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JAC-Antimicrobial Resistance

Effect and sustainability of a stepwise implemented multidisciplinary antimicrobial stewardship programme in a university hospital emergency department

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Objectives: To explore effectiveness and sustainability of guideline adherence and antibiotic consumption after establishing treatment guidelines and initiating antimicrobial stewardship (AMS) ward rounds in a university hospital emergency department (ED).

Methods: Data were gathered retrospectively from 2017 to 2021 in the LMU University Hospital in Munich, Germany. Four time periods were compared: P1 (pre-intervention period); P2 (distribution of guideline pocket cards); P3 (reassessment after 3 years); and P4 (refresher of guideline pocket cards and additional daily AMS ward rounds for different medical disciplines). Primary outcome was adherence to guideline pocket cards for community-acquired pneumonia, cystitis, pyelonephritis and COVID-19-associated bacterial pneumonia. Secondary outcomes were reduction in antibiotic consumption and adherence to AMS specialist recommendations.

Results: The study included 1324 patients. Guideline adherence increased in P2 for each of the infectious diseases entities. After 3 years (P3), guideline adherence decreased again, but was mostly on a higher level than in P1. AMS ward rounds resulted in an additional increase in guideline adherence (P1/P2: 47% versus 58.6%, $P=0.005$; P2/P3: 58.6% versus 57.3%, $P=0.750$; P3/P4: 57.3% versus 72.5%, $P<0.001$). Adherence increased significantly, not only during workdays but also on weekends/nightshifts. Adherence to AMS specialist recommendations was excellent (91.3%). We observed an increase in use of narrow-spectrum antibiotics and a decrease in the application of fluoroquinolones and cephalosporins.

Conclusions: Establishing treatment guidelines in the ED is effective. However, positive effects can be diminished over time. Daily AMS ward rounds are useful, not only to restore but to further increase guideline adherence significantly.

Introduction

Antimicrobial resistance remains a challenging global health threat that causes more than a million deaths annually.[1] Inappropriate use of antibiotics contributes to the expansion of antimicrobial resistance.[2] Emergency department (ED) medical staff especially prescribe high numbers of antimicrobials. Due to the specific environment of the ED with the need for quick

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decisions and high patient turnover, elevated rates of inappropriate use of antimicrobials are reported.[3,4]

Antimicrobial stewardship programmes (ASPs) can reduce the use of antimicrobials and the spread of resistant pathogens.[5,6] The ED is therefore an important field for ASPs, due to its unique linking position between the outpatient and inpatient sector.[7] ASP studies that specifically target the ED are of the utmost interest.[8]

The ED is characterized by the involvement of multiple medical disciplines, irregular physical presence of ED staff due to shift work and high patient turnover. This setting makes antimicrobial stewardship (AMS) interventions particularly challenging. ASPs have therefore to adapt to the specific environment of the ED.[9] There are some ASPs that proved to be effective in the ED.[10,11] So far, limited reports emphasize the importance of multidisciplinary AMS teams and the direct involvement of ED staff for effective AMS outcomes.[12–14] The combination of guideline distribution and education proved to be effective in the paediatric ED setting.[15]

However, effects of ASPs have been described not to last over longer periods of time.[16,17] No data are available on long-term effects of such programmes in the difficult setting of the ED. The optimal combination of ASP interventions in the ED setting is therefore unclear.[18]

Here, we investigated the effect of an AMS intervention consisting of the distribution of treatment recommendations and teaching sessions on guideline adherence and antibiotic consumption and reviewed sustainability of this ASP after 3 years. We hypothesized, that additional daily AMS ward rounds could further improve the quality of antimicrobial prescriptions.

Methods

Ethics

The study was approved by the institutional review board of the Ludwig-Maximilians-Universität (LMU), München, Germany (Project: 22-0097). Patient data were analysed anonymously.

Study design

We conducted a single-centre, retrospective study in the interdisciplinary ED at the LMU University Hospital in Munich, Campus Großhadern, over a 4 year period. The LMU University Hospital is a tertiary-care hospital, including transplantation medicine, with an inpatient treatment capacity of approximately 2000 beds. The ED counts around 40 000 visits per year. A broad spectrum of medical specialities is present 24/7 in the ED; most patients are seen by residents of internal medicine, surgery and neurology who are supervised by attending physicians of the same medical discipline. Paediatric emergencies are not seen in the ED at Campus Großhadern. Two wards are closely associated with the ED itself. One intermediate care unit (IMC) for critically ill patients and one general ward, which works as a buffer zone for patients waiting for admission to in-hospital wards or transfer to external healthcare providers. The ED and ED-associated wards are all attended by the same doctors. For persons requiring in-hospital treatment, patient flow is usually straight to in-hospital wards or to the ED IMC or ED general ward.

The AMS department is a multidisciplinary team consisting of specialists in infectious diseases, hospital pharmacy and clinical microbiology.

The AMS department prepared a hospital-adjusted treatment guideline for typical infectious diseases entities seen in the ED. Treatment recommendations focused on empirical antibiotic therapy and were prepared in accordance with existing national or international treatment guidelines and after consulting different medical disciplines of the hospital. Initially, treatment guidelines were distributed to the ED staff as pocket cards and posters in September 2018. Guidelines were not disseminated across the whole hospital, but could also be accessed electronically via the hospital intranet. Training sessions took place at that time. After 3 years, in October 2021, the AMS department initiated daily AMS ward rounds in the ED. AMS ward rounds were conducted from Monday to Friday twice daily during day shifts in internal medicine, surgery and neurology in the ED and the ED-associated wards. Recommendations given by the AMS ward round team consisted of all kinds of treatment recommendations like diagnostic procedures, choice of substance, dosing optimization or switch to oral therapy. There is no permanent presence of urologists in the ED. Staff of the department of urology, therefore, were trained in an educational session about empirical treatment of urinary tract infections (UTIs).

The primary outcome was adherence to local treatment guidelines. Secondary outcomes were changes in antibiotic consumption and adherence to AMS specialist recommendations.

Study periods

Four time periods of 3 months each were assessed: P1, P2, P3 and P4. P1 was the pre-intervention period (September 2017–November 2017). This was before initiating AMS activities in the ED. There were no treatment guidelines and no training sessions. P2 involved the distribution of treatment guidelines/training sessions in the ED (September 2018–November 2018). P3 was the reassessment period after 3 years (May 2021–July 2021). P4 involved redistribution of treatment guidelines and daily AMS ward rounds in the ED (October 2021–December 2021) (Figure 1).

Data

We included ED patients with documented community acquired pneumonia (CAP), cystitis or pyelonephritis. COVID-19-associated bacterial pneumonia was added as an additional entity due to its importance for AMS principles in periods P3 and P4. Focus was on these common specific infectious diseases entities, as they are treated by all medical disciplines represented in the ED. Patients under the age of 18 years, those with a simultaneously existing infectious disease diagnosis other than the ones explicitly studied, and/or intensified immunosuppression were excluded.

Data for selected patients were extracted from the electronic medical record system and included age, sex, Charlson comorbidity index (CCI) and choice of empirical antibiotic substance. The information was analysed retrospectively for the appropriateness of the chosen antibiotic therapy according to treatment guidelines. Adherence to AMS ward round recommendations and antibiotic consumption was evaluated as well. In P1, adherence was defined as concordance to the recommendations in the later distributed treatment guidelines.

Measurement of antibiotic consumption

Antibiotic consumption was measured in DDD/100 patients for the ED (without the ED IMC unit and the ED general medical ward) in the different study periods (P1–P4).

Statistical methods

Variation between the different study periods for continuous variables was analysed with the Kruskal–Wallis rank sum test. For categorial variables, the chi-squared test was used. Statistical significance was set at $P < 0.05$.

IBM SPSS Statistics (Version 29.0.0.0; SPSS, Inc.) was used for analysing data.

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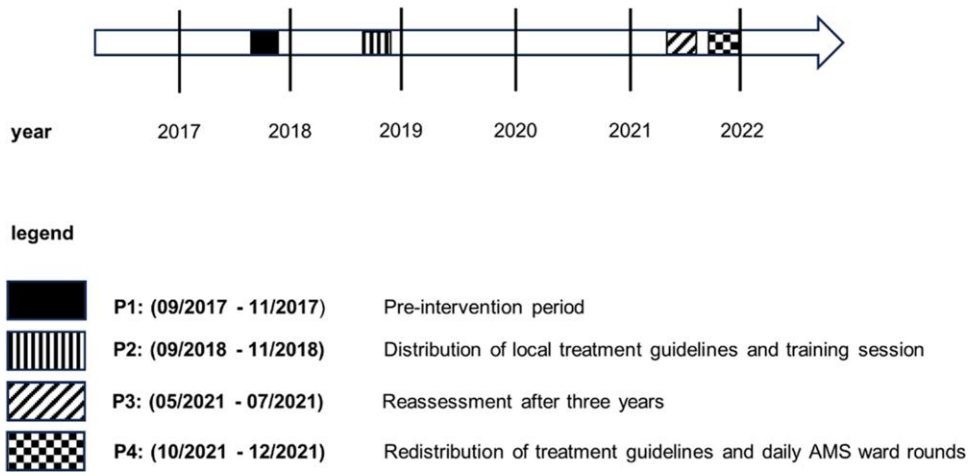

Figure 1. AMS intervention timeline.

Results

Patient characteristics

In total, 1324 patients were included in the study. More patients were analysed during P4 due to the high volume of COVID-19 cases in Autumn 2021 (Table 1).

Increased guideline adherence after distribution of local treatment guidelines

There was a good acceptance and utilization of treatment guideline pocket cards. This was seen by a significant increase in guideline adherence for all infectious diseases entities together (P1 versus P2: 47% versus 58.6%, $P=0.005$). The effect could especially be seen for CAP (P1 versus P2: 30% versus 64.6%, $P<0.001$). For cystitis and pyelonephritis, there was also an increase in guideline adherence but it did not reach statistical significance (cystitis: P1 versus P2: 42.4% versus 46%, $P=0.537$; pyelonephritis: P1 versus P2: 68.3% versus 77.3%, $P=0.225$) (Figure 2).

Additional positive effect on guideline adherence after implementation of AMS ward rounds

Initiating AMS ward rounds, we found an additional significant increase in overall guideline adherence (P3 versus P4: 57.3% versus 72.5%, $P<0.001$), for COVID-19-associated bacterial pneumonia (P3 versus P4: 77.8% versus 87.6%, $P=0.043$) and for CAP (P3 versus P4; 52.3% versus 71.9%, $P=0.042$). Adherence was >70% in these three groups. It also rose for cystitis (P3 versus P4: 48.3% versus 52.5%, $P=0.516$) and pyelonephritis (P3 versus P4: 54% versus 59.6%, $P=0.531$) but did not reach statistical significance (Figure 2).

Adherence to AMS team recommendations

In total, 449 recommendations were given during the intervention. Implementation of recommendations was excellent overall (91.3%). For the different medical specialities, adherence of internal medicine was higher than that of surgery and neurology (internal medicine versus surgery: 92.6% versus 86.3%, $P=0.125$; internal medicine versus neurology: 92.6% versus 87.2%, $P=0.205$) For the different wards, adherence on the ED general medical ward was superior to that on the ED IMC unit and the ED itself (ED general medical ward versus ED IMC: 95.3% versus 88.3%, $P=0.049$; ED general medical ward versus ED: 95.3% versus 91.9%, $P=0.272$) (Figures S1 and S2, available as Supplementary data at *JAC-AMR* Online).

Influence of medical discipline on guideline adherence

Adherence to guideline recommendations was compared for the departments of internal medicine, surgery and neurology. After distribution of local treatment guidelines, adherence to guidelines increased significantly for internal medicine (P1 versus P2: 41.7% versus 62.7%, $P<0.001$) and neurology (P1 versus P2: 10% versus 41.2%, $P=0.028$). By contrast, guideline adherence showed rather a trend towards poorer adherence for the department of surgery (P1 versus P2: 61.5% versus 45.7%, $P=0.221$).

After implementation of AMS ward rounds, an additional increase in guideline adherence for internal medicine (P3 versus P4: 60.1% versus 81%, $P<0.001$) and neurology (P3 versus P4: 58.3% versus 70.6%, $P=0.436$) could be observed. The latter did not reach statistical significance, probably due to the low number of cases. For surgery, guideline adherence remained on the same level (P3 versus P4: 56.7% versus 55%, $P=0.890$) (Figure 3).

Influence of AMS team presence on guideline adherence

We compared guideline adherence between regular working hours (Monday to Friday, 8 a.m. to 5 p.m.) and nightshifts/weekends. We could see a statistically significant increase in guideline adherence during regular working hours (P1 versus P2: 39.8% versus 60.0%, $P=0.004$). On weekends/nightshifts, there was also an increase in adherence, which was not statistically significant (weekend: P1 versus. P2: 50.8% versus 57.8%, $P=0.165$). The AMS intervention in P4 was conducted during regular working hours. AMS ward rounds then brought an additional statistically significant effect on guideline adherence during these times (P3 versus P4: 62.1% versus 76.7%, $P=0.012$) as well as on weekends/nightshifts (P3 versus P4: 55.0% versus 70.1%, $P<0.001$) (Figure 4).

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Table 1. Patient characteristics, P1–P4

	P1	P2	P3	P4	Total	*P* value
No. of patients	300	285	295	444	1324	
Age, years, median (range)	68 (18–95)	71 (18–104)	62 (18–96)	69 (18–99)	68 (18–104)	$P=0.005$
No. of women (%)	190 (63.3)	181 (63.5)	175 (59.3)	247 (55.6)	793 (60)	$P=0.093$
Diagnosis						
CAP, *n* (%)	60 (20.0)	82 (28.8)	44 (14.9)	57 (12.8)	243 (18.4)	$P<0.001$
COVID-19, pneumonia, *n* (%)	/	/	72 (24.4)	210 (47.3)	282 (21.3)	$P<0.001$
Cystitis, *n* (%)	158 (52.7)	137 (48.1)	116 (39.3)	120 (27.0)	531 (40.1)	$P<0.001$
Pyelonephritis, *n* (%)	82 (27.3)	66 (23.1)	63 (21.4)	57 (12.9)	268 (20.2)	$P<0.001$
CCI, median (range)	4 (0–14)	4 (0–13)	2 (0–12)	3 (0–13)	4 (0–14)	$P<0.001$
CCI, *n*	7	8	0	1	16	
Discipline, *n* (%)						
Internal medicine	144 (48)	151 (53.0)	153 (51.9)	274 (61.7)	722 (54.5)	$P=0.001$
Surgery	26 (8.7)	35 (12.3)	30 (10.2)	40 (9.0)	131 (9.9)	$P=0.433$
Neurology	20 (6.7)	17 (6.0)	12 (4.1)	34 (7.7)	83 (6.3)	$P=0.26$
Urology	102 (34.0)	77 (27.0)	83 (28.1)	84 (18.9)	346 (26.1)	$P<0.001$
Others	8 (2.6)	5 (1.7)	17 (5.7)	12 (2.7)	42 (3.2)	$P=0.031$

Due to missing data, 16 patients were excluded from statistical analysis for CCI in P1, P2 and P4. In P3, patients were younger and had a lower CCI. More patients were seen in internal medicine in P4, also because of the high volume of COVID-19 cases in the ED.

Antibiotic consumption

Overall, the antibiotic consumption remained on a similar level throughout the investigation period. There was a noticeable drop in P3, which was conducted in the summer months. In addition, the increase in antibiotic consumption in P4 could be completely explained by the additional application of azithromycin in moderate and severe CAP.

Regarding the antibiotic substances, the application of fluoroquinolones was substantially reduced (P1 versus P4: 3.1 versus 0.7 DDD/100 patients). A similar effect could be seen for ceftriaxone and cefuroxime, but to a lesser extent (Table S1). The most prominent increase was the usage of azithromycin (P1 versus P4: 0.0 versus 1.7 DDD/100 patients), clearly intended by the AMS specialists as combination therapy in moderate to severe CAP. Similarly, the application of cefpodoxime for pyelonephritis (P1 versus P4: 0.0 versus 0.3 DDD/100 patients) and pivmecillinam for uncomplicated cystitis (P1 versus P4: 0.0 versus 0.3 DDD/100 patients) could be introduced with AMS ward rounds. A mild increase in broad-spectrum antibiotics could be observed in the investigation period (piperacillin/tazobactam: P1 versus P4: 1.2 versus 1.7 DDD/100 patients; meropenem: P1 versus P4: 0.1 versus 0.3 DDD/100 patients); for narrow-spectrum substances, an increase was also noted (ampicillin/sulbactam: P1 versus P4: 0.3 versus 0.5 DDD/100 patients).

Overall, the application of antibiotic substances has become much more diverse over the years (Figure 5).

Discussion

Here, we conducted an ASP with high intensity in the ED of a large university hospital over a 4 year period. The distribution of treatment pocket cards had a valuable effect on guideline adherence and choice of antibiotics. AMS ward rounds further increased guideline adherence and brought improvement in the selection of antibiotics. AMS experts were integrated into the ED workflow and positively accepted by the ED staff.

We show here for the first time the long-term effects of an AMS intervention in a multidisciplinary university hospital ED. A decrease in guideline adherence could be observed 3 years after implementation of treatment guidelines, confirming that positive behavioural change can get lost over time, as is described for the inpatient sector.[16] Data on the necessity of regular and persisting multidisciplinary AMS presence in the ED is just emerging.[13,15] While our study confirms these findings, it additionally shows the evaluation over a period of 4 years for various infectious diseases entities and medical disciplines and demonstrates the benefit of AMS ward rounds.

In our study, the ASP was more effective for internal medicine and neurology than for surgery. Differences in antibiotic prescribing between medical disciplines have been described before.[19] Antibiotic prescribing in the ED is complex and not every decision is guided by seniors or ID specialists.[20] Moreover, the analysed infectious diseases entities in this study are not typically surgical. The picture could be different for specific surgical diagnoses like appendicitis or cholecystitis. Due to the specialization of our hospital in complex surgical procedures and transplantation medicine, less complex surgical cases are usually transferred to another hospital campus. Treated numbers of uncomplicated appendicitis and cholecystitis were therefore too low to be integrated in this study.

As junior physicians rotate in the ED in their early years of training, we see the ED as optimal terrain for education on behalf of AMS. Junior physicians are not only eager in acquiring knowledge about appropriate antimicrobial prescribing but can also positively influence other sectors of the hospital once they complete their rotations in the ED.[21–23] Little is known about the attitudes of ED staff towards AMS in the ED.[24] As continuous external AMS advice

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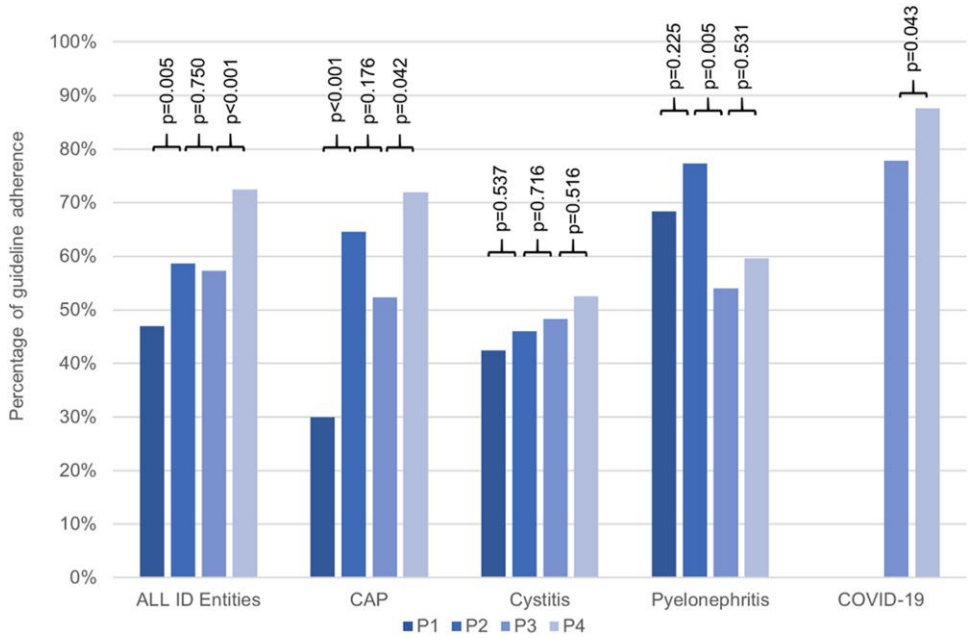

Figure 2. Percentage of guideline adherence for all infectious diseases (ID) entities as well as CAP, cystitis, pyelonephritis and COVID-19-associated bacterial pneumonia, P1–P4 (chi-squared test).

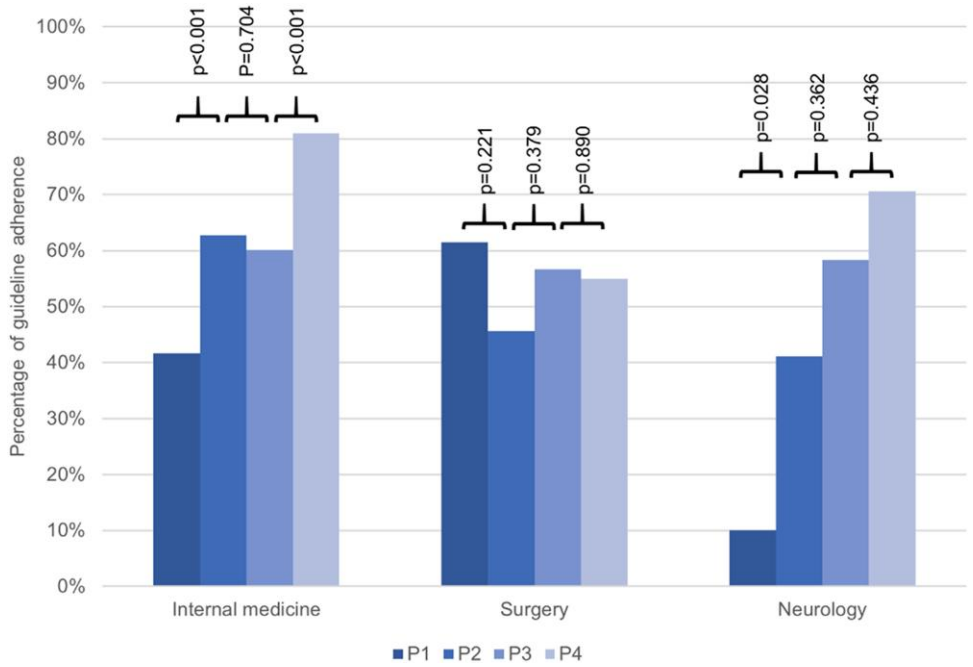

Figure 3. Percentage of guideline adherence for internal medicine, surgery and neurology, P1–P4, evaluated for all infectious diseases entities (chi-squared test).

can easily be perceived as annoying and presumptuous, this is an even more delicate matter for the stressful environment of the ED. Nevertheless, acceptance of AMS team recommendations was excellent for all medical disciplines and on all wards, confirming the importance of collaborative AMS in the ED.[12–14]

A reduction in total antibiotic consumption could be observed in P3. We rather explain this important change in seasonal variation due to the investigation period (summer) than to a behavioural change in antibiotic prescription.[25] Total antibiotic consumption remained on the same level between P1 and P4.

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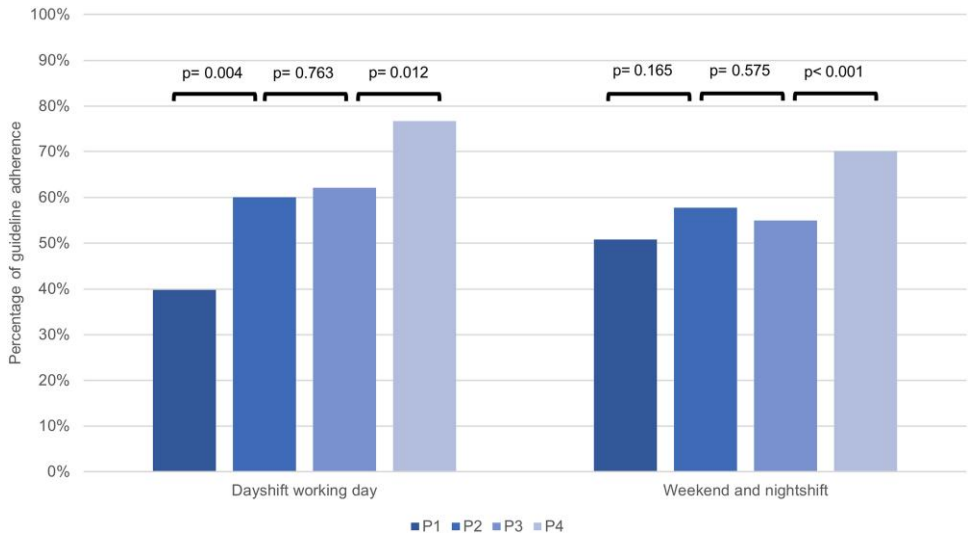

Figure 4. Percentage of guideline adherence on AMS intervention time versus non-intervention time, P1–P4. Regular working hours: Monday to Friday 8 a.m. to 5 p.m. (chi-squared test).

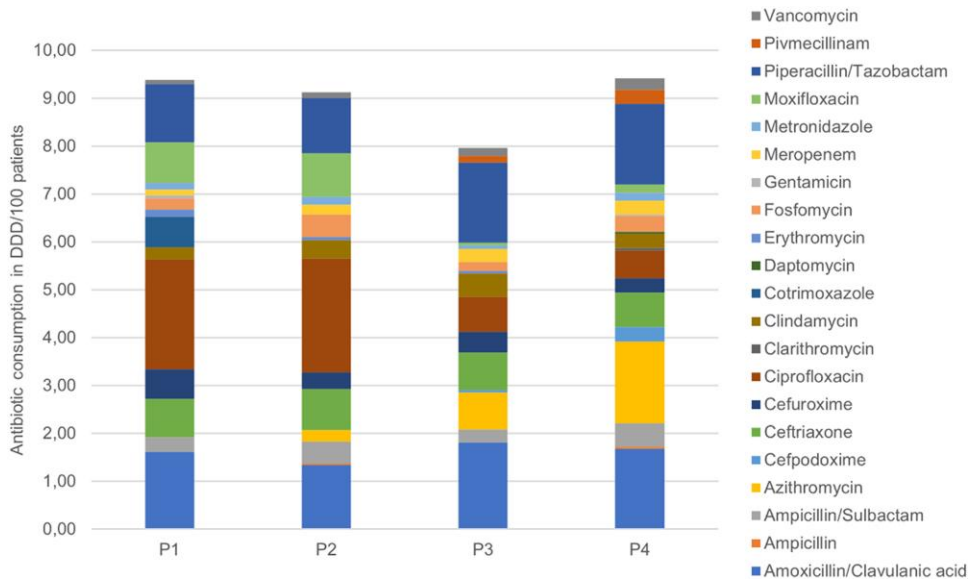

Figure 5. Antibiotic consumption for the P1–P4 in the ED, evaluated as DDD/100 patients.

However, a substantial percentage of applied antibiotics in P4 was the additional application of azithromycin in moderate and severe CAP. This is in accordance with national and international guidelines and an important part of the improvement of the antibiotic treatment of CAP in our ED. The finding demonstrates that AMS interventions can lead to increased antibiotic consumption in some cases.

Moreover, important AMS goals could be achieved. One study showed a decrease in hospital acquired *Clostridioides difficile*, and a decrease of MRSA and ESBL-producing coliforms after reduced consumption of ceftriaxone and ciprofloxacin.[26] In our study, fluoroquinolones especially could be effectively reduced over the years. A reduction in the use of cephalosporins could also be observed but to a lower extent than fluoroquinolones. Additionally, there was an increase in the application of narrow-spectrum antibiotics and substances that were not known by ED staff before the AMS intervention (e.g. pivmecillinam, cefpodoxime). All in all, we observed a much more diverse repertoire of antibiotics used in the ED over the study period.

A major limitation to our study was the addition of COVID-19-associated bacterial pneumonia in periods P3 and P4. Due to the importance of responsible use of antimicrobials, also during the COVID-19 pandemic, we found it indispensable to include COVID-19 in our study.[27,28] In addition, P3 had to be

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conducted in summer, which makes it difficult to compare with the other study periods. The reason for this choice was the timing of the research grant that funded the second part of the project and which was limited to a 12 month period, including preparation, analysis and evaluation of the study. AMS ward rounds could therefore not be extended over a 3 month period, although a longer investigation period would have provided more information. As we tried to highlight the importance and effectiveness of AMS ward rounds in the ED, we chose an immediate pre-ward rounds period (P3), which therefore fell in Summer 2021.

An official drug-safety warning concerning the application of fluoroquinolones in October 2018 could have contributed to the noticeable reduction of these substances over the investigation periods.

In this study, we could show that regular presence and ward rounds by a multidisciplinary AMS team can bring rapid behavioural change in the application of antimicrobials. As ED crowding can have a negative impact on guideline adherence,[29] consultation of an AMS expert can reduce cognitive workload for the ED healthcare professionals. The improved ED staff performance on weekends and during nightshifts when no AMS expert consultation was available further underlines the specific efficacy of AMS ward rounds. For ICU physicians, speed of processing information and perceptual reasoning was impaired after a nightshift.[30] As nightshifts in the ED show similarities with the ICU, we conclude that AMS coverage of the ED can support reasonable decision-making during the night hours.

Hospital ASPs should therefore also cover the ED. ED staff must be made aware of their pivotal role in optimal utilization of antimicrobials and its impact for the individual patient but also on the community.

We conclude that implementation of local therapy guidelines impacts the adequacy of antibiotic prescriptions in the ED positively. However, these effects can be diminished over time. We can show that AMS ward rounds in the ED are well received and lead to further and rapid improvement in the use of antibiotics. AMS specialists should therefore be an integral part of emergency medicine teams.

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Transparency declarations

None to declare.

Supplementary data

Figures S1 and S2 and Table S1 are available as Supplementary data at *JAC-AMR* Online.

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