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# Bacteraemia due to *E.coli* in urinary tract infections in adults: a prospective epidemiological study following implementation of guidelines in a regional hospital

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## Abstract

**Background** Several countries have established action plans for antibiotic stewardship programs (ASPs), which recognise the clinical and public health issues of antimicrobial resistance. We evaluated the impact of a multimodal ASP, implemented in 2017 to improve urinary source E.coli bacteraemia in a secondary care hospital in Catalonia, Spain.

**Methods** Prospective, post-intervention, epidemiological study in a single hospital in Catalonia. Patients were included if they were aged ≥ 18 years, were admitted to the hospital for any cause between January 1, 2017 and December 31, 2022, and had urinary-source E.coli bacteraemia. The primary endpoint was adherence to antimicrobial treatment guidelines for urinary-source E.coli bacteraemia. Secondary endpoints included, appropriate antimicrobial treatment use based on in vitro sensitivity; the degree of error in appropriate use of empirical antimicrobial treatments by guideline adherence (yes/no); and the percentage of E. coli antibiotic resistance in these patients.

**Results** Of the 297 patients with urinary-source E.coli bacteraemia, the majority were female (57.9%), and the mean (SD) age was 79.0 (16.9) years. Most urinary-source E.coli bacteraemias were community-acquired ($n = 194$, 65.3%) vs. healthcare system- ($n = 78$, 26.3%) or hospital- ($n = 25$, 8.4%) acquired. Adherence rates to antimicrobial treatment guidelines were high across all years (91.4%; range 83.0% to 97.8%), as was the appropriateness of use based on in vitro sensitivity (93.0%; range: 89.4% to 97.8%). The degree of error in appropriate use of empirical antimicrobial treatments was 3.0% (range: 0% to 6.5%) when guidelines were followed and 50.0% (33.3% to 66.7%) when guidelines were not followed. The percentage of urinary-source E.coli bacteraemia which were resistant to treatment with quinolones (44.7% vs. 22.4%; $p = 0.014$) and ESBLs (21.3% vs. 12.2%; $p = 0.058$) reduced significantly from 2017 to 2022. No cases of carbapenem resistance occurred.

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**Conclusions** This prospective, single centre study reports a high level of appropriate antimicrobial use, based on both guideline recommendations and in vitro sensitivity testing. Our ASP has been applied successfully over 6 years, resulting in improvements in the empirical antimicrobial treatment of urinary-source E.coli bacteraemia, and a reduction in antimicrobial resistance.

**Keywords** Antimicrobial stewardship program, Bacteraemia, *Escherichia coli*, Guideline adherence, Prospective study, Urinary tract infections, Antimicrobial resistance

## Background

Bloodstream infections are a major cause of morbidity and mortality in patients admitted to hospital and immediate initiation of appropriate antibiotics in patients with bacteraemia is critical to improve poor patient outcomes and to reduce mortality rates [1–5]. In high-income countries, *Escherichia coli* (*E.coli*) is the most common cause of gram-negative bacteraemia, with urinary tract infections (UTIs) being the main source of *E.coli* bacteraemia (>50% of cases) [5, 6]. The estimated incidence of *E.coli* bacteraemia is 48 per 100,000 person-years, and this had been shown to be increasing in some regions [6, 7].

Although there have been improvements in rapid microbiologic testing, the turnaround time still takes up to 72 h, and therefore clinicians often initiate empiric antibiotic therapies [6]. Empiric treatment may have some negative consequences for patients' health, including not being effective for the pathogen or being associated with unnecessary toxicity due to treatment-related adverse events [8]. In addition, unnecessary broad spectrum empiric treatment has been shown to exacerbate the risk of antimicrobial resistance [8]. Resistance to antibiotics is a worldwide problem, especially in hospitalized patients [8, 9]. Emerging multidrug resistant *E.coli* strains, such as extended-spectrum beta-lactamase (ESBL) producing *E.coli*, are difficult to treat, and are associated with a higher risk of bacteraemias and death [7, 10]. The major drivers for the increasing prevalence of antimicrobial resistance are the misuse and overuse of antimicrobial agents, which affect not only the efficaciousness of treatments but also prolong the duration of hospitalisations, negatively affect patients' quality of life, and increase hospital resource use [8]. To combat this, several countries have established action plans for antibiotic stewardship programs (ASPs), which recognise the clinical and public health issues of antimicrobial resistance [8].

To combat antimicrobial resistance in Catalonia (Spain), the Catalan Health Service created the Programme for the Surveillance of Healthcare-Related Infections named VINCat in 2006 [11–14]. A part of the program includes the establishment of a standardized surveillance program for bacteraemia of urinary tract origin caused by *E. coli* in hospitals in Catalonia [13]. This includes the application of an ASP in hospitals, the community, and long-term care facilities.

The objective of this prospective, post-intervention, epidemiological study was to evaluate the impact of an ASP, implemented in 2017 in a single hospital in Catalonia, including investigation of how adherence to clinical antimicrobial treatment guidelines can positively impact bacteraemia of urinary tract origin caused by *E.coli.*

## Methods

### Hospital ASP

The study is settled in a secondary acute care hospital of 150 beds for acute care. In 2017 an institutional ASP was launched, with an infectious disease specialist, a microbiologist and a pharmacist being responsible for the program. The ASP program consists of daily revisions to all in-hospital antibiotic treatments, with prompt feedback about the adequacy or inadequacy of antibiotic treatment provided to the prescribers, either by phone or by written notes. The antimicrobial stewardship team also advises prospectively on the duration of every antibiotic prescribed in the hospital. At the same time, institutional protocols for the most common infections were redacted, with the collaboration of other hospital specialists. In 2017, a new protocol for the diagnosis and treatment of urinary infections was implemented at our hospital that is based on local microbiology and patterns of resistance (See supplementary appendix for further details). This protocol is updated yearly and disseminated throughout all hospital services. It is communicated in a general session and subsequently copies of the information and algorithm are left in all medical offices of the hospital, including the doctor's office in the emergency room. In addition, all local protocols, including the urinary infection protocol, are easily accessible to all healthcare personnel via the main page of the hospital intranet. As part of the ASP for our centre, urinary infections and bacteraemias are reviewed daily and feedback is constantly provided to prescribers. Prescribers are informed of possible errors due to non-adherence to the protocol and an email is sent to the Emergency department coordinator.

### Study design and population

All patients who were aged ≥ 18 years, were admitted to the surgical or medical hospital wards for any cause between January 1, 2017 and December 31, 2022, and

had bacteraemia of urinary tract origin caused by *E.coli* were included in the study. Daily data on E. coli bacteraemia were transmitted from the microbiology laboratory to the clinical investigators. Bacteraemia of urinary tract origin caused by E. coli was defined as any E. coli isolation in a blood culture from a patient with a simultaneous urine culture showing $>10^5$ colony-forming units/mL and compatible symptoms, in the absence of an alternative focus [15]. Bacteraemia was further classified according to the acquisition setting: hospital-acquired if identified >48 h after admission and before discharge; community-acquired if identified in the community or within 48 h of admission in patients who had been discharged from a healthcare facility >4 weeks before symptom onset; and healthcare-associated if occurring within 48 h of admission in patients living in the community but with regular healthcare contact. The latter included patients receiving medical care at home, residing in nursing or social health centres, undergoing chronic haemodialysis or peritoneal dialysis, attending day hospitals on a regular basis, or with a hospital admission within the previous 4 weeks [15].

For each patient meeting the inclusion criteria, the principal investigator collected the following variables from medical records: age, sex, source of bacteraemia, hospitalisation ward at the time of diagnosis (medical, surgical, or intensive care unit [ICU]), acquisition category, empirical antimicrobial treatment (active ingredient and dose), adherence of empirical antimicrobial treatment to therapeutic guidelines (yes/no), adequacy of empirical antimicrobial treatment in light of antibiotic susceptibility results (yes/no), and resistance profile of the isolate (E. coli producing extended-spectrum β-lactamases [ESBL] [yes/no], carbapenem-resistant E. coli [yes/no], or quinolone-resistant E. coli [yes/no]). Antibiotic sensitivity and ESBL production were assessed using the breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). This process adhered to the guidelines recommended by the Spanish Antibiogram Committee (COESANT) and the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). A strain was considered sensitive if classified as 'susceptible' or 'susceptible, increased exposure.' The broth microdilution method was utilized to determine susceptibility [16]. The antibiotics commonly tested in the laboratory are the following: amikacin, amoxicillin-clavulanate, cefuroxime, third-generation cephalosporins, ciprofloxacin, cotrimoxazole, gentamicin and ertapenem.

### Endpoints

The primary endpoint was adherence to antimicrobial treatment guidelines for treatment of bacteraemia due to *E.coli* infections of urinary origin. Secondary endpoints included, adequacy of the empirical antimicrobial treatment, based on in vitro sensitivity results; the degree of non-compliance, defined as the percentage of empirical treatments that did not adhere to the guidelines (yes/no); the percentage of bacteraemias due to *E.coli* infection of urinary origin which were resistant to quinolones, carbapenems, and resistant by ESBLs production, over time.

### Study conduct

During the course of the study, no diagnostic tests were made, or samples taken from, any participant other than those required by routine care. The study complied with the principles of the Declaration of Helsinki, with international human rights, and with the legislation regulating biomedicine and personal data protection. All data were treated as confidential, and records were accessed anonymously. This study was approved by the Ethics Committee of Bellvitge Hospital (Ref. PR066/18). Patient data were anonymized, and so the requirement for informed consent was waived by the Ethics Committee of Bellvitge Hospital.

### Statistical analysis

Variables of interest were analysed graphically by year from 2017 to 2022. Demographic variables were analysed using descriptive statistics. Categorical variables are presented as the number and percentage in each category whereas continuous variables are presented as mean (standard deviation [SD]) values. The dataset used in the analysis was complete, and thus no missing data handling was required. P values were calculated using the Pearson test for continuous variables with normal distribution, the Spearman test for continuous variables non-normally distributed and the chi-square test based on the correlation coefficient for categorical variables. Statistical analyses were performed using the R program (version 4.2.1).

## Results

### Study population

In total, 297 patients with bacteraemia due to *E.coli* infection of urinary origin were included in the study between 2017 and 2022. The majority of the patients were female (57.9%), and the mean (SD) age was 79.0 (16.9) years (Table 1). The majority of bacteraemias due to *E.coli* infection of urinary origin were acquired in the community ($n = 194$, 65.3%) compared with healthcare system-acquired ($n = 78$, 26.3%) or hospital-acquired ($n = 25$, 8.4%) infections (Table 1); however, the number acquired in the healthcare system increased from 2017 to 2022. Bacteraemia due to *E.coli* infection of urinary origin was most commonly diagnosed in general medicine, general surgery and ICU departments, with most cases identified in general medical wards (Table 1).

**Table 1** Patient demographics, hospitalisation characteristics and antibiotic use, by year

| | 2017 *N* = 47 | 2018 *N* = 48 | 2019 *N* = 52 | 2020 *N* = 45 | 2021 *N* = 56 | 2022 *N* = 49 | Total *N* = 297 | *P*-value |
|---|---|---|---|---|---|---|---|---|
| Age, years, mean (SD) | 74.4 (16.9) | 71.2 (21.2) | 73.0 (17.9) | 73.1 (15.4) | 76.2 (14.9) | 78.3 (13.8) | 74.4 (16.9) | 0.042 |
| Female sex, n (%) | 26 (55.3) | 27 (56.2) | 29 (55.8) | 31 (68.9) | 29 (51.8) | 30 (61.2) | 172 (57.9) | 0.669 |
| **Acquisition, n (%)** | | | | | | | | |
| Community-acquired | 37 (78.7) | 34 (70.8) | 26 (50.0) | 28 (62.2) | 37 (66.1) | 32 (65.3) | 194 (65.3) | 0.257 |
| Hospital-acquired | 4 (8.5) | 4 (8.3) | 6 (11.5) | 8 (17.8) | 0 (0.0) | 3 (6.1) | 25 (8.4) | 0.289 |
| Healthcare system-acquired | 6 (12.8) | 10 (20.8) | 20 (38.5) | 9 (20.0) | 19 (33.9) | 14 (28.6) | 78 (26.3) | 0.058 |
| Hospital admission area, n (%) | | | | | | | | 0.597 |
| ICU | 2 (4.3) | 3 (6.3) | 3 (5.8) | 4 (8.9) | 1 (1.8) | 4 (8.2) | 17 (5.7) | - |
| Medical wards | 32 (68.1) | 35 (72.9) | 36 (69.2) | 29 (64.4) | 40 (71.4) | 36 (73.5) | 208 (70.0) | - |
| Surgical wards | 13 (27.7) | 10 (20.8) | 13 (25.0) | 12 (26.7) | 15 (26.8) | 9 (18.4) | 72 (24.2) | - |
| **Number of antibiotics, n (%)** | | | | | | | | 0.422 |
| 1 | 41 (87.2) | 43 (89.6) | 51 (98.1) | 45 (100.0) | 54 (96.4) | 43 (87.8) | 277 (93.3) | |
| 2 | 6 (12.8) | 5 (10.4) | 1 (1.9) | 0 (0.0) | 2 (3.6) | 6 (12.2) | 20 (6.7) | |

ICU, intensive care unit

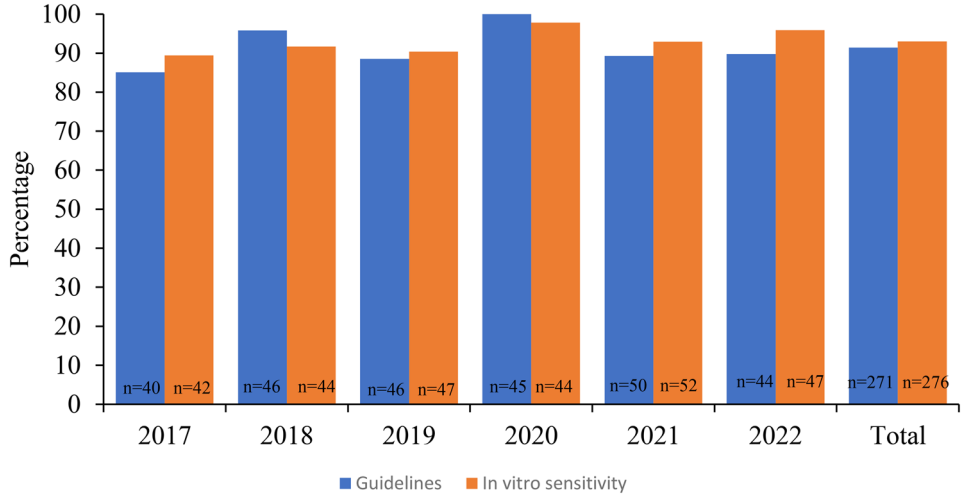


**Fig. 1** Adherence to antimicrobial treatment guidelines for the treatment of bacteraemia due to *E.coli* infections of urinary origin and appropriate use of empirical antimicrobial treatments based on in vitro sensitivity, by year

### Primary endpoint

The rates of adherence to antimicrobial treatment guidelines for the treatment of bacteraemia due to *E.coli* infections of urinary origin were high across all years studied after the implementation of the ASP (91.4%; range 83.0% to 97.8%; Fig. 1).

### Secondary endpoints

Adequacy of the empirical antimicrobial treatment, based on in vitro sensitivity results was high across all 6 years (Fig. 1). The degree of error in appropriate use of empirical antimicrobial treatments was low when guidelines were followed (Fig. 2) but was significantly higher when treatments were nonadherent to the guidelines (3.0%; range 0% to 6.5% vs. 50.0%; range 33.3% to 66.7%). With regards to antimicrobial resistance patterns, the percentage of bacteraemia due to *E.coli* infections of urinary origin which were resistant to treatment with quinolones significantly reduced over time from 44.7% in 2017 to 22.4% in 2022 ($p = 0.014$; Fig. 3). Similarly, there was a trend towards a decrease in bacteraemia due to *E.coli* infections of urinary origin which were resistant to ESBL over time from 21.3% in 2017 to 12.2% in 2022 ($p = 0.058$). No cases of *E.coli* resistance to carbapenems occurred (Table 2).

## Discussion

In this prospective epidemiology study from a single hospital in Catalonia, after the introduction of our ASP there was a high level of appropriate use of antimicrobial treatments based on both guideline adherence and in vitro sensitivity testing, with a low degree of error when the guidelines were followed. In addition, it was shown that cases of antimicrobial resistance decreased over time in our hospital, suggesting that our ASP was having a positive effect. Notably, no additional infection control

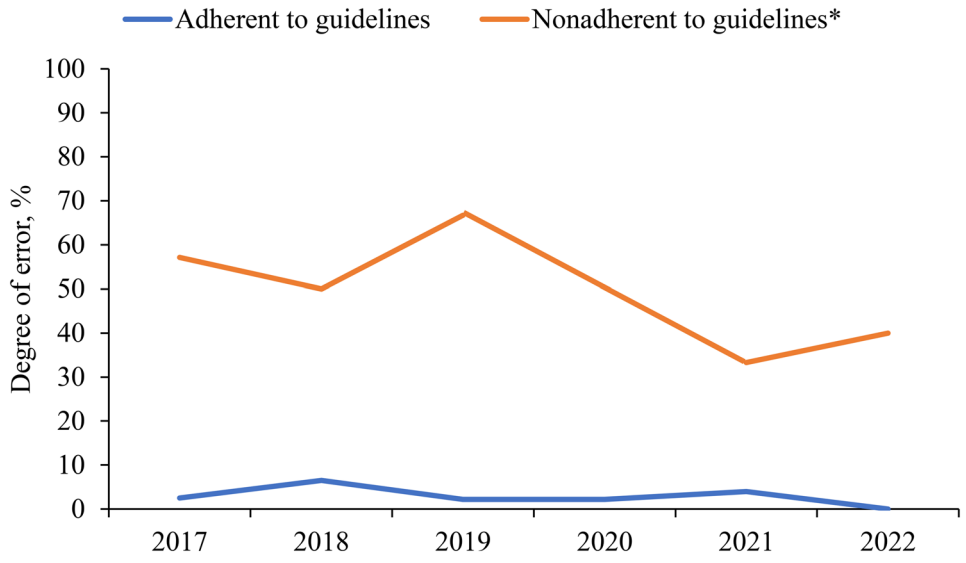


**Fig. 2** Degree of error in the appropriate use of empirical antimicrobial treatments, by guideline adherence. *All treatments in 2020 were adequate according to the guidelines and therefore no degree of error in appropriate use of empirical antimicrobial treatment was included in the graph for 2020

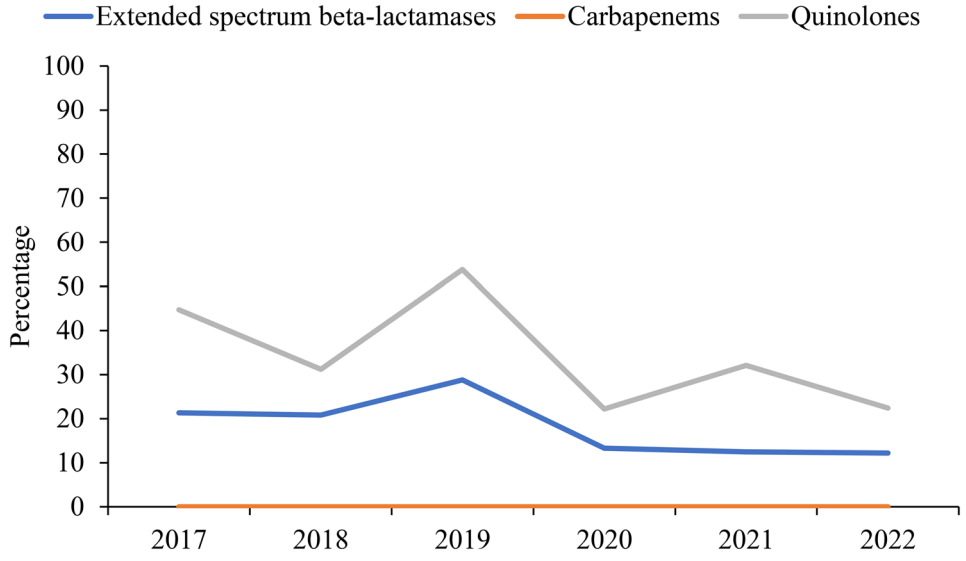


**Fig. 3** Antimicrobial resistance patterns, over time

**Table 2** *Escherichia coli* resistance by year

| | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | p.trend | N |
|---|---|---|---|---|---|---|---|---|
| | *N = 47* | *N = 48* | *N = 52* | *N = 45* | *N = 56* | *N = 49* | | |
| BLEE, N (%) | 10 (21.3%) | 10 (20.8%) | 15 (28.8%) | 6 (13.3%) | 7 (12.5%) | 6 (12.2%) | 0.058 | 297 |
| Carbapenems, N (%) | 1 (2.13%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0.134 | 297 |
| Quinolones, N (%) | 21 (44.7%) | 15 (31.2%) | 28 (53.8%) | 10 (22.2%) | 18 (32.1%) | 11 (22.4%) | 0.014 | 297 |

measures were implemented during the study period, and there were no changes in the antibiotic prescribing guidelines during this time.

Several pre- and post-intervention studies have compared antimicrobial prescribing patterns before and after the introduction of ASPs [17–22]. Although the methodologies used for the ASPs differed between studies, they all reported positive effects from the introduction of the ASPs, including reductions in antimicrobial consumption due to elimination of inappropriate prescribing practices and shortening of hospital stays [17–22]. Several studies reported that the implementation of ASPs reduced both overall use and duration of antimicrobial treatment, including carbapenems, without affecting overall

safety [18–21]. A pre- and post-ASP intervention study based in a urology department of a single hospital in Barcelona reported a 9% decrease in defined daily doses (DDD)/1000 patient days for carbapenem use during the intervention period. Similarly, a single-centre, pre- and post-intervention study reported a reduction in the utilization of broad-spectrum antimicrobials with no significant differences in clinical outcomes [20]. Thirdly, a single-centre, pre- and post-intervention study of gram-negative bacteraemia treatment reported shorter duration of treatment, earlier switch to oral treatment and lower 30-day readmission rates [18]. Fourthly, a single-centre, pre- and post-intervention study to assess the effect of implementing an infectious disease specialist-led ASP showed a significant decrease from the pre- to the post-intervention periods for overall high-end antibiotic density with no significant differences in the incidence rates of clinical outcomes [19]. Finally, a single-centre study which assessed the long-term effect of bedside interventions by an antibiotic stewardship team reported that the duration of third- and fourth-generation pseudomonal cephalosporin and carbapenem use significantly decreased in the post-intervention period ($p < 0.01$) [22]. In addition, in-hospital mortality was significantly lower in the post-intervention group and 30-day mortality and in-hospital mortality in patients with resistant gram-negative bacteraemia were significantly lower in the post-intervention group [22].

Although we did not investigate costs associated with antimicrobial use in our study, two single-centre, pre- and post-intervention studies reported cost-savings through the implementation of ASPs, without compromising clinical outcomes [18, 19].

Enterobacteriaceae resistance to multiple classes of antimicrobials is increasing worldwide and continued efforts are needed to prevent their spread [23–26]. Hospitals, and particularly ICUs, are important settings for the development and spread of antibiotic resistant bacteria, mainly due to patients being exposed to heavy antibiotic use, a high density patient population, and frequent contact with healthcare staff and the risk of cross infection [27]. Data from Spanish hospitals which are part of the Study for Monitoring Antimicrobial Resistance Trends (SMART) showed that there was a slight increase in ESBL-producing *E.coli* isolates from 2011 to 2017 [28, 29]. In contrast to this, the data for antimicrobial resistance patterns from our hospital showed that there was a reduction in the percentage of bacteraemia due to E.coli infections of urinary origin that were resistant to quinolones and to ESBL from 2017 to 2022, despite an increased risk in healthcare system-acquired infections. In the case of quinolones, this decrease in resistance coincided with a decrease in their use. However, we believe that Antimicrobial Stewardship Programs (ASPs) can reduce resistance overall, if their use aligns with clinical guidelines. This downward trend in antimicrobial resistance has also been shown in other studies after the implementation of ASPs [23, 30]. Together these studies provide support to show that the implementation of ASPs can curb the development of antimicrobial resistance.

The results from all hospitals included in the VINCAT ASP have been published [30]. Although many hospitals in the Catalonia region of Spain were following the same protocol, the results from our hospital were generally better than those for the region as a whole, suggesting that our ASP model may be more robust [31]. In our hospital the rates of adherence to antimicrobial treatment guidelines were high across all years (91.4%; range: 85.1% to 100.0%), whereas the overall adherence rate for the region was 79.5% during the period from 2017 to 2021, meaning that adherence at our hospital was higher than that of the whole region. A similar trend was seen for appropriateness in view of the in vitro sensitivity in our hospital (93.0%; range: 89.4% to 97.8%), which was also higher than the total appropriateness in view of in vitro sensitivity for Catalonia (88.1%). The degree of error when guidelines were followed was low from 2017 to 2022 in our hospital (3.0%; range: 0% to 6.5%). The degree or error for Catalonia region was 5.9% from 2017 to 2021.

There are some differences in patient populations between our hospital and the data for the Catalonia region as a whole. Firstly, our data was collected from 2017 to 2022, whereas the data for the Catalonia region was collected from 2017 to 2021. In our hospital, patients had a higher mean age (79.0 years vs. 72.7 years), a higher percentage of community-acquired infections (65.3% vs. 59.3%) and a lower percentage of healthcare system-acquired (26.3% vs. 29.9%) and hospital-acquired (8.4% vs. 10.2%) infections vs. the region as a whole [31]. Despite these differences, the principal reason for better results in our hospital may be the robustness of our ASP. This robustness is due to the daily revisions made to all in-hospital antibiotic treatments, with feedback about the adequacy or inadequacy of antibiotic treatment provided to the prescribers either by phone or written notes. Specifically, we provide physicians with daily emails regarding the centres' antimicrobial therapies, including possible errors of non-adherence of the guide. Judging by the comparison with other centers in our region, the hospital ASP appears to be influencing community resistance and not just hospital resistance. This could be due to the influence our hospital has on its catchment area and the local primary care physicians, as well as the volume of community patients our hospital actually manages, given that the program also includes the Emergency Department.

Furthermore, the COVID-19 pandemic occurred during the study period, and it could be hypothesized that

it influenced the observed variations in antimicrobial resistance. However, since our hospital showed a more favourable trend in resistance evolution compared with other hospitals in the surrounding area, it is unlikely that the observed findings can be explained by the impact of the pandemic.

A strength of this study is the 6-year follow period which allowed sufficient time for trends in outcomes to be observed; however, the results presented herein are from a single hospital, which may limit the generalizability of the results. Another limitation was that the clinical evolution of patients was not followed up in order to determine mortality rates associated with bacteraemia from *E.coli* infection of urinary sources.

## Conclusions

This prospective study from a single hospital in Catalonia (Spain) reports a high level of appropriate antimicrobial use, based on both guideline recommendations and in vitro sensitivity testing. The results suggest that our ASP has been applied successfully over the last 6 years and has resulted in improvements in the empirical antimicrobial treatment of bacteraemia from *E.coli* infection of urinary sources, and a reduction in the number of cases of antimicrobial resistant *E.coli*.

### Abbreviations

| | |
|---|---|
| ASP | Antibiotic stewardship programs |
| CI | Confidence interval |
| DDD | Defined daily doses |
| *E.coli* | *Escherichia coli* |
| ESBL | Extended-spectrum beta-lactamase |
| ICU | Intensive care unit |
| IR | Incidence rate |
| SD | Standard deviation |
| UTI | Urinary tract infection |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-11987-z.

Supplementary Material 1

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### Author contributions

DB-A designed the study, contributed to data analysis and interpretation, reviewed and approved the final version. CP-L cured the data, JC did the statistical analysis and reviewed and approved the final version of the manuscript. AFS, CC, SS, EJ, EM-R, JG-P contributed to the field work and reviewed and approved the final version of the manuscript.

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### Data availability

The dataset used in the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of Bellvitge Hospital (Ref. PR066/18). Patient data were anonymized, and so the requirement for informed consent was waived by the Ethics Committee of Bellvitge Hospital.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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