bacterial co-infection [10]. According to a recent systematic review performed on 3834 hospitalized patients with COVID-19, the overall pooled proportion of patients who had laboratory-confirmed bacterial co-infections, was 7% [11]. Rawson et al. reported a similar finding of 8% prevalence of bacterial/fungal co-infection during hospital admission [12]. The same authors reported wide use of broad-spectrum antibiotics, despite paucity of evidence for bacterial co-infections and lack of antimicrobial stewardship considerations [12]. Based on the reviewed papers, we estimate the prevalence of bacterial co-infection to be less than 10% in hospitalized patients with COVID-19.

3.1.2. The Prevalence of UTI Co-Infections in COVID-19

The prevalence of urinary tract co-infections in patients affected by COVID-19 has not been investigated explicitly. The majority of the reviewed reports focused on pneumological co-infections. However, the prevalence of UTI co-infections in patients with COVID-19 can be extrapolated from some of the reviewed studies. Firstly, Bardi et al. reported the prevalence of UTI of 8% in 140 patients admitted to the intensive care unit, most of which were catheter-associated urinary tract infections [13]. Moreover, Karaba et al. reported a prevalence of 3% in 1016 patients admitted to five hospitals in the US [14]. A recent paper concluded that in more than 60% of patients hospitalized with COVID-19 and urinary tract co-infections, the UTIs were probably over-diagnoses [15]. Hence, the true prevalence of UTI associated to COVID-19 seems to be very low.

3.1.3. Antibiotic Prescriptions and Antimicrobial Stewardship Considerations in COVID-19

In a study addressing both outpatients and hospitalized patients, the prevalence of bacterial co-infections in COVID-19 positive patients was 3.5% in outpatients and 14.3% in hospitalized patients, respectively [16]. Over-prescription of antibiotics in COVID-19 positive patients can increase selective pressure for development of antimicrobial resistance and collateral damage, such as *Clostridium difficile* infections [17]. As highlighted by Huttner et al., the over-prescribing of antibiotics may be due to lowered adherence to international guidelines on the use of antibiotics. The authors emphasize that physicians involved in the

management of COVID-19 positive patients have a high workload and show high levels of stress [18,19]. Furthermore, the higher rate of telemedicine within primary care, secondary care, and outpatient services also increased the number of antimicrobial prescriptions due to safety-netting and reduced access to laboratory diagnostics [17]. On the other hand, reduced access to pharmacies has limited the number of self-administered antibiotics, but rare antimicrobial stewardship initiatives within local healthcare environments have reduced the awareness of correct use of antibiotics during the pandemic [17,20]. The net effect of these COVID-19 related changes in clinical practice is an increased number of antibiotic prescriptions. Finally, as economic and health care resources were allocated to controlling the SARS-CoV-2 pandemic, our attention to antimicrobial resistance and antimicrobial stewardship diminished [20]. Huttner BD et al. now ask healthcare professionals to assess the impact of the COVID pandemic on antibiotic usage and resistance in all settings (community, nursing homes, and hospitals) [19]. However, the jury is still out in regards the impact of the COVID pandemic on antimicrobial stewardship programs and long-term rates of antimicrobial resistance [17].

3.2. Recommendations

3.2.1. The COVID-19 Pandemic: An Excellent Reminder of Antimicrobial Stewardship Principles

It might be said that the COVID-19 pandemic made us forget the need for antimicrobial stewardship in clinical practice, both in community as well as in the hospital setting. Although we still lack data about the long-term effects of COVID-19 on antimicrobial resistance, it is time to remind ourselves that antibiotic stewardship principles must be adhered to in order to avoid not only direct long-term effects of COVID-19, but also serious collateral damages on global health [19]. Several authors underline the importance of sticking to international guidelines in the management of urinary tract infections.

3.2.2. Think Twice before Prescribing Antimicrobials to COVID-19 Positive Patients!

As bacterial co-infections in COVID-19 patients are relatively rare (<10%) [13–15], prescription of antibiotics in COVID-19 patients should be avoided in patients without signs and/or symptoms related to bacterial infections [19]. Serum biomarkers, such as C-reactive protein and/or procalcitonin may play a role in the decision-making process before antibiotic prescription, but further investigations are required [15,19]. The white blood cells (WBC) count is generally considered as an index for bacterial infection, but its specificity in patients with SARS-CoV2 infection is low due to its vulnerability to several factors, such as the presence of inflammatory status or asymptomatic bacteriuria that could increase the level of WBCs. On the other hand, procalcitonin seems to be a useful marker to discriminate between SARS-CoV2 and bacterial infection. Hann J et al. highlighted that a non-elevated procalcitonin level on admission to a healthcare center predicts the absence of bacterial co-infection. Procalcitonin might therefore facilitate implementation of antibiotic stewardship principles [21]. The ability of procalcitonin to discriminate between viral infection alone and viral infection with bacterial co-infection is due to the fact that viral infections are associated with high production of interferon-γ by macrophages, which inhibits TNF-α in the immune response [22].

3.2.3. Asymptomatic Bacteriuria Is Not a Risk Factor for Future Complications in COVID-19 Patients

Asymptomatic bacteriuria is generally over-treated in COVID-19 positive hospitalized patients [15]. This is due to the erroneous assumption that asymptomatic bacteriuria increases the risk of complications in COVID-19 positive patients, which often get indwelling urinary catheters during hospitalization with SARS-CoV-2 [15]. According to Geehan Suleymant al., the COVID-19 pandemic did not have a negative impact on CAUTI rates, even though the rate of indwelling urinary catheters increased [23]. Another aspect to take into account is that during the first wave of pandemic, the number of infectious disease episodes treated with antibiotics decreased, without evidence for an increase in complica-

tions [24]. This is an indirect demonstration of a general over-diagnosis and overtreatment of infectious diseases, resulting in overuse of antibiotics.

Delirium is not generally considered a "systemic sign of infection", but it should be taken into account in elderly patients. Decision about antibiotic treatment is complex and challenging in patients with bacteriuria and delirium in connection with SARS-CoV-2 infection [25]. Some authors suggest avoiding treatment for these patients, as no studies have shown benefit from antibiotic treatment in elderly patients with asymptomatic bacteriuria and delirium [25]. In a study performed before the COVID-19 pandemic, Dasgupta reported a significant further functional loss in patients who received antibiotics, compared with those who did not [26].

3.2.4. Antimicrobial Prophylaxis before Urological Procedures and Surgery in COVID-19 Positive Patients

The COVID-19 pandemic deferred the majority of scheduled urological surgical interventions, especially in the first wave of the pandemic. Only urgent and emergency surgical interventions were performed. In the opinion of the present panel, patients with COVID-19 who are supposed to undergo surgical procedures should get standard antimicrobial prophylaxis in line with international guidelines, even though there are no clinical trials supporting this recommendation. Recently, Antonello Vs et al. demonstrated a significant decrease (49%) in surgical site infection during the COVID-19 pandemic in comparison with a pre-COVID period. The authors highlight the importance of increased use of personal protective equipment and products in the operating theater [27].

3.2.5. Urosepsis and COVID-19

A possible alteration induced by SARS-CoV-2 in blood coagulation was addressed by Jue Js et al. [28]. Other reports demonstrated significant changes in platelet gene expression and function in COVID-19 patients and highlighted the role of SARS-CoV-2 in platelet activation and aggregation, resulting in thrombosis and coagulopathy [29]. On the basis of these observations, Cai et al. reported an increased risk of pulmonary embolism in a small cohort of patients with urosepsis and speculated that the findings are due to enhanced stimulation of thrombo-inflammatory mechanisms by the bacterial infection in association with the increased platelet activation due to SARS-CoV-2 co-infection [30]. Even though further studies are required to confirm these considerations, a higher level of attention is required in patients with urosepsis and COVID-19 infections as regards the risk of thromboembolism.

3.3. Limitations

This study, even if supported by a rigorous methodology according to the international guidelines [31], has a few limitations to take into account. Firstly, the lack of adequate data about the outpatients setting. Most included studies were performed in the hospital setting. The impact on COVID-19 pandemic in outpatients should be evaluated in depth, by using future studies in order to understand its impact on antimicrobial stewardship. Finally, the lack of data about the impact of COVID-19 pandemic on the healthcare systems costs for UTI management.

4. Conclusions and Final Remarks

In order to maintain a high adherence to antimicrobial stewardship principles, the management of UTIs in the COVID-19 pandemic should be based on the following considerations:

- Avoid using antibiotics in COVID-19 patients without any sign and/or symptoms related to bacterial infections.
- The presence of fever in the absence of symptoms related to UTIs is not an indication for the use of antibiotics.

- In case of symptoms related to UTIs, empirical antimicrobial treatment in accordance with international guidelines is the most appropriate practice.
- Asymptomatic bacteriuria is not a risk factor in patients affected by COVID-19 infection. The management of asymptomatic bacteriuria should also be in line with international guidelines, but elderly patients with bacteriuria and delirium require meticulous evaluation and continuous attention to a less harmful approach than antibiotic treatment.
- The care of COVID-19 patients is more difficult than for patients in a standard hospital setting. Isolation procedures might increase the use of urinary catheters and cause higher prevalence of catheter associated UTI and hospital acquired UTIs. The indications for catheterization in patients affected by COVID-19 requires careful considerations.
- Patients affected by COVID-19 have the same risk as non-COVID-19 patients to develop infectious complications after urological procedures. There is no evidence to deviate from international guidelines on antimicrobial prophylaxis before urological surgical procedures.
- Before prescription of antibiotic therapy, physicians must consider all possible collateral damages caused by antibiotics.
- It is urgently required to change current practice of preemptive broad-spectrum antibiotic prescription in COVID-19 patients. We must pay more attention to available evidence and the principles of antimicrobial stewardship!
- Please don't forget to consider the patient's quality of life in association with antimicrobial stewardship in everyday clinical practice! [32].

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References

1. Coronavirus Pandemic (COVID-19)—The Data. Available online: https://ourworldindata.org/coronavirus-data (accessed on 19 November 2021).
2. WHO Coronavirus (COVID-19). Available online: https://COVID19.who.int (accessed on 19 November 2021).
3. Barycka, K.; Szarpak, L.; Filipiak, K.J.; Jaguszewski, M.; Smereka, J.; Ladny, J.R.; Turan, O. Comparative effectiveness of N95 respirators and surgical/face masks in preventing airborne infections in the era of SARS-CoV2 pandemic: A meta-analysis of randomized trials. *PLoS ONE* **2020**, *15*, e0242901. [CrossRef] [PubMed]
4. Estrada, A.D.B.; Parra, J.C.; Carracedo, E.F.; Míguez, A.M.; Martínez, A.R.; Rubio, E.M.; Rubio-Rivas, M.; Agudo, P.; Fernández, F.A.; Perez, V.E.; et al. Inadequate use of antibiotics in the COVID-19 era: Effectiveness of antibiotic therapy. *BMC Infect. Dis.* **2021**, *21*, 1144.
5. International Severe Acute Respiratory and Emerging Infection Consortium. COVID-19 Report. 2020. Available online: https://media.tghn.org/medialibrary/2020/04/ISARIC_Data_Platform_COVID-19_Report_8APR20.pdf (accessed on 12 December 2021).
6. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G.; Group, P. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Ann. Intern. Med.* **2009**, *151*, 264–269. [CrossRef] [PubMed]
7. Köves, B.; Cai, T.; Veeratterapillay, R.; Pickard, R.; Seisen, T.; Lam, T.B.; Yuan, Y.; Bruyere, F.; Wagenlehner, F.; Bartoletti, R.; et al. Benefits and Harms of Treatment of Asymptomatic Bacteriuria: A Systematic Review and Meta-analysis by the European Association of Urology Urological Infection Guidelines Panel. *Eur. Urol.* **2017**, *72*, 865–868. [CrossRef]
8. Wang, Z.; Yang, B.; Li, Q.; Wen, L.; Zhang, R. Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. *Clin. Infect. Dis.* **2020**, *71*, 769–777. [CrossRef] [PubMed]

9. Wu, C.; Chen, X.; Cai, Y.; Xia, J.; Zhou, X.; Xu, S.; Huang, H.; Zhang, L.; Zhou, X.; Du, C.; et al. Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern. Med.* **2020**, *180*, 934–943. [CrossRef] [PubMed]
10. Wan, S.; Xiang, Y.; Fang, W.; Zheng, Y.; Li, B.; Hu, Y.; Lang, C.; Huang, D.; Sun, Q.; Xiong, Y.; et al. Clinical features and treatment of COVID-19 patients in northeast Chongqing. *J. Med. Virol.* **2020**, *92*, 797–806. [CrossRef]
11. Lansbury, L.; Lim, B.; Baskaran, V.; Lim, W.S. Co-infections in people with COVID-19: A systematic review and meta-analysis. *J. Infect.* **2020**, *81*, 266–275. [CrossRef]
12. Rawson, T.M.; Moore, L.S.P.; Zhu, N.; Ranganathan, N.; Skolimowska, K.; Gilchrist, M.; Satta, G.; Cooke, G.; Holmes, A. Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. *Clin. Infect. Dis.* **2020**, *71*, 2459–2468. [CrossRef]
13. Bardi, T.; Pintado, V.; Gomez-Rojo, M.; Escudero-Sanchez, R.; Azzam Lopez, A.; Diez-Remesal, Y.; Martinez Castro, N.; Ruiz-Garbajosa, P.; Pestaña, D. Nosocomial infections associated to COVID-19 in the intensive care unit: Clinical characteristics and outcome. *Eur. J. Clin. Microbiol. Infect. Dis.* **2021**, *40*, 495–502. [CrossRef]
14. Karaba, S.M.; Jones, G.; Helsel, T.; Smith, L.L.; Avery, R.; Dzintars, K.; Salinas, A.B.; Keller, S.C.; Townsend, J.L.; Klein, E.; et al. Prevalence of Co-infection at the Time of Hospital Admission in COVID-19 Patients, A Multicenter Study. *Open Forum Infect. Dis.* **2020**, *8*, ofaa578. [CrossRef] [PubMed]
15. Van Laethem, J.; Wuyts, S.C.M.; Pierreux, J.; Seyler, L.; Verschelden, G.; Depondt, T.; Meuwissen, A.; Lacor, P.; Piérard, D.; Allard, S.D. Presumed Urinary Tract Infection in Patients Admitted with COVID-19: Are We Treating Too Much? *Antibiotics* **2021**, *10*, 1493. [CrossRef] [PubMed]
16. Langford, B.J.; So, M.; Raybardhan, S.; Leung, V.; Westwood, D.; MacFadden, D.R. Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis. *Clin. Microbiol. Infect.* **2020**, *26*, 1622–1629. [CrossRef] [PubMed]
17. Rawson, T.M.; Moore, L.S.P.; Castro-Sanchez, E.; Charani, E.; Davies, F.; Satta, G. COVID-19 and the potential long-term impact on antimicrobial resistance. *J. Antimicrob. Chemother.* **2020**, *75*, 1681–1684. [CrossRef]
18. Lai, J.; Ma, S.; Wang, Y.; Cai, Z.; Hu, J.; Wei, N. Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. *JAMA Netw. Open* **2020**, *3*, e203976. [CrossRef]
19. Huttner, B.D.; Catho, G.; Pano-Pardo, J.R.; Pulcini, C.; Schouten, J. COVID-19: Don't neglect antimicrobial stewardship principles! *Clin. Microbiol. Infect.* **2020**, *26*, 808–810. [CrossRef]
20. Borek, A.J.; Maitland, K.; McLeod, M.; Campbell, A.; Hayhoe, B.; Butler, C.C.; Morrell, L.; Roope, L.S.J.; Holmes, A.; Walker, A.S.; et al. Impact of the COVID-19 Pandemic on Community Antibiotic Prescribing and Stewardship: A Qualitative Interview Study with General Practitioners in England. *Antibiotics* **2021**, *10*, 1531. [CrossRef]
21. Han, J.; Gatheral, T.; Williams, C. Procalcitonin for patient stratification and identification of bacterial co-infection in COVID-19. *Clin. Med.* **2020**, *20*, e47. [CrossRef]
22. Müller, B.; Becker, K.L.; Schächinger, H.; Rickenbacher, P.R.; Huber, P.R.; Zimmerli, W.; Ritz, R. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. *Crit. Care Med.* **2000**, *28*, 977–983. [CrossRef]
23. Geehan Suleyman, M.D.; Rita Kassab, D.O.; Smitha Gudipati, M.D.; Ramesh Mayur, M.D.; Indira Brar, M.D. 779. COVID-19 Pandemic and Catheter-associated Urinary Tract Infection Trends. *Open Forum Infect. Dis.* **2021**, *8*, S486–S487. [CrossRef]
24. van de Pol, A.C.; Boeijen, J.A.; Venekamp, R.P.; Platteel, T.; Damoiseaux, R.A.M.J.; Kortekaas, M.F.; van der Velden, A.W. Impact of the COVID-19 Pandemic on Antibiotic Prescribing for Common Infections in The Netherlands: A Primary Care-Based Observational Cohort Study. *Antibiotics* **2021**, *10*, 196. [CrossRef] [PubMed]
25. Reyes, R.; Bono, G.; Finucane, T.E. So-called Urinary Tract Infection in the Era of COVID-19. *J. Am. Geriatr. Soc.* **2020**, *68*, 1927–1928. [CrossRef] [PubMed]
26. Dasgupta, M.; Brymer, C.; Elsayed, S. Treatment of asymptomatic UTI in older delirious medical in-patients: A prospective cohort study. *Arch. Gerontol. Geriatr.* **2017**, *72*, 127–134. [CrossRef] [PubMed]
27. Antonello, V.S.; Dallé, J.; Antonello, I.C.F.; Benzano, D.; Ramos, M.C. Surgical Site Infection after Cesarean Delivery in Times of COVID-19. *Rev. Bras. Ginecol. Obstet.* **2021**, *43*, 374–376. [CrossRef] [PubMed]
28. Jue, S.; Alameddine, M. COVID-19 Coagulopathy: Considerations for Urologists. *J. Urol.* **2020**, *204*, 640–641. [CrossRef]
29. Manne, B.K.; Denorme, F.; Middleton, E.A.; Portier, I.; Rowley, J.W.; Stubben, C.; Petrey, A.C.; Tolley, N.D.; Guo, L.; Cody, M.; et al. Platelet gene expression and function in COVID-19 patients. *Blood* **2020**, *136*, 1317–1329. [CrossRef]
30. Cai, T.; Tandogdu, Z.; Wagenlehner, F.M.E.; Bjerklund Johansen, T.E. Re: COVID-19 Coagulopathy: Considerations for Urologists. *J. Urol.* **2020**, *204*, 848–849. [CrossRef]
31. Bramer, W.M.; Rethlefsen, M.L.; Kleijnen, J.; Franco, O.H.; Bramer, W.M.; Rethlefsen, M.L.; Kleijnen, J.; Franco, O.H. Optimal database combinations for literature searches in systematic reviews: A prospective exploratory study. *Syst. Rev.* **2017**, *6*, 245. [CrossRef]
32. Cai, T.; Verze, P.; Bjerklund Johansen, T.E. The Quality of Life Definition: Where Are We Going? *Uro* **2021**, *1*, 14–22. [CrossRef]