



Successful implementation of a bundle to prevent increased excessive-spectrum antimicrobial use under new EUCAST susceptibility definitions: a quasi-experimental study in a tertiary hospital

P. Duch-Llorach^{a,b,c}, A.F. Simonetti^{a,b}, A. Figueras-Roig^a, A. Rivera^{b,d,e}, E. Fernández de Gamarra-Martínez^{b,f,g}, L. Gras-Martin^{b,c,f}, M-E. Moreno-Martínez^{b,f,g}, J. Ruiz Ramos^{b,f}, B. Zarate-Tamames^{b,c,f}, F. Navarro^{b,d,e}, J. López-Contreras^{a,b,c,†}, L. Escolà-Vergé^{a,b,c,h,*,†}

^a Infectious Diseases Division, Internal Medicine Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

^b Institut de Recerca Sant Pau (IR SANT PAU), Barcelona, Spain

^c Medicine Department, Universitat Autònoma de Barcelona, Barcelona, Spain

^d Microbiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

^e Genetics and Microbiology Department, Universitat Autònoma de Barcelona, Barcelona, Spain

^f Pharmacy Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

^g School of Health Sciences Blanquerna, University Ramon Lull, Barcelona, Spain

^h CIBERINFEC, Instituto de Salud Carlos III, Madrid, Spain

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SUMMARY

Background: This study evaluated the effectiveness of an implementation-bundle to prevent increased targeted excessive-spectrum antibiotics for wild-type *Pseudomonas aeruginosa* (PA) infections, following the introduction of 2019 EUCAST susceptibility categories redefinition.

Methods: This was a single-centre, quasi-experimental study at a tertiary University Hospital. All consecutive adult patients with wild-type PA infections between July 2023 and April 2024 were included and analysed across three-month periods: before the EUCAST update (Period 1), after the update with audit-feedback (Period 2), and after the update without audit-feedback (Period 3). The implementation-bundle included: (1) in-person educational sessions before the introduction of the redefinition; and (2) in antimicrobial susceptibility reports, replacing 'I' with 'SE', with a clarifying footnote and dosing information. An audit-feedback intervention was conducted during the first three months after the introduction of the redefinition. Selective reporting of antimicrobial susceptibility testing results was already in place in our hospital. Primary outcomes included targeted meropenem, and ceftolozane/tazobactam prescriptions; secondary outcomes were optimal anti-pseudomonal dosing and infectious diseases (IDs) consultations.

* Corresponding author. Address: C/ Sant Quintí, 89, Block A, 5th Floor, Module 2, 08025 Barcelona, Spain. Tel.: +34 93 556 56 24; fax: +34 93 553 71 40. E-mail address: Laura.Escola@uab.cat (L. Escolà-Vergé).

† These authors contributed equally to this work.

Findings: Among 158 patients (55 Period 1, 60 Period 2, 43 Period 3), targeted meropenem prescriptions did not increase (7.3% vs 6.7% ($P=0.898$) vs 0% ($P=0.071$)). No patients received targeted ceftolozane/tazobactam. ID consultations decreased (56.4% vs 38.3% ($P=0.053$) vs 34.9% ($P=0.034$)) and correct anti-pseudomonal dosing improved (70.9% vs 93.3% ($P=0.002$) vs 95.3% ($P=0.002$)). Risk factors for targeted meropenem prescriptions included age <65 years, immunosuppression, septic shock, intensive care unit admission, and empirical excessive-spectrum antimicrobial use.

Conclusion: This implementation-bundle enabled the introduction of EUCAST susceptibility categories redefinition without increasing targeted excessive-spectrum antibiotics or ID consultations, while optimizing dosing.

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Introduction

In January 2019, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) changed the definitions of the susceptibility categories 'S' and 'I'. The category 'S' now stands for 'Susceptible, standard dosing regimen', while 'I' has been redefined as 'Susceptible, increased exposure', aiming to improve the interpretation of antimicrobial susceptibility by taking dosage and exposure levels into account [1,2]. These changes aimed to optimize treatment by encouraging higher dosages for less susceptible bacteria. However, potential misinterpretations have led to concerns, particularly with *Pseudomonas aeruginosa* (PA) infections, where formerly 'S' strains for most antipseudomonal agents were reclassified as 'I', while remaining 'S' only for meropenem and ceftolozane/tazobactam [3–5].

Following the EUCAST update, an observed increase in meropenem and ceftolozane/tazobactam prescriptions for wild-type PA has been reported in some centres, accompanied by heightened infectious diseases (IDs) consultations [6–8]. After receiving susceptibility test results, over-prescription primarily involved initiating (42.5%) or switching to (30%) meropenem, with a smaller proportion continuing empiric therapy (27.5%) [6]. Studies also revealed limited physician awareness of the revised definitions [9]. However, there has been a positive shift towards appropriately targeted higher dosages of anti-pseudomonal antibiotics [6–8].

To address these challenges, different strategies have been proposed to guide antibiotic choices more effectively. Studies suggest that implementing selective reporting can mitigate inappropriate broad-spectrum antibiotic use [7,10–14]. Other recommendations include replacing the 'I' category with a clearer term such as 'S*', 'S+', 'SDD' or 'SE' and providing detailed footnotes in susceptibility reports to enhance understanding among clinicians [3–6]. Targeted education for healthcare professionals about the new EUCAST criteria is also crucial for successful implementation [9,15].

In response to these issues, our hospital introduced the revised EUCAST definitions in October 2023, accompanied by an implementation-bundle.

This study aimed to evaluate the effectiveness of this implementation-bundle in preventing overuse of targeted excessive-spectrum anti-pseudomonal therapy (meropenem and ceftolozane/tazobactam), avoiding increased ID consultations, and promoting optimal doses of anti-pseudomonal antibiotics for PA wild-type phenotype for β -lactams infections.

Methods

Study design, size, setting, and participants

Single-centre, quasi-experimental, and multi-disciplinary study conducted at University Hospital de la Santa Creu i Sant Pau, a tertiary-care hospital in Barcelona, Spain, with a capacity of 624 beds.

The updated EUCAST antimicrobial susceptibility definitions were introduced on 16th October 2023, along with the antimicrobial susceptibility report changes proposed in the implementation-bundle. The implementation of the updated EUCAST definitions was postponed until late 2023 due to disruptions during the COVID-19 pandemic, technical challenges in updating information technology (IT) systems, and the need to refine our strategy to prevent increased excessive-spectrum antimicrobial use observed in other centres [6,8]. The study was structured into three periods. Period 1 encompassed the three months (15th July 2023 to 15th October 2023) before introducing the EUCAST definitions update in the antimicrobial susceptibility reports. Period 2 covered the initial three months (16th October 2023 to 15th January 2024) following the definitions update, during which a prospective audit and feedback intervention was conducted to evaluate the effectiveness of the bundle and correct deviations. This involved reviewing treatments twice weekly, at least 24 h after antimicrobial susceptibility testing results were available, and providing feedback to prescribers in cases of inappropriate treatment. Period 3 comprised the subsequent three months (16th January 2024 to 15th April 2024) without the audit and feedback intervention.

All consecutive adult patients with positive clinical samples for PA with wild-type phenotype for β -lactams (susceptible to ceftazidime, cefepime, piperacillin-tazobactam, and meropenem) between 15 July 2023 and 15 April 2024 were identified through the Microbiology Information System and included. Exclusion criteria were not hospitalized patients, PA isolation considered colonization and therefore not treated, documented beta-lactam allergy, or co-infection with extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales requiring carbapenem therapy.

Implementation-bundle

The implementation-bundle included: (1) in-person training sessions conducted before the introduction of the new

definitions, between June and September 2023, by the Antimicrobial Stewardship Multi-disciplinary Team across all major departments; (2) antimicrobial susceptibility reports adopting the acronym 'SE' instead of 'I', with a clarifying footnote 'SE = susceptible, increased exposure'; and (3) a hyperlink to the EUCAST dosing table [16] at the bottom of the antimicrobial susceptibility reports.

Before the bundle, selective reporting of the antimicrobial susceptibility testing results had already been used in our hospital for many years.

Data collection and variables

Data extracted from electronic medical records included demographics, comorbidities, microbiological data, antibiotic treatments, ID consultations, infection characteristics, microbiological recurrence, relapse of the PA infection, 30-day related readmission, 30-day mortality rates, and complications related to antibiotic use such as *Clostridioides difficile* infection and *Enterococcus faecium* bacteraemia.

During Period 2, interventions were recorded. Data was recorded prospectively for Period 2 and retrospectively for Periods 1 and 3.

Definitions

Empirical treatment was defined as the initial choice of antibiotics made before receiving microbiological data results.

Targeted treatment was defined as the antibiotic given to the patient >24 h after the antibiotic susceptibility results were available, but before the prospective audit and feedback intervention of the Period 2.

Post-audit targeted treatment was defined as the antibiotic administered 24 h after the feedback intervention, when necessary, during Period 2.

The correct antipseudomonal dose was determined based on the EUCAST recommendations [16].

Excessive-spectrum antimicrobial therapy was defined as treatment with carbapenem or ceftolozane/tazobactam for PA infections that are susceptible to ceftazidime, cefepime, and piperacillin-tazobactam.

Septic shock was defined by the requirement for vasopressors to maintain a mean arterial pressure of ≥ 65 mm Hg, unresponsive to fluid resuscitation [17].

Nosocomial, healthcare-associated and community-acquired infections were defined according to Friedman criteria [18].

History of colonization or infection for ESBL-producing Enterobacterales was defined as a positive sample for ESBL-producing Enterobacterales within the six months preceding the current infection episode.

Moderate to severe chronic kidney disease (CKD) was defined as either ongoing dialysis or consistently elevated creatinine levels above 3 mg/dL [19].

ID consultations were identified through written evidence in the patient's electronic medical chart; only those related to the index infection were included.

Microbiological recurrence was defined as a new positive microbiological sample for PA from the same site within 30 days after ceasing antibiotics. Infection relapse involved this positive sample along with clinical symptoms indicating infection,

and 30-day related readmission was defined as hospital readmission due to the infection relapse.

Outcomes

The primary outcome was the proportion of patients receiving excessive-spectrum anti-pseudomonal antimicrobial therapy as a targeted treatment.

Secondary outcomes included the proportion of patients receiving correct antipseudomonal dose as targeted treatment, consultation rates to ID, 30-day all-cause mortality, bacteraemia caused by *E. faecium*, infection due to *C. difficile*, microbiological recurrence, infection relapse, and 30-day related readmission.

Statistical methods

The analysis was performed using the Statistical Package for Social Sciences (SPSS), version 29. Data were summarized using descriptive statistics. Medians and interquartile ranges (IQRs) were used to present continuous variables, while percentages were employed for categorical variables. Chi-squared tests were used to compare dichotomous variables across different periods, and Kruskal–Wallis tests were utilized for continuous variables. Univariate analysis was conducted to identify risk factors related to excessive-spectrum antimicrobial therapy. Statistical significance was determined by a *P*-value of less than 0.05 (two-tailed).

Results

Cohort description

During the study periods, 158 hospitalized adult patients with infections due to PA wild-type phenotype for β -lactams were included: 55 in Period 1, 60 in Period 2, and 43 in Period 3 (flowchart of included patients in Figure 1).

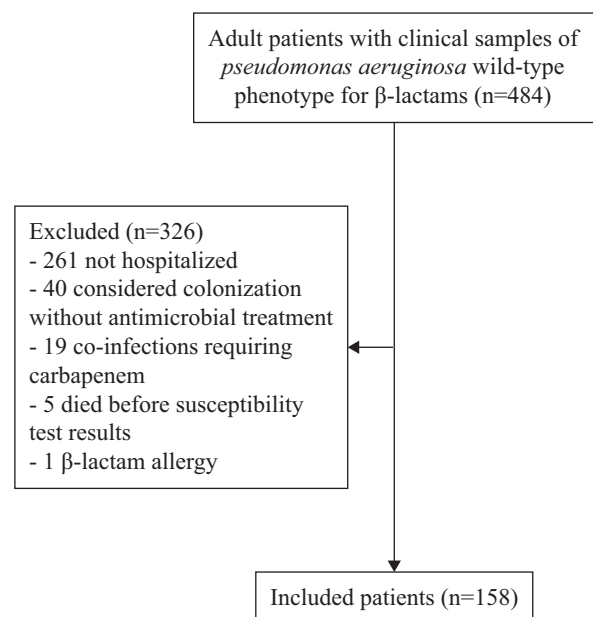


Figure 1. Flowchart of included patients.

Table 1
Demographic and clinical characteristics of patients

Variables	Overall (N = 158)	Period 1: Before EUCAST update (N = 55)	Period 2: After EUCAST update, with prospective audit-feedback (N = 60)	Period 3: After EUCAST update, without prospective audit-feedback (N = 43)	P
Patient characteristics					
Male sex	99 (62.7)	34 (61.8)	41 (68.3)	24 (55.8)	0.427
Age >65 years	118 (74.7)	40 (72.7)	41 (68.3)	37 (86)	0.115
Median (IQR)	72.9 (17.8)	70.1 (15.9)	71.7 (18.1)	79.2 (16.8)	0.008
Charlson comorbidity score >3	51 (32.3)	20 (36.4)	19 (31.7)	12 (27.9)	0.668
Median (IQR)	3 (2)	3 (3)	3 (2)	3 (2)	0.897
COPD	58 (36.7)	14 (25.5)	23 (38.3)	21 (48.8)	0.055
Congestive heart failure	48 (30.4)	19 (34.5)	15 (25)	14 (32.6)	0.504
Solid tumour diagnosed within the past 5 years	45 (28.5)	20 (36.4)	15 (25)	10 (23.3)	0.271
Peripheral vascular disease	28 (17.7)	9 (16.4)	7 (11.7)	12 (27.9)	0.098
History of a cerebrovascular accident	22 (13.9)	10 (18.2)	5 (8.3)	7 (16.3)	0.273
Haematologic tumour diagnosed within the past 5 years	19 (12)	5 (9.1)	13 (21.7)	1 (2.3)	0.008
Dementia	17 (10.8)	7 (12.7)	6 (10)	4 (9.3)	0.838
Moderate to severe CKD	10 (6.3)	2 (3.6)	3 (5)	5 (11.6)	0.236
History of ESBL-producing Enterobacterales infection or colonization within the previous 6 months	9 (5.7)	3 (5.5)	4 (6.7)	2 (4.7)	0.905
Immunosuppression	39 (24.7)	13 (23.6)	17 (28.3)	9 (20.9)	0.674
Immunosuppressive treatment	14 (8.9)	7 (12.7)	6 (10)	1 (2.3)	0.184
Neutropenia	7 (4.4)	2 (3.6)	5 (8.3)	0	0.120
Haematopoietic stem cell transplant	7 (4.4)	2 (3.6)	5 (8.3)	0	0.120
Solid organ transplant	3 (1.9)	2 (3.6)	1 (1.7)	0	0.419
Infection characteristics					
Site of infection					
Low respiratory tract	66 (41.8)	19 (34.5)	29 (48.3)	18 (41.9)	0.326
Genitourinary tract	29 (18.4)	7 (12.7)	10 (16.7)	12 (27.9)	0.143
Skin and soft tissue	26 (16.5)	9 (16.4)	9 (15)	8 (18.6)	0.888
Bone/joints	14 (8.9)	7 (12.7)	3 (5)	4 (9.3)	0.344
Gastrointestinal tract	13 (8.2)	7 (12.7)	5 (8.3)	1 (2.3)	0.177
Catheter-related bacteraemia	7 (4.4)	5 (9.1)	2 (3.3)	0	0.083
Primary bacteraemia	1 (0.6)	0	1 (1.7)	0	0.440
Vascular graft infection	1 (0.6)	1 (1.8)	0	0	0.390
Malignant external otitis	1 (0.6)	0	1 (1.7)	0	0.440
Bacteraemia due to <i>Pseudomonas aeruginosa</i>	25 (15.8)	13 (23.6)	9 (15)	3 (7)	0.079
Gram-negative rod co-infection	32 (20.3)	14 (25.5)	9 (15)	9 (20.9)	0.376
Septic shock	12 (7.6)	6 (10.9)	5 (8.3)	1 (2.3)	0.271
Infection acquisition					
Healthcare-associated	64 (40.5)	18 (32.7)	27 (45)	19 (44.2)	0.346
Nosocomial	55 (34.8)	22 (40)	18 (30)	15 (34.9)	0.531
Community acquired	39 (24.7)	15 (27.3)	15 (25)	9 (20.9)	0.768
Patient location					
Medical ward	91 (57.6)	31 (56.4)	29 (48.3)	31 (72.1)	0.054
Surgical ward	49 (31)	19 (34.5)	21 (35)	9 (20.9)	0.245
Intensive care	18 (11.4)	5 (9.1)	10 (16.7)	3 (7)	0.250

All data presented as N (%), unless stated otherwise. CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESBL, extended-spectrum beta lactamase; EUCAST, European Committee on Antimicrobial Susceptibility Testing; IQR, interquartile range.

Table 1 summarizes patients' demographics and clinical characteristics across all three periods. While most characteristics were similar, significant differences were observed in the median age (70.1 (IQR 15.9) vs 71.7 (IQR 18.1) vs 79.2 (IQR

16.8), $P=0.008$), and the prevalence of haematologic tumours (9.1% (5/55) vs 21.7% (13/60) vs 2.3% (1/43), $P=0.008$). There was a non-significant variation in chronic obstructive pulmonary disease (COPD) percentages (25.5% (14/55) vs 38.3%

(23/60) vs 48.8% (21/43), $P=0.055$). PA bacteraemia and septic shock were more frequent in Period 1 compared with Periods 2 and 3, but these differences were not statistically significant ($P=0.079$ and $P=0.271$, respectively).

Primary outcome

Antibiotic treatments and patient outcomes are summarized in Table II. No increase in the proportion of targeted excessive-spectrum antimicrobial therapy was observed: 7.3% (4/55) in Period 1, 6.7% (4/60) in Period 2 ($P=0.898$ compared with Period 1), and 0% in Period 3 ($P=0.071$ compared with Period 1). In the study, all excessive-spectrum antimicrobial prescriptions were meropenem.

Among the 31 patients who received empirical meropenem, eight (25.8%) received targeted excessive-spectrum therapy compared with none (0%) of the 127 patients who did not receive empirical meropenem. This difference was statistically significant ($P<0.001$).

Risk factors for receiving targeted meropenem included age <65 years ($P=0.001$), immunosuppression ($P=0.011$), septic shock ($P=0.001$), intensive care unit (ICU) admission ($P<0.001$), and empirical excessive-spectrum antimicrobial therapy ($P<0.001$) (Table III).

In Period 2, the proportion of targeted excessive-spectrum treatments reduced from 6.7% (4/60) to 5% (3/60) after the audit and feedback intervention ($P=0.697$).

Secondary outcomes

There was no increase in ID consultations following antimicrobial susceptibility reports for PA infections across the study periods: 56.4% (31/55) in Period 1, 38.3% (23/60) in Period 2 ($P=0.053$ compared with Period 1), and 34.9% (15/43) in Period 3 ($P=0.034$ compared with Period 1).

There was a significant increase in correct anti-pseudomonal dosing of targeted treatment: from 70.9% (39/55) in Period 1–93.3% (56/60) in Period 2 ($P=0.002$ compared with Period 1), and 95.3% (41/43) in Period 3 ($P=0.002$ compared with Period 1). In Period 2, the proportion of correct anti-pseudomonal dosing increased from 93.3% (56/60) to 98.3% (58/59) following the audit and feedback intervention ($P=0.177$).

The 30-day all-cause mortality rate decreased from 18.2% (10/55) in Period 1–13.3% (8/60) in Period 2 ($P=0.475$ compared with Period 1), and 4.7% (2/43) in Period 3 ($P=0.043$ compared with Period 1).

The remaining secondary outcomes showed no statistically significant differences when comparing Periods 1, 2, and 3 (Table II).

Discussion

We implemented the revised EUCAST definitions, accompanied by in-person training sessions, the introduction of the acronym 'SE' instead of 'I', along with a clarifying footnote, and a hyperlink to the EUCAST dosing table [16] in the antimicrobial susceptibility reports. Additionally, a prospective audit and feedback intervention was conducted during the first three months following the introduction of the new nomenclature. These interventions were implemented upon an

existing framework of selective reporting in antimicrobial susceptibility testing results. In our cohort with the proposed measures, no increase in the use of antipseudomonal excessive-spectrum agents was observed, while significantly improving dosing accuracy, in managing PA infections, and without an increase of ID consultations.

In contrast to our results, other centres that directly adopted the new definitions reported higher consumption [6–8]. To mitigate the increase in targeted excessive-spectrum antibiotic consumption (which rose to 25.3% following the nomenclature change), a Swiss hospital implemented selective reporting in antimicrobial susceptibility testing, which successfully reduced the increase following the introduction of the new definitions (down to 8.4%). However, despite this reduction, excessive-spectrum antimicrobial use remained higher than levels observed before the introduction of the new definitions (previously 3.4%) [7]. These findings are consistent with other studies showing that selective reporting can mitigate inappropriate excessive-spectrum antibiotic use [7,10–13], but may not be enough.

In our cohort, we observed a non-significant reduction in targeted excessive-spectrum antimicrobial therapy use, contrasting with the previous study where selective reporting reduced usage but remained above pre-nomenclature change levels. These findings suggest that our multi-modal approach achieved more substantial improvements [7].

In previous studies, the rise in excessive-spectrum antibiotic use was primarily attributed to initiating excessive-spectrum therapy based on misinterpreting susceptibility test results [6,7]. In contrast, our cohort showed that all cases of excessive-spectrum therapy resulted from continuation of empirical treatment. This suggests that our implementation-bundle reduced misinterpretation, although there is still room for improvement. Further reductions in the continuation of excessive-spectrum empirical treatment could likely be achieved with the support of the antimicrobial stewardship team.

Our study observed a decrease in ID consultation rates following the implementation of the new definitions, in contrast to the increases reported in previous studies [6,7]. In our opinion, this shows that our implementation-bundle enhanced prescriber confidence and understanding of the revised susceptibility criteria, thereby reducing the need for specialist input [9,15].

Previous studies showed an improvement in correct dosing following the change in nomenclature [6,7], consistent with our findings. This highlights the importance of adopting these new definitions to enhance dosing accuracy.

The sustained positive outcomes, also in the absence of feedback-based audits, highlight the effectiveness of our approach with the initial educational and systemic interventions. However, maintaining these long-term results will likely require continuous information campaigns by the antimicrobial stewardship teams.

Our analysis identified several risk factors for targeted excessive-spectrum therapy, including age <65 years, septic shock, ICU admission, and empirical use of excessive-spectrum antibiotic. The presence of septic shock is a recognized factor in previous studies [6,7]. Probably one of the most prevalent instances requiring intervention to curtail targeted excessive-spectrum antimicrobial therapy use is among critically ill patients, such as those with septic shock or admitted to ICU.

Table II
Antibiotic treatment and patient outcomes

Variables	Overall (N = 158)	Period 1: Before EUCAST update (N = 55)	Period 2: After EUCAST update, with prospective audit-feedback (N = 60)	Period 3: After EUCAST update, without prospective audit-feedback (N = 43)	P (Period 2 vs 1)	P (Period 3 vs 1)
Treatment						
Empiric treatment						
Piperacillin/tazobactam	44 (27.8)	18 (32.7)	19 (31.7)	7 (16.3)	0.903	0.064
Non-antipseudomonal antibiotic	40 (25.3)	11 (20)	12 (20)	17 (39.5)	1.000	0.034
Meropenem	31 (19.6)	14 (25.5)	14 (23.3)	3 (7)	0.791	0.017
Cefepime	10 (6.3)	4 (7.3)	6 (10)	0	0.604	0.071
No antibiotic	10 (6.3)	1 (1.8)	3 (5)	6 (14)	0.352	0.021
Ciprofloxacin	8 (5.1)	3 (5.5)	1 (1.7)	4 (9.3)	0.268	0.463
Levofloxacin	5 (3.2)	2 (3.6)	1 (1.7)	2 (4.7)	0.508	0.801
Ceftazidime	5 (3.2)	1 (1.8)	2 (3.3)	2 (4.7)	0.611	0.419
Ceftolozane/tazobactam	3 (1.9)	0	2 (3.3)	1 (2.3)	0.172	0.256
Imipenem	2 (1.3)	1 (1.8)	0	1 (2.3)	0.294	0.860
Targeted treatment (prior to the prospective audit-feedback intervention, if necessary, in period 2)						
Piperacillin/tazobactam	54 (34.2)	13 (23.6)	26 (43.3)	15 (34.9)	0.026	0.221
Ceftazidime	40 (25.3)	17 (30.9)	13 (21.7)	10 (23.3)	0.260	0.400
Ciprofloxacin	39 (24.7)	15 (27.3)	9 (15)	15 (34.9)	0.106	0.417
Cefepime	13 (8.2)	3 (5.5)	7 (11.7)	3 (7)	0.238	0.755
Meropenem	8 (5.1)	4 (7.3)	4 (6.7)	0	0.898	0.071
Levofloxacin	2 (1.3)	2 (3.6)	0	0	0.136	0.206
Non-antipseudomonal antibiotic	2 (1.3)	1 (1.8)	1 (1.7)	0	0.950	0.374
Ceftolozane/tazobactam	0	0	0	0	—	—
Correct anti pseudomonal dose of the targeted treatment	136 (86.1)	39 (70.9)	56 (93.3)	41 (95.3)	0.002	0.002
Actions taken after receiving the antimicrobial susceptibility report (prior to the prospective audit-feedback intervention in period 2)						
Switch of antibiotic therapy	92 (58.2)	35 (63.6)	31 (51.7)	26 (60.5)	0.195	0.748
Empiric therapy continued	56 (35.4)	19 (34.5)	26 (43.3)	11 (25.6)	0.335	0.339
Initiation of antibiotic therapy without prior empiric treatment	10 (6.3)	1 (1.8)	3 (5)	6 (14)	0.352	0.021
ID recommendation following prospective audit-feedback						
No recommendation needed			53 (88.3)			
Recommendation			7 (11.7)			
Antibiotic change			3 (5)			
Dose adjustment			2 (3.3)			
Initiation of therapy			1 (1.7)			
Cessation of therapy			1 (1.7) ^a			
Correct anti pseudomonal dose of the post-audit targeted treatment			58/59 (98.3)			
ID consultations	69 (43.7)	31 (56.4)	23 (38.3)	15 (34.9)	0.053	0.034
Outcomes						
30-day all-cause mortality	20 (12.7)	10 (18.2)	8 (13.3)	2 (4.7)	0.475	0.043
Median days of hospital stay after sample collection (IQR)	12 (12)	13 (14)	11 (8)	10 (10)	0.428	0.181
Bacteraemia due to <i>Enterococcus faecium</i>	2 (1.3)	2 (3.6)	0	0	0.136	0.206
Infection due to <i>Clostridioides difficile</i>	0	0	0	0	—	—
Microbiological recurrence of <i>Pseudomonas aeruginosa</i> at 30 days of discontinuation of antibiotic	19 (12)	7 (12.7)	7 (11.7)	5 (11.6)	0.862	0.869
Infection relapse (microbiological recurrence along with clinical symptoms indicating infection)	13 (8.2) ^b	5 (9.1)	7 (11.7)	1 (2.3)	0.652	0.166
30-day related readmission	8 (5.1)	4 (7.3)	3 (5)	1 (2.3)	0.611	0.269

All data presented as N (%), unless stated otherwise.

EUCAST, European Committee on Antimicrobial Susceptibility Testing; ID, infectious diseases; IQR, interquartile range.

^a The isolation of *P. aeruginosa* was considered significant, but the audit recommended cessation of antimicrobial therapy as the treatment duration was sufficient.

^b Most infection relapses (76.9%, 10/13) occurred in patients with low respiratory tract infections.

Table III

Risk factors associated with targeted meropenem

	No targeted meropenem (N = 150)	Targeted meropenem (N = 8)	Univariate OR (95% CI)	P
Patient characteristics				
Male sex	95 (63.3)	4 (50)	0.579 (0.139–2.408)	0.447
Age >65 years	116 (77.3)	2 (25)	0.098 (0.019–0.506)	<0.001
Charlson comorbidity score >3	50 (33.3)	1 (12.5)	0.286 (0.034–2.387)	0.219
COPD	56 (37.3)	2 (25)	0.560 (0.109–2.868)	0.481
Congestive heart failure	46 (30.7)	2 (25)	0.754 (0.147–3.875)	0.734
Solid tumour	44 (29.3)	1 (12.5)	0.344 (0.041–2.880)	0.304
Peripheral Vascular Disease	28 (18.7)	0	0.25 (0.01–4.51)	0.178
History of a cerebrovascular accident	21 (14)	1 (12.5)	0.878 (0.103–7.499)	0.905
Haematologic tumour	17 (11.3)	2 (25)	2.608 (0.487–13.965)	0.247
Dementia	17 (11.3)	0	0.45 (0.02–8.12)	0.313
Moderate to severe CKD	10 (6.7)	0	0.79 (0.04–14.6)	0.451
History of ESBL-producing Enterobacterales	9 (6)	0	0.88 (0.05–16.36)	0.476
Immunosuppression	34 (22.7)	5 (62.5)	5.686 (1.292–25.017)	0.011
Infection characteristics				
Site of infection				
Low respiratory tract	62 (41.3)	4 (50)	1.419 (0.342–5.893)	0.628
Genitourinary tract	28 (18.7)	1 (12.5)	0.622 (0.074–5.265)	0.661
Skin and soft tissue	25 (16.7)	1 (12.5)	0.714 (0.084–6.064)	0.757
Bone/joints	14 (9.3)	0	0.55 (0.03–10.1)	0.365
Digestive	12 (8)	1 (12.5)	1.643 (0.186–14.486)	0.652
Catheter-related bacteraemia	6 (4)	1 (12.5)	3.429 (0.362–32.491)	0.255
Bacteraemia due to <i>Pseudomonas aeruginosa</i>	22 (14.7)	3 (37.5)	3.491 (0.778–15.663)	0.085
Gram-negative rod coinfection	31 (20.7)	1 (12.5)	0.548 (0.065–4.625)	0.575
Septic shock	9 (6)	3 (37.5)	9.400 (1.932–45.730)	0.001
30-Day all-cause mortality	19 (12.7)	1 (12.5)	0.985 (0.115–8.454)	0.989
ID consult	67 (44.7)	2 (25)	0.413 (0.081–2.113)	0.274
Infection setting				
Healthcare-associated	61 (40.7)	3 (37.5)	0.875 (0.202–3.800)	0.859
Nosocomial	50 (33.3)	5 (62.5)	3.333 (0.766–14.513)	0.092
Community acquired	39 (26)	0	0.17 (0.01–2.94)	0.097
Patient location				
Medical ward	89 (59.3)	2 (25)	0.228 (0.045–1.170)	0.056
Surgical ward	48 (32)	1 (12.5)	0.304 (0.036–2.537)	0.245
Intensive care	13 (8.7)	5 (62.5)	17.564 (3.765–81.948)	<0.001
Empiric treatment				
No active treatment	50 (33.3)	0	0.12 (0.01–2.07)	0.048
Piperacillin/tazobactam	44 (29.3)	0	0.14 (0.01–2.49)	0.071
Excessive-spectrum antimicrobial therapy	28 (18.7)	8 (100)	73.07 (4.1–1303.18)	<0.001
Anti-pseudomonal cephalosporins	15 (10)	0	0.51 (0.03–9.35)	0.347
Quinolones	13 (8.7)	0	0.6 (0.03–10.96)	0.385

All data presented as N (%), unless stated otherwise. CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESBL, extended-spectrum beta lactamase; ID, infectious diseases; OR, odds ratio.

De-escalating antimicrobial therapy in critically ill patients remains a contentious issue [20], with its greatest potential benefit likely seen in those with microbiologically verified infections requiring longer antimicrobial therapy [21]. Some studies have shown de-escalation to be safe also in critically ill patients, supporting the implementation of antimicrobial stewardship programmes in the ICU [21–23]. These programmes can help reduce the use of broad-spectrum antibiotics, limit the development of antimicrobial resistance, and improve overall patient outcomes [23].

Our study has some limitations. First, being a single-centre study limits its generalizability. The small sample size, particularly the eight patients receiving targeted meropenem, may weaken the robustness of the risk factor analysis. Due to the nature of the study in the context of an antimicrobial stewardship intervention that included all patients in that period, a formal sample size calculation was not performed, so we cannot rule out with certainty the possibility of a type 2 error. The low number of PA bacteraemia cases limits our ability to draw specific conclusions about the impact of the intervention

on PA bloodstream infections' management. Additionally, variations in cohort characteristics across study periods could introduce selection bias, affecting the comparability of results. The selection of three consecutive periods, and the small sample size of each one, makes it difficult to rule out the existence of possible seasonal biases. Seasonal epidemiological patterns may have influenced clinical presentations and antimicrobial prescribing, adding complexity to the interpretation of findings. Although the differences in patient severity between periods were not statistically significant, they warrant consideration, as they may impact the comparability of outcomes across study periods. A final limitation is that the educational sessions occurred before the introduction of the new EUCAST definitions, which may have influenced prescribing patterns in the first period, potentially underestimating the true impact of the implementation bundle.

Despite these limitations, the consistent improvement across three key variables (reduced excessive-spectrum antibiotic use with no new prescriptions initiated after susceptibility test results, better dosing, and fewer ID consultations) suggests that the intervention was effective, reducing the likelihood of a beta error.

In conclusion, our implementation-bundle which included the adoption of the 'SE' acronym with a clarifying footnote ('SE = susceptible, increased exposure'), appropriate dosing information, in-face educational sessions, and a prospective audit and feedback intervention during the first three months after the introduction of the new definitions implemented upon a previous existing framework of selective reporting in antimicrobial susceptibility testing results successfully facilitated the transition to the new EUCAST definitions in our centre. This approach avoided an increase of targeted excessive-spectrum antibiotics and ID consultations for PA infections while also improving dosage of these antipseudomonal drugs. Importantly, these positive outcomes were sustained even without ongoing feedback-based audits, indicating the effectiveness and robustness of the intervention without additional strain on healthcare resources.

To maintain these benefits, it is likely essential to have continuous information campaigns conducted by the multi-disciplinary antimicrobial stewardship teams. These findings highlight the importance of comprehensive implementation strategies, including clear communication and education, to enhance antimicrobial stewardship efforts.

Author contributions

P.D.L. had full access to all the study data and assumes responsibility for the integrity of the data and the accuracy of the data analysis. A.F.S. and L.E.-V. conceived and designed the study. A.F.S., L.E.-V., E.F.G.-M., L.G.-M., M.-E.M.-M., J.R.R., and B.Z.-T. took part in the prospective audit-feedback intervention. A.R. provided the PA isolation database via the Microbiology Information System. L.E.-V., A.F.S. and P.D.L. collected and analysed the data, and wrote and revised the manuscript. A.F.R. and P.D.L. collected data. A.R., E.F.G.-M., L.G.-M., M.-E.M.-M., J.R.R., B.Z.-T., F.N. and J.L.-C. critically reviewed the manuscript. All authors read and approved the final manuscript.

Conflict of interest statement

P.D.L. received support for attending meetings and/or travel from Menarini, Pfizer, and Rovi. B.Z.-T. received

payment or honoraria for lectures from GlaxoSmithKline. J.L.-C. received support for attending meetings and/or travel from Pfizer, AstraZeneca, and MSD; payments or honoraria for lectures from Pfizer, Hartmann, AstraZeneca, Guerbet, and Unió Consorci Formació; and research grants or contracts from Pfizer, GSK, AstraZeneca, Marató TV3, Shionogi, and Summit. L.E.-V. received support for attending meetings from Angelini, MSD, and Pfizer. All other authors have no conflicts of interest to declare.

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Ethics statement

The study was approved by the Ethics Committee at the Hospital de la Santa Creu i Sant Pau. Informed consent was waived because of the study's design.

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