

Supplementary material

Table S1. Differences between the pre-intervention period and the antimicrobial stewardship program period regarding pre-post analysis of antimicrobial consumption.

Outcomes	Pre-Intervention period	ASP period	P value
Total J01+J02	148.2±16.2	112.0±21.7	<0.001
Antibiotics (J01)	107.5±9.3	71.2±11.7	<0.001
Antifungals (J02)	40.8±11.3	40.8±11.7	0.954
Carbapenems	11.7±2.0	7.1±3.2	<0.001
Piperacillin-tazobactam	6.9±1.6	14.9±4.0	<0.001
Antipseudomonal cephalosporins	15.9±3.3	6.9±4.0	<0.001
Quinolones	34.8±4.6	10.9±4.8	<0.001
Amikacin	5.1±0.8	5.5±1.7	0.782
Glycopeptides	7.3±1.9	4.9±2.4	0.009

Data are presented as mean±standard deviation of quarterly defined daily doses per 100 occupied bed days. P values represent the results from Student's t-test or Mann-Whitney U, according to the data distribution. ASP, antimicrobial stewardship program.

Table S2. Trend analysis of antimicrobial consumption (2009-2019).

Outcomes	QPC (%)	95% CI	P value
Total J01+J02	-1.455	(-2.011 to -0.896)	<0.001
Antibiotics (J01)	-1.622	(-1.925 to -1.317)	<0.001
Antifungals (J02)	-0.857	(-1.813 to 0.108)	0.082
Carbapenems	-2.787	(-3.666 to -1.899)	<0.001
Piperacillin-tazobactam	1.220	(-0.201 to 2.662)	0.093
Antipseudomonal cephalosporins	-1.301	(-4.205 to 1.690)	0.390
Quinolones	-4.381	(-5.963 to -2.773)	<0.001
Amikacin	-0.605	(-1.911 to 0.718)	0.368
Glycopeptides	-2.621	(-3.614 to -1.618)	<0.001

Data are presented as quarterly defined daily doses per 100 occupied bed days. QPC, quarterly percentage change. CI, confidence interval.

Table S3. Frequency of most relevant gram-negative microorganisms and *Candida* spp. as causative agents of bloodstream infections (2009–2019).

Microorganism	Number (%) N = 522
Gram-negative microorganisms	493
<i>Escherichia coli</i>	273 (55.4)
ESBL <i>E. coli</i>	36 (13.2)
<i>Klebsiella pneumoniae</i>	116 (23.5)
ESBL <i>K. pneumoniae</i>	26 (22.4)
<i>Pseudomonas aeruginosa</i>	82 (16.6)
MDR <i>P. aeruginosa</i>	13 (15.9)
<i>Candida</i> spp.	29

ESBL, extended-spectrum β-lactamase. MDR, multidrug-resistant.

Table S4. Mortality of patients with the most relevant gram-negative microorganisms and *Candida* spp. causing bloodstream infections (2009-2019).

Microorganism	Number of patients	Number of deaths on day +7 (%)	Number of deaths on day +30 (%)
MDR microorganisms	104	13 (12.5)	29 (27.9)
ESBL <i>Escherichia coli</i>	36	2 (5.6)	6 (16.7)
ESBL <i>Klebsiella pneumoniae</i>	26	2 (7.7)	4 (15.4)
MDR <i>Pseudomonas aeruginosa</i>	13	3 (23.1)	6 (46.2)
<i>Candida</i> spp.	29	6 (20.7)	13 (44.8)
Non-MDR microorganisms	396	23 (5.8)	56 (14.1)
<i>Escherichia coli</i>	237	13 (5.5)	35 (14.8)
<i>Klebsiella pneumoniae</i>	90	6 (6.7)	13 (14.4)
<i>Pseudomonas aeruginosa</i>	69	4 (5.8)	8 (11.6)

MDR, multidrug-resistant. ESBL, extended-spectrum β -lactamase.

Table S5. Differences between the pre-intervention period and the antimicrobial stewardship program period regarding pre-post analysis of incidence and mortality rate of multidrug-resistant bloodstream infections.

Outcomes	Pre-Intervention period	ASP period	P value
Incidence density	1.11 \pm 0.76	0.82 \pm 0.61	0.210
Early mortality	0.05 \pm 0.16	0.12 \pm 0.19	0.308
Late mortality	0.15 \pm 0.32	0.26 \pm 0.27	0.226

Data are presented as mean \pm standard deviation of quarterly incidence density and all-cause crude death rate on day +7 (early mortality) and +30 (late mortality) per 1000 occupied bed days. P values represent the results from Student's t-test or Mann-Whitney U, according to the data distribution. ASP, antimicrobial stewardship program.

Table S6. Trend analysis of the incidence and mortality rate of multidrug-resistant bloodstream infections (2009-2019).

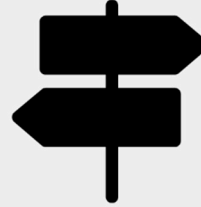
Outcomes	QPC (%)	95% CI	P value
Incidence density	-0.325	(-2.049 to 1.431)	0.709
Early mortality	-0.697	(-1.657 to 0.272)	0.154
Late mortality	-0.608	(-1.545 to 0.337)	0.201

Data are presented as quarterly incidence density and all-cause crude death rate on day +7 (early mortality) and +30 (late mortality) per 1000 occupied bed days. QPC, quarterly percentage change. CI, confidence interval.

PRIOAM CORE INTERVENTIONS

5 STEPS FOR ANTIMICROBIAL STEWARDSHIP

01 LOCAL GUIDELINES
Consensual and updated clinical guidelines for common infectious syndromes



02 EDUCATIONAL INTERVIEWS
Face-to-face structured interviews with prescribers about antimicrobial therapy of the case

03 CLINICAL SESSIONS
Regular clinical sessions tackling practical aspects of common infections



04 INSTITUTIONAL SUPPORT
Incorporation of the ASP objectives into the annual agreement signed by the hospital director

05 REGULAR FEEDBACK
Quarterly reports to departments on evaluation of annual goals



Figure S1. Description of the core elements of PRIOAM.

Date of interview: Centre
 Clinical department Episode number
 Advisor: Prescriber
 Antimicrobial agent(s)
 Clinical indication:
 Perioperative prophylaxis
 Diagnosis without microbiological confirmation
 Diagnosis with microbiological confirmation
 Describe

Perioperative prophylaxis

1. Was prophylaxis indicated? Yes No
 2. Was the chosen agent appropriate? Yes No
 3. Was the administration timing appropriate? Yes No
 4. Was the total number of doses appropriate? Yes No

Empirical antimicrobial treatment

1. Was empirical treatment initiation indicated? Yes No
 2. Was the timing of treatment initiation appropriate? Yes No
 3. Were microbiological samples collected?
 It was not indicated:
 Not performed
 It was indicated:
 Performed
 Not performed or incorrectly performed
 4. Was the chosen agent appropriate? Yes No
 5. Was the dosing appropriate? Yes No
 6. Was the way of administration appropriate? Yes No
 7. If other therapeutic measures were indicated, were they performed correctly?
 They were not indicated and not performed
 They were indicated and correctly performed
 They were indicated, but not correctly performed
 8. Is the planned treatment duration appropriate? Yes No

Targeted antimicrobial treatment

1. Was antimicrobial treatment indicated? Yes No
 2. Was the timing of the treatment initiation appropriate? Yes No
 3. Was the interpretation of the microbiological results correct? Yes No
 4. Was the chosen agent appropriate? Yes No
 5. Was the chosen agent the most appropriate? Yes No
 6. Was the dosing appropriate? Yes No
 7. Was the way of administration appropriate? Yes No
 8. If other therapeutic measures were indicated, were they performed correctly?
 They were not indicated and not performed
 They were indicated and correctly performed
 They were indicated, but not correctly performed
 1. Is the planned treatment duration appropriate? Yes No

Figure S2. Form for PRIOAM educational interviews.