A Pilot Study: Interrupted Time-Series Analysis of the Impact of the COVID-19 Pandemic on Antimicrobial Stewardship in a Secondary Care Setting in the United Kingdom

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Abstract

This pilot study examines the impact of the COVID-19 pandemic on antimicrobial stewardship (AMS) practices in a UK secondary care setting. An interrupted time-series analysis compared antibiotic prescribing patterns for respiratory tract infections (RTIs) before (2019) and during (2020) the pandemic. The study, involving 80 admissions, highlights shifts in AMS practices. Community Acquired Pneumonia (CAP) was the most frequent diagnosis. Compliance with AMS practices, based on the PHE SMTF toolkit, showed 100% for clinical indication and drug allergy documentation. However, CURB-65 Score compliance remained at 60%, and other AMS interventions varied, with decreased compliance during the pandemic. RTI admissions peaked at 15 in December 2019, declined to 9 in June and September 2020. The study emphasizes the need for adaptable AMS strategies during health crises to mitigate antimicrobial resistance and maintain effective patient care. Future research should focus on developing resilient AMS frameworks for global health emergencies.

Introduction

Antimicrobial resistance (AMR) is emerging as a silent and rapidly accelerating threat, posing a severe challenge to global health security. This hidden crisis demands urgent attention and action to prevent a future where common infections become untreatable and medical procedures carry increased risks1. The introduction of penicillin in the 1920s was a transformative era in infection management, significantly reducing mortality rates2. Despite these advances, inappropriate antibiotic prescriptions have led to rising AMR, projected to cause 10 million deaths annually by 20503. In 2019, AMR was responsible for over 1.2 million deaths globally4.

Antimicrobial stewardship (AMS) plays a pivotal role in the UK's five-year AMR strategy to combat antimicrobial resistance effectively5. The effective implementation of AMS is imperative to combat AMR, promoting judicious antibiotic use to optimize treatment outcomes and minimize resistance6. The 'Start Smart, Then Focus' (SSTF) toolkit, developed by Public Health England (PHE) in 2015, offers a structured approach to evidence-based antimicrobial stewardship in inpatient care settings. SSTF provides evidence-based guidance for secondary care clinicians and leaders, designed to reduce the risk of AMR while safeguarding the quality of care for patients with infections7. The UK Health Security Agency (UKHSA) updated this SSTF toolkit in 2023. This toolkit emphasizes timely and responsible antibiotic use, starting with the rapid initiation of effective therapies followed by mandatory reviews within the first 24–72 hours8. By implementing AMS principles, this approach aims to standardize and optimize antimicrobial use across various healthcare settings. The goal is to improve antibiotic prescribing practices, enhance treatment outcomes, and reduce the emergence of resistance, thus fostering sustainable healthcare practices and improving patient safety. This comprehensive strategy highlights the critical importance of AMS in maintaining the efficacy of antibiotics and ensuring the health and safety of patients across the UK9.

The COVID-19 pandemic has significantly impacted global healthcare systems, leading to increased inappropriate antibiotic use and contributing to rising AMR rates10. Despite WHO guidelines advising against antibiotics unless a secondary bacterial infection is evident, 70% of COVID-19 patients were administered antimicrobials11-12. It is imperative to explore and provide an in-depth analysis to understand antibiotic prescribing and antimicrobial stewardship and the essential steps needed to combat the growing danger of antimicrobial resistance13. This is particularly crucial during emergencies or crises that disrupt the healthcare system, such as the COVID-19 pandemic. Implementing practical solutions and enhancing AMS practices is vital to mitigating the threat of AMR effectively5. The World Health Organization (WHO) has promoted the global implementation of AMS practices, aligning its efforts with the UK's Five-Year AMR Strategic Plan (2024–2029) to confront antimicrobial resistance by optimizing antibiotic prescribing and enhancing effective AMS strategies5-11.

This pilot study aimed to evaluate the need and feasibility of assessing antibiotic prescribing practices and AMS implementation in respiratory infections during the COVID-19 pandemic at a secondary care setting in the UK. The goal is to provide practical solutions and enhance AMS practices to mitigate the threat of AMR.

Results

This pilot study, which retrospectively investigates antibiotic use based on patient records, involved 80 admissions. The patient demographics were as follows: 39 (49%) were male and 41 (51%) were female. The mean age at admission was 76 years (± 14.8), with a range of 26–99 years. Regarding admission specialty, 39 were for general medicine, 18 for elderly medicine, 7 for surgery, 3 for cardiology, 3 for respiratory medicine, 1 for accident & emergency, and 1 for other specialties, including endocrinology and diabetic medicine. There were 4 ordinary admissions and 76 urgent admissions. Upon discharge, 66 patients were released, and 14 had died (Table 1).

Table 1
Demographic Characteristics and Admissions (n = 80).

Characteristics		Admissions (n = 80)
Sex	Male (%)	39 (49%)
	Female (%)	41 (51%)
Age at admission	Mean ± SD	76 ± 14.8
	Range (26–99)	
Admission Specialty	General Medicine	39
	Elderly Medicine	18
	Surgery	7
	Cardiology	3
	Respiratory Medicine	3
	Accident & Emergency	1
	Others'[1]	1
Patient Classification	Ordinary and Routine Admission	4
	Urgent Admission	76
Discharge Method	Discharge	66
	Died	14

[1] The 'other' consultant specialities include endocrinology, diabetic medicine, acute internal medicine, thoracic medicine, neurology, and rheumatology.

Table 1. Demographic Characteristics and Admissions (n = 80).

Figure 1 illustrates the number of respiratory tract infection (RTI) admissions at eight different time points in 2019 and 2020. Notably, admissions peaked in December 2019 with 15 cases, coinciding with the onset of the COVID-19 pandemic. In March 2020, admissions decreased to 10, followed by a further decline to 9 in both June and September 2020. There was a slight increase in December 2020, with admissions rising to 11 cases. This pattern indicates fluctuations in RTI admissions correlating with the early stages and progression of the COVID-19 pandemic.

Figure 1. The Number of Respiratory Tract Infection Admissions Across Eight Seasonal Time Points in 2019 and 2020 (n = 80 Admissions).

Table 2 below compares the Length of Stay (LOS) in 2019 and 2020. The average LOS was almost the same between 2019 and 2020. The SD was 16 in 2019, while in 2020, the SD was 13.

Table 2
Length of Stay in Days (2019–2020).

Length of Stay in Days	2019	2020
Mean	16	15
Median	11	10
Range	1-119	1–97
Standards Deviation	16	13

Table 2. Length of Stay in Days (2019–2020).

Figure 2 presents the number of respiratory tract infection (RTI) admissions from March 2019 to December 2020, categorized by diagnosis and totaling 80 admissions. Community Acquired Pneumonia (CAP) was the most frequent, with 24 admissions, peaking at 5 in December 2020. Non-Specific Diagnoses (URTI, Pneumonia) followed with 23 admissions, peaking at 6 in June 2020. Hospital Acquired Pneumonia (HAP) had 10 admissions, with peaks of 3 in both March and June 2020. Ventilator Pneumonia (VAP) had 6 admissions, with 3 in June 2019. Bronchiectasis also had 6 admissions, evenly spread. COVID-19 pneumonia accounted for 5 admissions, peaking at 2 in March 2020. COPD infective exacerbation had 4 admissions, while Viral Pneumonia had the lowest frequency with 2 admissions, one each in March and September 2019.

Figure 2. Seasonal Trends in Respiratory Tract Infection Admissions in 2019 and 2020 (Total number = 80 admissions).

Figure 3 summarizes the compliance with AMS practices across eight-time points in 2019 and 2020, based on the PHE SMTF toolkit. The data reveals that clinical indication and drug allergy documentation consistently achieved 100% compliance across all records. However, other AMS interventions exhibited variability. Notably, the CURB-65 Score for Pneumonia Severity was not commonly included in most patient records, despite hospital guidelines requiring its use for antibiotic classification, with compliance remaining at 60% in both 2019 and 2020. Clinical practice guidelines and the IV-to-Oral switch were the most frequently applied interventions in both years. In contrast, the implementation of streamlining/de-escalation, antibiotic change, and discontinuation showed higher compliance rates before the pandemic (30%, 40%, and 50%, respectively) but decreased during the pandemic. Overall, the figure highlights the variations and consistencies in AMS practices before and during the COVID-19 pandemic, emphasizing areas of strong compliance and those needing improvement.

Figure 3. Compliance with Antimicrobial Stewardship Practices Across Eight Seasonal Time Points in 2019 and 2020.

Discussion

The findings from this pilot study provide valuable insights into the impact of the COVID-19 pandemic on antimicrobial stewardship practices in a secondary care setting in the UK. This study utilized an interrupted time-series analysis to compare antibiotic prescribing patterns before (2019) and during (2020) the pandemic, focusing on respiratory tract infections.

With regards to the demographic characteristics and admissions, this study included 80 patient admissions, with a balanced gender distribution (49% male, 51% female) and a mean age of 76 years. The majority of admissions were for general medicine (39) and elderly medicine (18), reflecting the high vulnerability of these groups to RTIs and the critical need for effective AMS practices in these areas. The predominance of urgent admissions (76 out of 80) highlights the acute nature of these cases and the necessity for prompt and appropriate antibiotic use. A meta-analysis of 59 studies from the Netherlands in 2020, involving 36,470 patients, found that men and individuals aged 70 and above face higher risks of COVID-19 infection, severe disease, ICU admission, and death. The study highlights significant age and sex disparities in COVID-19 outcomes14.

Regarding the Seasonal Trends in RTI Admissions, findings from this study illustrate the fluctuation in RTI admissions over eight-time points in 2019 and 2020. The data shows a peak in admissions in December 2019, coinciding with the onset of the COVID-19 pandemic, followed by a decline in 2020. This pattern suggests that the initial surge in COVID-19 cases may have influenced RTI admissions, either through increased awareness and testing or through changes in patient behavior and healthcare access during lockdowns. A 2021 study in America revealed a 33.7% decrease in daily hospital admissions for urgent conditions during the COVID-19 pandemic compared to 2019. Significant declines were seen in gastroenterology (-29.6%) and cardiovascular (-44.7%) admissions. The study underscores the importance of public awareness campaigns to reassure the public about the safety of seeking necessary medical care during the pandemic15.

For the LOS, the average LOS remained consistent between 2019 and 2020, with a mean of 15–16 days. However, the standard deviation decreased from 16 in 2019 to 13 in 2020, indicating a slight reduction in variability of hospital stays during the pandemic. This could reflect more standardized treatment protocols or the impact of pandemic-related healthcare policies on patient management. A 2022 study in China examined 563,680 emergency admissions in 2020 and 709,583 in 2019, finding that the COVID-19 pandemic increased 28-day in-hospital mortality from 2.9–3.6% (aHR = 1.22). The first and third waves had significantly higher mortality than inter-wave periods. The average length of stay decreased by 0.40 days, notably shorter for patients with mental disorders and cerebrovascular disease16.

For RTI Diagnoses and Antibiotic Use, CAP was the most common diagnosis across the study period, with significant cases of HAP and non-specific RTIs. The emergence of COVID-19 pneumonia cases in 2020 highlights the direct impact of the pandemic on respiratory infection trends. The variability in diagnoses emphasises the challenges of maintaining precise AMS during a health crisis, emphasizing the need for robust diagnostic and treatment protocols. As an example of pneumonia education, a Continuing Education Activity in Australia in 2024 highlights the complexities of bacterial pneumonia, including its symptoms, complications, and long-term impacts. This module emphasizes a multidisciplinary approach to manage the disease, offering practical strategies for diagnosis, treatment, and patient care. It aims to enhance clinician knowledge, improve patient outcomes, and promote a cohesive healthcare approach17. Additionally, the protocol preparation adheres to national and international guidelines, including NICE guidelines, and incorporates results from local antibiograms. It is frequently updated with changes in local or national resistance patterns, clinical situations, or emergencies such as the COVID-19 pandemic. Updated protocols and antimicrobial guidelines should be properly disseminated to healthcare professionals to maintain proper antibiotic prescribing and antimicrobial stewardship practices18-20.

For AMS Compliance with the SSTF toolkit, findings show high compliance with documenting clinical indications and drug allergies, consistently achieving 100%. However, compliance with the CURB-65 Score for pneumonia severity remained at 60%, indicating an area for improvement. The decrease in compliance with interventions such as streamlining/de-escalation and antibiotic changes during the pandemic suggests that the crisis may have disrupted standard AMS practices. The COVID-19 pandemic posed significant challenges to maintaining optimal antibiotic stewardship. The consistent use of documentation for clinical indications and drug allergies is commendable, but the variability in other AMS interventions points to the need for strengthened protocols and continuous monitoring. These findings align with the study by the study in Spain in 2021, which reported increased inappropriate antibiotic use during the COVID-19 pandemic. The study highlights the significant rise in inappropriate antibiotic prescriptions, exacerbating antimicrobial resistance concerns21.

Materials and methods

Study Design and Setting

To assess the impact of COVID-19 on antimicrobial stewardship, antibiotic prescribing was examined before and during the pandemic. Baseline data from 2019 served as a pre-pandemic reference, with measurements taken in the first week of March, June, September, and December. The same periods were analyzed during the 2020 pandemic, which corresponded to UK national lockdowns and the release of COVID vaccines22. This interrupted time-series approach accounted for seasonal variations in antibiotic prescribing patterns. This pilot study, conducted from 1 August 2021 to 28 February 2023, took place at one NHS Foundation Trust in the East of England, serving approximately 700,000 people with about 742 beds. This retrospective medical records review aimed to evaluate antibiotic stewardship and prescribing in adult patients aged 25 years and above during 2019 (pre-pandemic) and 2020 (during the pandemic).

Participants

Participants in this medical record review study included adults aged 25 years and above, including pregnant women and individuals with compromised immune systems, who were admitted to the secondary care setting during 2019 and 2020. The focus was particularly on those administered antibiotics for RTIs, covering instances of pneumonia across both years and extending to COVID-19 in 2020. Exclusion criteria were established for individuals who had a stay of less than 48–72 h in the accident and emergency (A&E) department, those not administered antibiotics, and paediatric patients. The research protocol underwent evaluation and received input from the Citizens' Senate, an entity championing patient care with substantial representation of the elderly demographic. This study has been officially registered with the ISRCTN registry. The ISRCTN registry is a primary registry related to WHO criteria and the International Committee of Medical Journal Editors (ICMJE), accepting all clinical research studies (ISRCTN 14825813) 23. It was also registered in Octopus, the global primary research record24.

Data Sources and Variables

Patient selection was based on electronic health record (EHR) entries identified by the respective ICD-10 codes for RTIs. This covered a range of conditions, encompassing both specific and indeterminate diagnoses. Specific conditions included CAP, COPD infective exacerbation, HAP, and VAP. In 2020, the selection criteria were expanded to include cases of COVID-19 pneumonia. Additionally, indeterminate diagnoses such as URTIs, LRTIs, and pneumonia were categorised as 'Unspecific' RTIs. The primary diagnosis of RTIs in these records played a crucial role in determining the initial or empirical antibiotic prescribed to the patients.

The sample size calculation was calculated based on Public Health England's estimation that 20% of all antibiotics prescribed in the UK might be inappropriate25. This study, a retrospective cross-sectional analysis serving the NHS Foundation Trust's population of around 700,000 in East England, spanned two significant years: 2019 and 2020. Utilising Minitab Statistical Software Version 21.1.0 and considering the service population, a 10% margin of error, and a 95% confidence interval, the required sample size was determined26. A total of 80 patient records were precisely selected to analyse antibiotic prescribing trends during the specified years.

For sampling, the systematic method was employed to consistently select patient medical record data from a larger dataset at the Trust. Initially, data from 4830 records (2755 from 2019 and 2075 from 2020) were extracted. After applying inclusion and exclusion criteria and eliminating duplicate records, the numbers were narrowed down to 1188 for 2019 and 939 for 2020. Subsequently, a random selection of 40 records for each year was conducted using Excel's RAND function27. This resulted in a total of 80 patient records. This approach streamlined the sampling process while ensuring a comprehensive representation of the patient population. The primary author (RA) extracted data from the electronic medical records of patients within the secondary care setting. These data included demographic characteristics and evaluated antibiotic prescribing practices based on the antimicrobial stewardship 'Start Smart, Then Focus' Toolkit from PHE, which was used as the gold standard for this study7.

This pilot study was conducted to provide an initial overview of the data and to evaluate the feasibility in addressing the research questions. Data were extracted from 80 patient medical records, 40 in 2019 and 40 in 2020. In this pilot test, two independent authors separately extracted data from 1% of the sample (four patient records) to validate the data extraction tool. An agreement rate of 80% or higher was used as a measure of the tool's validity28.To assess the tool's reliability, both authors independently extracted data from another 1% of the sample (four records). Inter-rater reliability was determined by independently comparing the percentage agreement in the data extracted. Any disagreements were resolved through discussion29. The result of the pilot study indicated that the data extraction tool was sufficient to address all the study objectives.

Statistical Methods

Descriptive analyses were conducted, presenting data on categorical or binary variables as numbers (n) and proportions (%). Initial data, including sex, age, admission specialty, patient classification, and discharge method, were described using numbers (n) and percentages (%) and further analyzed. The Chi-square test was utilized for categorical variables, and the Kruskal–Wallis test was applied to numerical variables. The study also examined the number of admitted patients with respiratory tract infections and their LOS in 2019 and 2020. Additionally, compliance with the SSTF toolkit was assessed. For advanced statistical analysis, IBM SPSS Statistics version 22.0, RStudio version 2022, and R version 4.2.2 were used30-31.

Conclusion

This pilot study highlights the profound impact of the COVID-19 pandemic on AMS practices within a secondary care setting in the UK. The interrupted time-series analysis comparing pre-pandemic (2019) and pandemic (2020) data reveals significant shifts in antibiotic prescribing patterns, particularly for RTIs. Community-acquired pneumonia was the most frequent, with notable increases during key pandemic phases. The pandemic disrupted standard AMS practices, resulting in decreased compliance with interventions such as streamlining, de-escalation, and antibiotic changes. The emergence of COVID-19 pneumonia and its impact on RTI trends underscores the necessity for adaptable AMS strategies during health crises. The study emphasizes the need for robust diagnostic and treatment protocols to maintain effective AMS during emergencies. Tailored AMS approaches that address the unique challenges posed by global health crises are crucial to mitigating antimicrobial resistance and ensuring patient safety. Future research should build on these insights to develop resilient AMS frameworks that can sustain optimal practices under the pressures of pandemics and other health emergencies, ensuring continuity and efficacy in patient care.

Declarations

Institutional Review Board Statement

Ethical approval for this study was granted by the Health Research Authority (HRA), with the Research Ethics Committee (REC) assigning reference number 22/EM/0161. In compliance with this approval, the study protocol underwent review and received approval from the University of Hertfordshire (UH) Ethics Committee under the reference LMS/PGR/NHS/02975.

Competing interests

The authors declare no competing interests.

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Author contributions

R.A.E. was responsible for data acquisition, with the study design and conceptualisation developed collaboratively by R.A.E., N.U. and Z.A.; R.A.E. carried out the literature review under N.U.'s and Z.A.'s supervision and further extracted relevant electronic data from patient records. The project dataset was constructed by R.A.E., who also verified, accessed, and analysed the data, guided significantly by N.U. and Z.A.; R.A.E. produced the initial draft of the study, guided by N.U. and Z.A. All authors contributed to data interpretation and the preparation and revision of the manuscript, sharing equal responsibility for the final decision to submit and approval of the final manuscript. Z.A. acted as the guarantor for the overall content of the research. Data were anonymised before analysis and securely stored within the University of Hertfordshire's (UH) dual secure system. R.A.E. analysed the anonymised data using UH's dual secure system. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The datasets presented in this article are not readily available, according to the institution's policy. Requests to access the datasets should be directed to r.a.elshenawy@herts.ac.uk.

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Figures

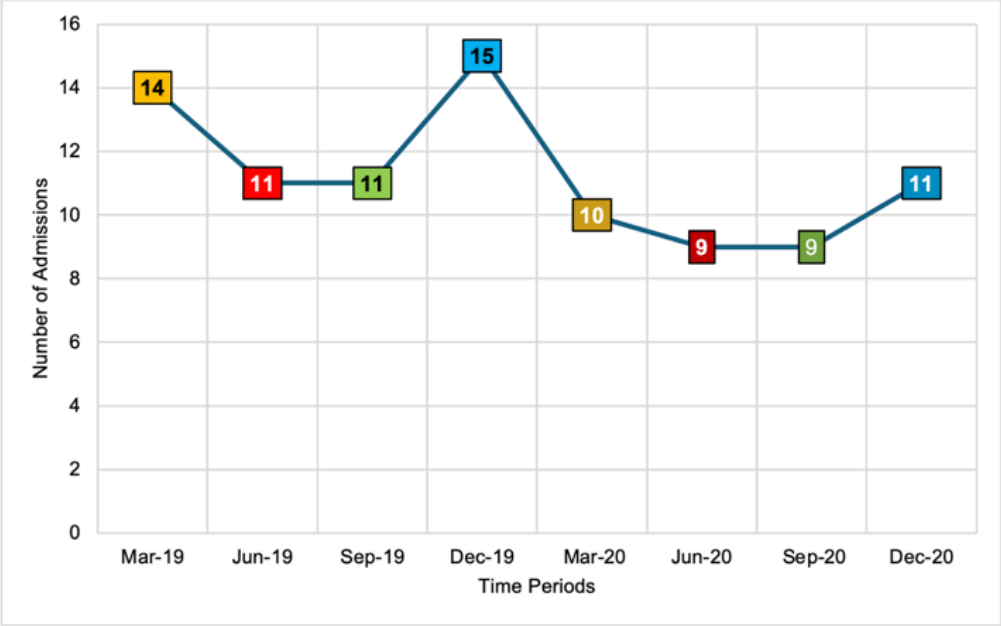

Figure 1

The Number of Respiratory Tract Infection Admissions Across Eight Seasonal Time Points in 2019 and 2020 (n= 80 Admissions).

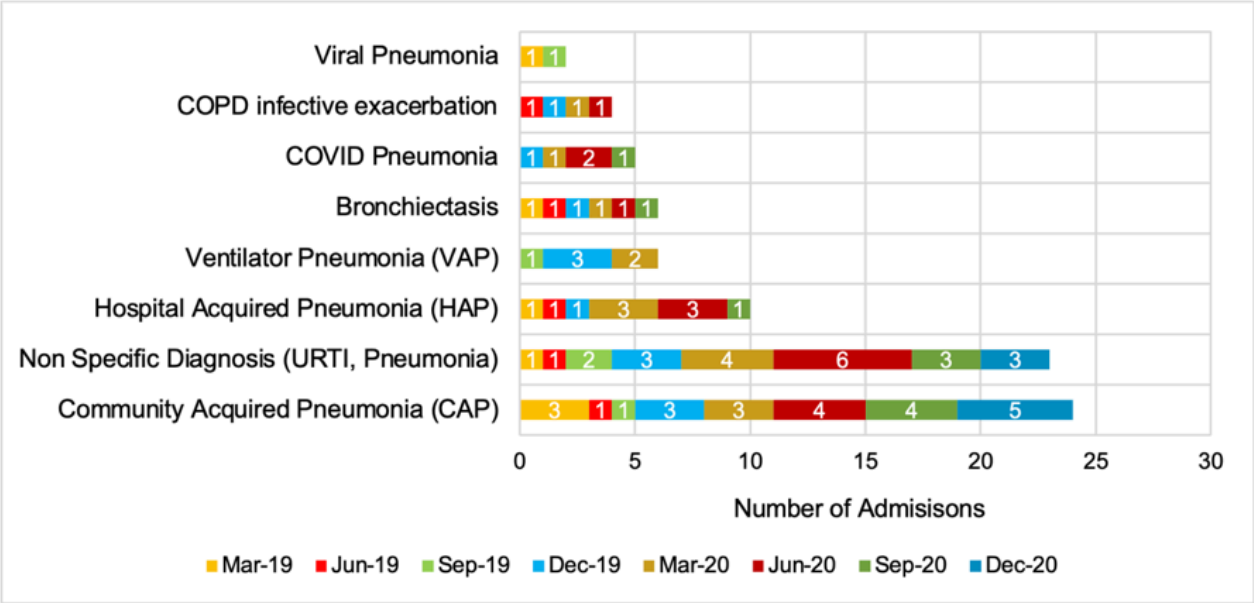

Figure 2

Seasonal Trends in Respiratory Tract Infection Admissions in 2019 and 2020 (Total number = 80 admissions).

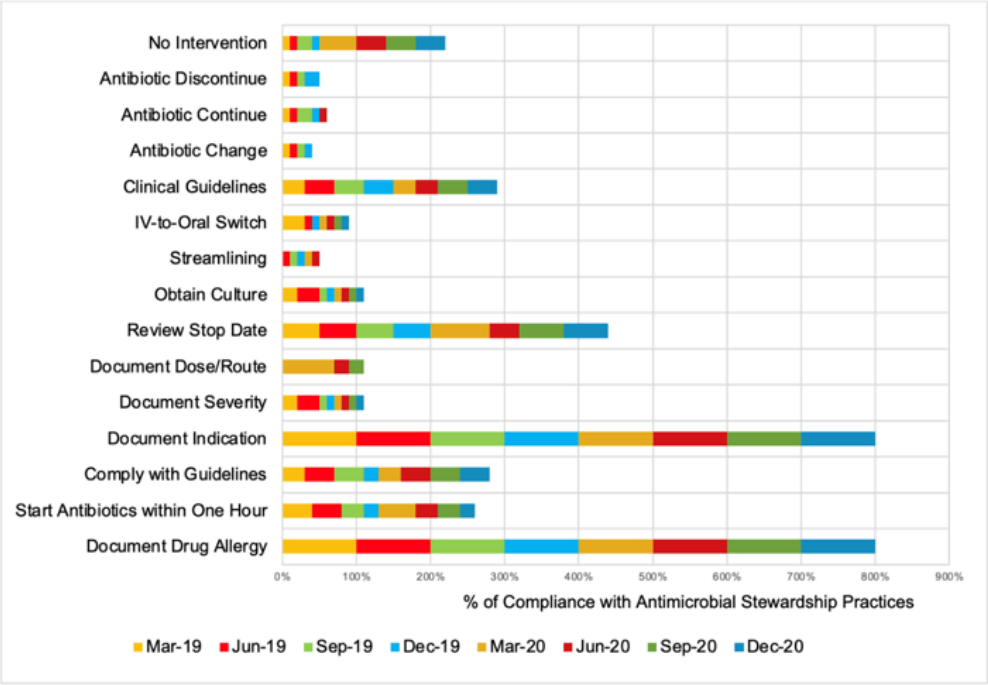

Figure 3

Compliance with Antimicrobial Stewardship Practices Across Eight Seasonal Time Points in 2019 and 2020.