A retrospective antibiotic prescribing assessment and examination of potential antibiotic stewardship targets in patients with COVID-19

Ryan W. Stevens 1*, Kelsey Jensen 2, Kirstin Kooda 1, Kristin Mara 3, John C. O’Horo 4,5 and Aditya Shah 4

1 Department of Pharmacy Services, Mayo Clinic, Rochester, MN, USA; 2 Department of Pharmacy Services, Mayo Clinic Health System, Austin, MN, USA; 3 Department of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, USA; 4 Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, USA; 5 Division of Infectious Diseases, Mayo Clinic, Rochester, MN, USA

*Corresponding author. E-mail: stevens.ryan@mayo.edu

Received 15 September 2021; accepted 18 October 2021

Objectives: Despite low rates of bacterial coinfection in patients admitted with COVID-19, antimicrobials are frequently prescribed. Our primary objective was to evaluate antimicrobial prescribing over time in patients admitted with COVID-19. The secondary objectives were to evaluate the role of ID providers in antimicrobial utilization, describe the rate of confirmed bacterial infection and determine factors associated with empirical antimicrobial prescribing in COVID-19.

Materials and methods: Retrospective review was performed for adult patients admitted to a tertiary care centre with COVID-19 between 1 March 2020 and 30 November 2020. Patient demographics, disease severity, risk factors for severe disease, clinical outcomes, antimicrobial prescribing and respiratory microbiological testing were collected and analysed. Prescribing trends were evaluated by month, and factors contributing to prescribing were established using univariate and multivariable analysis.

Results: Antibiotics were prescribed during admission in 37.9% of the study cohort, with 85.1% of patients who received antibiotics having therapy initiated within 48 h of admission. Antibiotic prescribing incidence increased with disease. Over the study period, antimicrobial prescribing rates decreased by 8.7% per month. Multivariable analysis found ICU admission, obtainment of procalcitonin values, intubation, heart failure, haemodialysis and nursing home residence were associated with empirical antimicrobial prescribing.

Conclusions: Unnecessary antimicrobial prescribing in patients with viral syndromes like COVID-19 continues to represent an area of concern. Antimicrobial stewardship efforts during COVID-19 should consider patient-specific factors associated with antibiotic prescribing. Recognition of such factors, in combination with application of well-established antimicrobial stewardship tactics, may serve to impact antimicrobial prescribing trends, even as patient volumes rise.

Introduction

During the COVID-19 pandemic, potential overuse of antimicrobials and resultant unintended consequences have been a concern of antimicrobial stewardship.1 This problem is driven by difficulty in differentiating between isolated viral illness and potential superimposed bacterial pneumonias or other infections. Bacterial or fungal coinfection have been estimated to occur in ~10% of COVID-19 patients, with some reports demonstrating lower rates.2–6 Despite low rates of bacterial coinfection, antimicrobial prescribing in inpatients with COVID-19 occurs in 50%–80% of admissions.7,5,5–9 Empirical antimicrobial prescribing in patients with COVID-19 has failed to demonstrate improvement in patient outcomes.7,10,11 The established overuse of antimicrobials in this patient population emphasizes the need for antimicrobial stewardship intervention, and application of fundamental stewardship strategies to patients with COVID-19 have been previously described.12–17

Early in the pandemic, we evaluated antimicrobial prescribing across the continuum of care in patients with COVID-19.6 However, at that time, only a small number of inpatients were able to be included. As the pandemic progressed and our institution entered its surge, we sought to perform a more thorough evaluation of inpatient antimicrobial prescribing practices. Our primary
The incidence of antimicrobial prescribing increased with disease severity, with 16.9% (32/189), 29.8% (72/242) and 64.6% (144/223) of patients receiving respiratory antimicrobials during their hospitalization for COVID-19 with 11, 20 and 24 being classified as mild, moderate or severe cases, respectively (P = 0.2). Procalcitonin (PCT) values were obtained within 24 h of admission in 170 (26%) patients. PCT values were more likely to be obtained in those with severe COVID-19 (P < 0.001) and median PCT values increased with increasing disease severity (P < 0.001). Formal consultation by ID occurred in 93.6% (612/654) of all cases. ID was more likely to be consulted in moderate (94.2%, 228/242) or severe cases (96.4%, 215/223) as compared with mild cases (89.4%, 169/189) (P = 0.014).

Antibiotic utilization

In the full cohort, 248 (37.9%) of patients received antimicrobials targeting suspected or confirmed bacterial respiratory infections. The incidence of antimicrobial prescribing increased with disease severity, with 16.9% (32/189), 29.8% (72/242) and 64.6% (144/223) of patients receiving respiratory antimicrobials during their hospitalization for COVID-19 with 11, 20 and 24 being classified as mild, moderate or severe cases, respectively (P = 0.2). Procalcitonin (PCT) values were obtained within 24 h of admission in 170 (26%) patients. PCT values were more likely to be obtained in those with severe COVID-19 (P < 0.001) and median PCT values increased with increasing disease severity (P < 0.001). Formal consultation by ID occurred in 93.6% (612/654) of all cases. ID was more likely to be consulted in moderate (94.2%, 228/242) or severe cases (96.4%, 215/223) as compared with mild cases (89.4%, 169/189) (P = 0.014).
admission in the mild, moderate and severe disease classifications, respectively \( (P < 0.01) \). Of the patients who received antibiotics, 85.5% (212/248) received empirical therapy within 48 h of hospital admission, with no significant difference identified between disease severities (90.9% mild versus 88.9% moderate versus 81.9% severe, \( P = 0.24 \)). This considered, antimicrobial therapy was administered as empirical therapy within 48 h of hospitalization in 15.9% (30/189), 26.4% (64/242) and 52.9% (118/223) of the total populations of mild, moderate and severe disease, respectively \( (P < 0.001) \). However, it should be noted that 52.9% (118/223) of patients admitted with severe disease were admitted as the result of direct admission transfer, and, of these, 59.3% (70/118) received antibiotics within 48 h of admission. The ID consultation team was responsible for antimicrobial initiation in only 1.6% (4/248) of all encounters where an antibiotic was prescribed; however, they recommended antimicrobial discontinuation in 42.7% (106/248) of all encounters with an antimicrobial prescribed.

Antimicrobial utilization data are described in Table 2. The median length of antimicrobial therapy was 5 days in the total population, with significantly longer median durations of therapy being observed in those with severe disease (mild: 1 day versus moderate: 2 days versus severe: 6 days, \( P < 0.01 \)). As such, total

| Table 1. Population demographics |
|----------------------------------|
| Characteristics                  | All patients \( (n = 654) \) | Mild disease \( (n = 189) \) | Moderate disease \( (n = 242) \) | Severe disease \( (n = 223) \) | \( P \) value |
| Age, years, mean \( \pm SD \)     | 63.6 \( \pm 17.1 \) | 62.1 \( \pm 18.2 \) | 65.3 \( \pm 15.6 \) | 63.1 \( \pm 17.6 \) | 0.12        |
| Male, %                          | 55.8                  | 52.4                  | 51.7                  | 63.2                  | 0.03        |
| Race, %                          |                       |                       |                       |                       | 0.42        |
| White                            | 76.1                  | 74.1                  | 81.4                  | 72.2                  |             |
| American Indian/Alaska Native    | 0.2                   | 0                     | 0                     | 0.4                   |             |
| Asian                            | 5.4                   | 6.3                   | 3.3                   | 6.7                   |             |
| Black or African American        | 7.6                   | 9                     | 6.6                   | 7.6                   |             |
| Native Hawaiian                  | 0.2                   | 0                     | 0                     | 0.4                   |             |
| Other                            | 8                     | 8.5                   | 7                     | 8.5                   |             |
| Unknown                          | 2.6                   | 2.1                   | 1.7                   | 4                     |             |
| Ethnicity, %                     |                       |                       |                       |                       | 0.45        |
| Hispanic or Latino               | 10.2                  | 9                     | 9.5                   | 12.1                  |             |
| Not Hispanic or Latino           | 84.6                  | 85.7                  | 86.8                  | 81.2                  |             |
| Unknown                          | 5.2                   | 5.3                   | 3.7                   | 6.7                   |             |
| BMI, mean \( \pm SD \)           | 32 \( \pm 8 \)         | 31.7 \( \pm 8.6 \)    | 32.3 \( \pm 7.8 \)    | 31.8 \( \pm 7.7 \)    | 0.69        |
| Charlson Comorbidity Index, mean \( \pm SD \) | 5.8 \( \pm 4.5 \) | 5.7 \( \pm 4.5 \) | 5.9 \( \pm 4.5 \) | 5.6 \( \pm 4.6 \) | 0.65        |
| Time between positive test and admission, days, median (IQR) | 1 (0, 6) | 1 (0, 5) | 3 (0, 7) | 1 (0, 5) | 0.06 |
| Length of stay, days, median (IQR) | 7 (5, 11) | 4 (3, 7) | 6 (5, 9) | 10 (7, 17) | <0.01 |
| PCT obtained within 24 h of admittance, % | 26 | 14.3 | 28.5 | 33.2 | <0.01 |
| PCT value, median (IQR) | 0.2 (0.1, 0.6) | 0.1 (0.1, 0.2) | 0.2 (0.1, 0.4) | 0.3 (0.1, 0.8) | <0.01 |
| Death, %                         | 10.6                  | 11.1                  | 3.7                   | 26                    | <0.01      |
| Transfer type, %                 |                       |                       |                       |                       | <0.01      |
| Local admission (i.e. no transfer) | 48                   | 63                    | 50.8                  | 32.7                  |             |
| ED transfer                      | 20                    | 21.2                  | 24                    | 14.4                  |             |
| Direct admission                 | 32                    | 15.9                  | 25.5                  | 52.9                  |             |
| Risk factors, %                  |                       |                       |                       |                       |             |
| Age >60 years                    | 62.8%                 | 58.2%                 | 66.5%                 | 62.8%                 | 0.21        |
| BMI >30                          | 54.1%                 | 50.8%                 | 55.4%                 | 55.6%                 | 0.55        |
| Hypertension                     | 55.4%                 | 51.3%                 | 59.5%                 | 54.3%                 | 0.22        |
| Heart failure                    | 14.7%                 | 12.7%                 | 16.5%                 | 14.3%                 | 0.53        |
| Congenital heart disease         | 2.1%                  | 0.5%                  | 2.1%                  | 3.6%                  | 0.1         |
| Coronary artery disease          | 17.7%                 | 22.2%                 | 17.4%                 | 14.3%                 | 0.11        |
| Chronic lung disease/asthma      | 25.4%                 | 24.3%                 | 25.2%                 | 26.5%                 | 0.88        |
| Diabetes                         | 35.6%                 | 30.7%                 | 36.4%                 | 39%                   | 0.2         |
| Immunocompromised                | 12.2%                 | 13.2%                 | 16.1%                 | 7.2%                  | 0.01        |
| Nursing home resident            | 7.5%                  | 5.3%                  | 9.1%                  | 7.6%                  | 0.33        |
| Chronic haemodialysis            | 3.8%                  | 3.2%                  | 5%                    | 3.1%                  | 0.51        |
| Chronic liver disease            | 6.6%                  | 5.8%                  | 7.9%                  | 5.8%                  | 0.6         |
| Pregnancy                        | 1.2%                  | 1.6%                  | 0.8%                  | 1.3%                  | 0.76        |
| Total risk factors, mean \( \pm SD \) | 1.7 \( \pm 1.4 \) | 1.6 \( \pm 1.2 \) | 1.7 \( \pm 1.4 \) | 1.8 \( \pm 1.5 \) | 0.9         |
cumulative antimicrobial spectrum scores were higher in the patients with severe disease; however, when the spectrum score per day of antimicrobial therapy was evaluated, no significant difference was identified between any of the severity groups ($P = 0.25$). Antimicrobial durations of therapy were found to be shorter in patients who received empirical therapy within 48 h of hospitalization versus those initiated on antibiotics 48 h after admission (5 days [IQR 1, 7] versus 6 days [IQR 3.5, 9], $P = 0.034$). 

A multiplicative decrease in antimicrobial prescribing rate over time of 8.7% per month was observed for all respiratory antimicrobials prescribing (incident rate ratio [IRR] per month: 0.92, 95% CI 0.86–0.95). This decrease in prescribing occurred despite an increase in COVID-19 related admissions during the study period (Figure 1). A statistically significant decrease in both total (51.8% [102/197] versus 31.9% [146/457], $P < 0.001$) and empirical (45.7% [90/197] versus 26.7% [122/457], $P < 0.01$) antibiotic prescribing was observed when comparing patients admitted before and after the implementation of the refined ASP flag.

### Microbiological testing

Respiratory cultures were collected in 15.9% (104/654) of patients in the full cohort with 7.7% collected from bronchoalveolar lavage, 55.3% from expectorated sputum and 36.9% from tracheal...
aspirate. Patients with severe disease were more likely to have bacterial respiratory cultures obtained than those with mild (34.1% [76/223] versus 3.7% [7/189], \( P < 0.01 \)) or moderate disease (34.1% [76/223] versus 8.7% [21/242], \( P < 0.001 \)). Additionally, time between admission and culture collection was longer in those with severe disease (3 days [IQR 1, 7]) as compared with mild (1 day [IQR 0, 1]) or moderate disease (1 day [IQR 0, 2]) (\( P = 0.003 \)). A total of 64 isolates were identified from positive respiratory cultures (Figure 2). A specific pathogen was identified in the respiratory cultures of 47.1% (49/104) of patients who had cultures collected, without variation between disease severities, with 42.9% (3/7), 42.9% (9/21) and 48.7% (37/76) of cultures demonstrating growth of a pathogen in mild, moderate and severe disease, respectively (\( P = 0.91 \)). Staphylococcus aureus was the most isolated pathogen and was isolated from 27 of the 49 patients with positive cultures, with 21 of 27 isolates being methicillin susceptible.

Factors associated with antimicrobial utilization

On univariate analysis (Table 3), factors found to be associated with empirical antimicrobial use included baseline coronary artery disease; residence in a nursing home; haemodialysis dependence; obtainment of a PCT value within 24 h of admission; admission to the ICU; intubation; calendar month of admission; transfer type (i.e. local admission versus direct admission transfer); evidence of infiltrate on chest imaging; severity of illness; and collection of respiratory cultures. Though collection of a PCT level within 24 h of admission was a factor associated with antimicrobial utilization, the median value was 0.2 ng/mL in both those who received empirical antimicrobials and those who did not (\( P = 0.03 \)). Admission by direct admission transfer was associated with a statistically significant increase in empirical antimicrobial utilization as compared with local admission (\( P < 0.001 \)) and admission by ED transfer (\( P = 0.01 \)).

On multivariable analysis (Table 3), pre-existing heart failure; residence in a nursing home; haemodialysis dependence; obtainment of a PCT value within 24 h of admission; ICU admission, intubation; evidence of infiltrate on chest imaging; and collection of respiratory tract cultures were associated with empirical antimicrobial prescribing.

Discussion

The unnecessary utilization of antimicrobials in viral respiratory syndromes has long drawn the attention of antimicrobial stewards.16 This has been acutely highlighted by the SARS-CoV-2 pandemic with early antimicrobial prescribing rates as high as 80%.2,3,5,9

During the first 9 months of the pandemic, we observed an overall rate of antimicrobial prescribing of 37.9%. Furthermore, 85.4% of patients that received antimicrobial therapy received their first dose within 48 h of admission. This high rate of empirical prescribing is starkly contrasted with a low rate of bacterial culture obtainment and isolation of a bacterial pathogen from respiratory cultures obtained during the hospital stay. During the study period, both active and passive methodologies were implemented to attempt to reduce unnecessary antibacterial prescribing in COVID-
This was accompanied by a high rate of formal ID consultation, with ID providers rarely being responsible for antibiotic initiation, but often recommended discontinuation. These interventions, likely along with the accumulation of time and experience with managing COVID-19, appear to have contributed to the observed trend in decreasing antimicrobial prescribing over time. Our study concluded with an empirical prescribing rate of 24.3% in November of 2020 despite the largest number of admissions in a single month during the study period (n = 243). While our rate of antimicrobial prescribing is notably lower than observed rates in other early publications, opportunities for improvement in antimicrobial prescribing in COVID-19 remain. Furthermore, the decrease in respiratory antibacterial prescribing over time demonstrates the utility of both passive and active antimicrobial stewardship techniques and the significance of ID involvement.

Use of a multivariable analysis, regarding empirical antimicrobial prescribing, identified that patients in the ICU potentially benefit from closest ASP review. Patients admitted to the ICU had the highest rate of culture collection amongst the disease severities and were also the most likely to receive antimicrobial therapy. Additionally, patients admitted to the ICU received therapy for significantly longer than those outside of the ICU, and intubation appeared to further increase the probability of empirical antimicrobial prescribing.

Though potentially a result of empirical prescribing practices rather than the cause, obtainment of PCT values and respiratory cultures occurred more commonly in ICU patients. Specifically, regarding respiratory cultures, the median time to culture obtainment was 3 days and antimicrobial initiation occurred within the first 24–48 h in 52.9% of that population. This may indicate that cultures were being obtained to guide therapy rather than determine its necessity. PCT is often touted as a tool to decrease antimicrobial use in adult ICU patients. One study found the sensitivity and specificity of a PCT cut-off of 0.25 ng/mL in identifying bacterial respiratory coinfections to be poor at 0.71 and 0.53, respectively. This yielded a positive predictive value of 0.015 and negative predictive value of 0.995. As such, some have concluded that PCT may lack utility for identifying patients with concurrent bacterial infection, but may be a tool to rule out bacterial coinfection and reduce unnecessary antimicrobial prescribing; however, this strategy is not supported by current community-acquired pneumonia guideline recommendations. We noted that despite the median PCT value of 0.18, obtainment of PCT was significantly associated with receipt of respiratory antibiotics, which suggests either misapplication of the test or outright disbelief in the pneumonia threshold drawn from ICU literature. Our findings appear to illuminate an uncertainty regarding the utility of PCT given higher rates of PCT obtainment alongside longer durations of therapy in ICU patients. Clinical suspicion seems to supersede PCT values in antimicrobial decision-making. These factors should be further investigated.

Our study is not without limitations. First, inclusion of data from a single institution limits external validity of our findings. Our institution is based in a rural, primarily Caucasian setting and may not reflect the outcomes of more populous and diverse urban institutions, where the burden of COVID-19 may differ due to differences in demographic characteristics. Second, we specifically set out to evaluate the rate of respiratory bacterial coinfection and did not evaluate the incidence of other bacterial coinfections and/or antimicrobial use related to other syndromes. This may have contributed to our rate of antimicrobial prescribing being lower than that observed in other publications that have accounted for other bacterial coinfections. Additionally, diagnosis with a bacterial respiratory tract infection required culture obtainment and not all patients included had respiratory tract cultures obtained, which may have led to underestimation of the true incidence of bacterial coinfection. Finally, our institution had the continuous presence of ID providers within an expert COVID-19 panel comprised of several disciplines including radiology, critical care and haematology. Such bandwidth may not be possible in other institutions, especially in areas of high disease prevalence. Hence, our results may not reflect the experience of institutions who struggled to provide a
typical provider-to-patient ratio during periods of surge. These limitations considered; our study adds to the body of evidence suggesting low rates of bacterial respiratory coinfection in patients with COVID-19 and confirms the key role of multidisciplinary care with ID involvement in antimicrobial stewardship. It also confirms key targets for ASP initiatives to steward antimicrobials in this population (i.e. increasing disease severity and receipt of mechanical ventilation).3,7,9

Despite low rates of respiratory bacterial coinfection in patients with COVID-19, antimicrobials are commonly prescribed. The potentially unnecessary use of antibacterial therapy in these patients may be more common in patients on haemodialysis, admitted from nursing homes and/or with greater disease severity. Ongoing vigilance regarding the stewardship of antimicrobials remains of utmost importance in this patient population. The application of longstanding antimicrobial stewardship tactics, such as prospective audit with intervention and feedback, educational strategies and multidisciplinary team involvement, are likely to have an ongoing role in addressing antimicrobial overuse in COVID-19. Institutional ASPs should take an active role in intervening on unnecessary antimicrobial use in these patients by specifically understanding their local prescribing patterns, trending these patterns over time and identifying patient populations most likely to derive benefit from programmatic interventions.

### Table 3. Univariate and multivariable analysis of factors potentially associated with empirical antimicrobial prescribing

|                              | Univariate              | Multivariablea          |
|------------------------------|-------------------------|-------------------------|
|                              | OR (95% CI)             | P value                 |
| Age >60 years (Y versus N)   | 1.09 (0.77–1.53)        | 0.63                    |
| Male sex (Y versus N)        | 1.11 (0.80–1.55)        | 0.54                    |
| BMI >30 (Y versus N)         | 1.19 (0.86–1.66)        | 0.30                    |
| Hypertension (Y versus N)    | 0.89 (0.64–1.23)        | 0.47                    |
| Heart failure (Y versus N)   | 0.70 (0.43–1.14)        | 0.15                    |
| Congenital heart disease (Y versus N) | 1.58 (0.54–4.61) | 0.40                    |
| Coronary artery disease (Y versus N) | 0.61 (0.39–0.97) | 0.037                   |
| Chronic lung disease/asthma (Y versus N) | 1.17 (0.80–1.69) | 0.42                    |
| Diabetes (Y versus N)        | 1.25 (0.89–1.76)        | 0.19                    |
| Immunocompromising condition (Y versus N) | 0.94 (0.57–1.56) | 0.81                    |
| Nursing home (Y versus N)    | 2.13 (1.19–3.83)        | 0.012                   |
| Dialysis (Y versus N)        | 2.34 (1.05–5.22)        | 0.038                   |
| Chronic liver disease (Y versus N) | 1.13 (0.59–2.16) | 0.72                    |
| Pregnancy (Y versus N)       | 0.69 (0.14–3.46)        | 0.65                    |
| Charlson Comorbidity Index, median (IQR) | 0.98 (0.95–1.02) | 0.36                    |
| PCT within 24 h of admittance (Y versus N) | 3.46 (2.40–4.98) | <0.001                  |
| ICU stay                     | Reference               | Reference               |
| No ICU stay                  |                         |                         |
| ICU stay—no intubation       | 3.53 (2.36–5.27)        | <0.001                  |
| ICU stay—intubated           | 8.48 (4.89–14.72)       | <0.001                  |
| Time between positive test and admission | 1.01 (0.99–1.02) | 0.57                    |
| Transfer type                | Reference               | Reference               |
| Local admission (i.e. no transfer) | 1.19 (0.75–1.88) | 0.46                    |
| ED transfer                  | 2.54 (1.75–3.68)        | <0.001                  |
| Direct admission             | 7.49 (3.41–16.47)       | <0.001                  |
| Radiographic changes (Y versus N) | 4.51 (1.96–10.40) | <0.01                  |
| Severity                     | Reference               | Reference               |
| Mild                         |                         |                         |
| Moderate                     | 1.91 (1.18–3.09)        | 0.009                   |
| Severe                       | 5.97 (3.72–9.53)        | <0.001                  |
| Respiratory cultures collected (Y versus N) | 5.06 (3.24–7.89) | <0.001                  |
| ID consulted (Y versus N)    | 1.38 (0.68–2.80)        | 0.37                    |

Y, yes; N, no.
aVariables included in the multivariable model were heart failure; nursing home residence; haemodialysis dependence; whether PCT values were collected within 24 h of admission; ICU stay/intubation; radiographic changes on chest imaging; and whether respiratory cultures were collected.
Funding
This study was carried out as part of our routine work, and with internal funding by a research grant from the Mayo Midwest Pharmacy Research Committee.

Transparency declarations
Dr O’Horo reports personal fees from Elsevier and Bates college, outside of the submitted work. All other authors: none to declare.

Author contributions
R.W.S. contributed to study design, data collection, data analysis and manuscript writing. K.J. contributed to study design, data collection, data analysis and manuscript revisions. K.K. contributed to study design, data collection, data analysis and manuscript revision. J.C.O. contributed to study design, data collection and data analysis. A.S. contributed to study design, data collection, data analysis and manuscript revision.

Supplementary data
Table S1 is available as Supplementary data at JAC-AMR Online.

References
1 CDC. Current Report: Antibiotic Use in the United States, 2020 Update: Progress and Opportunities. 2020. https://www.cdc.gov/antibiotic-use/stewardship-report/current.html.
2 Karaba SM, Jones G, Helsel T et al. Prevalence of co-infection at the time of hospital admission in COVID-19 patients, a multicenter study. Open Forum Infect Dis 2021; 8: ofaa578.
3 Langford BJ, So M, Raybardhan S et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clin Microbiol Infect 2021; 27: 520–31.
4 Lansbury L, Lim B, Baskaran V et al. Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect 2020; 81: 266–75.
5 Nori P, Cowman K, Chen V et al. Bacterial and fungal co-infections in COVID-19 patients hospitalized during the New York City pandemic surge. Infect Control Hosp Epidemiol 2021; 42: 84–8.
6 Stevens RW, Jensen K, O’Horo JC et al. Antimicrobial prescribing practices at a tertiary-care center in patients diagnosed with COVID-19 across the continuum of care. Infect Control Hosp Epidemiol 2021; 42: 89–92.
7 Moretto F, Sixt T, Devilliers H et al. Is there a need to widely prescribe antibiotics in patients hospitalized with COVID-19? Int J Infect Dis 2021; 105: 256–60.
8 Rawson TM, Moore LSP, Zhu N et al. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis 2020; 71: 2459–68.
9 Vaughn VM, Gandhi T, Petty LA et al. Empiric antibacterial therapy and community-onset bacterial co-infection in patients hospitalized with COVID-19: a multi-hospital cohort study. Clin Infect Dis 2021; 72: e533–41.
10 Buetti N, Mazzuchelli L, Lo Priore E et al. Early administered antibiotics do not impact mortality in critically ill patients with COVID-19. J Infect 2020; 81: e148–9.
11 Zhou F, Yu T, Du R et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395: 1054–62.
12 Davis MW, McManus D, Koff A et al. Repurposing antimicrobial stewardship tools in the electronic medical record for the management of COVID-19 patients. Infect Control Hosp Epidemiol 2020; 41: 1335–7.
13 Stevens MP, Patel PK, Nori P. Involving antimicrobial stewardship programs in COVID-19 response efforts: all hands on deck. Infect Control Hosp Epidemiol 2020; 41: 744–5.
14 Stevens RW, Estes L, Rivera C. Practical implementation of COVID-19 patient flags into an antimicrobial stewardship program’s prospective review. Infect Control Hosp Epidemiol 2020; 41: 1108–10.
15 Tande AJ, Stevens RW, Wermers RA et al. Leveraging existing strategies of medication stewardship to preserve and appropriately use critical supplies. Mayo Clin Proc 2020; 95 Suppl 9: S29–S32.
16 Barlam TF, Cosgrove SE, Abbo LM et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis 2016; 62: e51–77.
17 Henig O, Kehat O, Meijer SE et al. Antibiotic use during the COVID-19 pandemic in a tertiary hospital with an ongoing antibiotic stewardship program. Antibiotics 2021; 10: 1056.
18 Gerber JS, Hersh AL, Kronman MP et al. Development and application of an antibiotic spectrum index for benchmarking antibiotic selection patterns across hospitals. Infect Control Hosp Epidemiol 2017; 38: 993–7.
19 May M, Chang M, Dietz D et al. Limited utility of procalcitonin in identifying community-associated bacterial infections in patients presenting with coronavirus disease 2019. Antimicrob Agents Chemother 2021; 65: e02167–20.
20 Metlay JP, Waterer GW, Long AC et al. Diagnosis and Treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med 2019; 200: e45–67.
21 Tai DBG, Shah A, Dubeeri CA et al. The disproportionate impact of COVID-19 on racial and ethnic minorities in the United States. Clin Infect Dis 2021; 72: 703–6.