Journal of Health Economics and Outcomes Research

Online Supplementary Material

Budget Impact Analysis of Procalcitonin-Guided Antimicrobial Stewardship for Sepsis and Lower Respiratory Tract Infection in the United Arab Emirates. *JHEOR*. 2026;13(2):282-292. doi:10.36469/jheor.2026.175278

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This supplementary material has been provided by the authors to give readers additional information about their work.

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Table S1. Pathogen-specific antibiotic resistance rates (based on the UAE National AMR Surveillance Report 2024)[1]

	Antibiotic[a,b] resistance rate, %									
Pathogen (N)	**AMC**	**TZP**	**3GC (CRO/CTX)**	**FEP**	**Carbapenem (IPM/MEM)**	**AMK**	**FQ (CIP/LVX)**	**Macrolide**	**OXA**	**VAN**
E. coli (53 918)	14.6	6.0	35.2 / 36.8	23.2	1.0	1.9	35.6	—	—	—
S. aureus (24 771)	—	—	—	—	—	—	33.5	31.0	40.7	0.7
K. pneumoniae (21 594)	14.4	10.7	23.8 / 25.3	15.5	3.0	2.9	21.5	—	—	—
P. aeruginosa (12 625)	—	9.6	—	6.1	11.6	2.9	11.0	—	—	—
E. faecalis (6760)	—	—	—	—	—	—	22.6	—	—	0.4
S. pneumoniae (2958)	2.4	—	1.7 / 2.5	—	—	—	5.4	59.0	—	—
A. baumannii (2546)	—	12.0	—	8.1	5.8	5.4	10.2	—	—	—

Abbreviations: 3GC, third-generation cephalosporins; AMC, amoxicillin/clavulanic acid; AMK, amikacin; AMR, antimicrobial resistance; CIP, ciprofloxacin; CRO, ceftriaxone; CTX, cefotaxime; FEP, cefepime; FQ, fluoroquinolones; IPM, imipenem; LVX, levofloxacin; MEM, meropenem; OXA, oxacillin; TZP, piperacillin/tazobactam; UAE, United Arab Emirates; VAN, vancomycin.

[a]For each antibiotic class the table reports the specific agent used in the modelled empiric regimens (**Supplementary Table S4**), with CRO for 3GCs, and an FQ chosen by organism (CIP for Gram-negative bacilli and *S. aureus*; LVX for *E. faecalis* and *S. pneumoniae*, as CIP lacks reliable activity against these organisms). CTX is reported separately by the UAE National AMR Surveillance Report[1] and shown alongside CRO for transparency but was not used in the calculation. In relation to carbapenems, the UAE National AMR Surveillance Report[1] reports IPM and MEM separately; the column shows their mean, which was used for the carbapenem class (lower-bound) estimate. Regimens that specify MEM used the MEM-specific value (**Supplementary Table S4**).

[b]Only antibiotic classes relevant to the modeled regimens are included. Other agents reported in Section 4.4 of the UAE National AMR Surveillance Report[1] (e.g., ampicillin, ceftazidime, cefuroxime, ertapenem, fosfomycin, gentamicin, linezolid, nitrofurantoin, teicoplanin, tigecycline, tobramycin, trimethoprim/sulfamethoxazole) were not part of any modeled regimen and are omitted. AMK, macrolide and VAN are shown for context only: they appear solely as companion agents in combination regimens and do not enter the principal-agent calculation.

Table S2. Causative pathogen distribution by clinical subtype

Clinical subtype[a]	Pathogen distribution[b]	Source (adapted from)
CAP / pulmonary sepsis–CAP	*S. pneumoniae* 45.9% *S. aureus* 17.6% *K. pneumoniae* 16.2% *P. aeruginosa* 13.5% *E. coli* 6.8%	Batool et al[2]
HAP/VAP / pulmonary sepsis–HAP	*P. aeruginosa* 34.5% *K. pneumoniae* 22.1% *A. baumannii* 20.4% *S. aureus* 18.6% *E. coli* 4.4%	Ali et al[3]
Urinary-origin sepsis	*E. coli* 53.4% *E. faecalis* 14.1%[c] *K. pneumoniae* 12.9% *P. aeruginosa* 12.9% *S. aureus* 4.6% *A. baumannii* 2.1%	Tandoğdu et al[4]

Abbreviations: CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia.

[a]In relation to intra-abdominal / other sepsis, a regional pathogen distribution was available, but no empiric-regimen prescribing shares were defined, so this subtype was excluded from the resistance composite; its clinical weight is retained in **Supplementary Table S3** and the remaining sepsis subtype weights re-normalized (**Supplementary Table S4**).

[b]Each distribution is based on the figures originally reported by the source, restricted to the pathogens for which the UAE National AMR Surveillance Report[1] provides resistance data (**Supplementary Table S1**) and re-normalized to 100%. Specifically, for CAP / pulmonary sepsis–CAP: distribution of culture-positive isolates reported by Batool et al (*S. pneumoniae* 34%, *H. influenzae* 16%, *S. aureus* 13%, *Klebsiella* 12%, *P. aeruginosa* 10%, *Legionella* 6%, *E. coli* 5%, *Proteus* 2%) was re-normalized to 100% for *S. pneumoniae* (34% adjusted to 45.9%), *S. aureus* (13% adjusted to 17.6%), *K. pneumoniae* (12% adjusted to 16.2%), *P. aeruginosa* (10% adjusted to 13.5%) and *E. coli* (5% adjusted to 6.8%) only. For HAP / VAP / pulmonary sepsis–HAP: distribution of total number of isolates reported by Ali et al (*Pseudomonas* n=39, *Klebsiella* n=25, *Enterobacter* n=24, *Acinetobacter* n=23, *Staphylococcus* n=21, *Haemophilus* n=16, *E. coli* n=5, *Streptococcus* n=5 and *Stenotrophomonas* n=4) was re-normalized to 100% for *P. aeruginosa* (n=39 adjusted to 34.5%), *K. Pneumoniae* (n=25 adjusted to 22.1%), *A. Baumannii* (n=23 adjusted to 20.4%), *S. aureus* (n=21 adjusted to 18.6%) and E. coli (n=5 adjusted to 4.4%) only. For urinary-origin sepsis: distribution of overall pathogen numbers reported by Tandoğdu et

al (*E. coli* n=174, *Enterococcus* n=46, *Klebsiella* n=42, *P. aeruginosa* n=42, *Enterobacter* n=23, *Proteus* n=16, *S. aureus* n=15, fungi n=12, coagulase-negative staphylococci n=9, *Acinetobacter* n=7, other Gram-positive cocci n=5, *Citrobacter* n=4, other bacteria n=13) was re-normalized to 100% for *E. coli* (n=174 adjusted to 53.4%), *E. faecalis* (n=46 adjusted to 14.1%), *K. pneumoniae* (n=42 adjusted to 12.9%), *P. aeruginosa* (n=42 adjusted to 12.9%), *S. aureus* (n=15 adjusted to 4.6%) and *A. baumannii* (n=7 adjusted to 2.1%) only.

[c]For urinary-origin sepsis, *E. faecalis* (14.1%) was retained in the distribution, but because the UAE report provides no enterococcal resistance data for the beta-lactam/carbapenem agents used in the modelled regimens, it is treated as susceptible under the not-reported = susceptible convention. As enterococci are intrinsically resistant to cephalosporins, this conservatively understates urinary-origin resistance.

Table S3. Clinical subtype weights (based on expert panel meeting)

Syndrome	**Subtype**	**Weight**
Sepsis	Pulmonary sepsis–CAP	20%
Sepsis	Pulmonary sepsis–HAP/VAP	40%
Sepsis	Urinary-origin sepsis	25%
Sepsis	Intra-abdominal/other sepsis[a]	15%
LRTI	CAP	60%
LRTI	HAP/VAP	40%

Abbreviations: CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; LRTI, lower respiratory tract infection; VAP, ventilator-associated pneumonia

[a]Intra-abdominal/other sepsis was excluded from the resistance composite as no reproducible regimen-level estimate was available; the weights for pulmonary sepsis (60%) and urinary-origin sepsis (25%) were re-normalized to 70.6% and 29.4% for the calculation.

Table S4. Empiric regimens, their share of prescribing and weighted resistance (based on expert panel meeting)

Subtype (weight)[a]	Regimen	Share	Principal agent	Antibiotic resistance rate by principal agent, %[b]	Antibiotic resistance rate by subtype, %[b]
Patients with suspected sepsis in the ICU					
Pulmonary sepsis–CAP (33.3% of pulmonary)	Ceftriaxone + fluoroquinolone	30%	Ceftriaxone	7.02	4.35
	Piperacillin/tazobactam + azithromycin	50%	Piperacillin/ tazobactam	3.44	
	Piperacillin/tazobactam + levofloxacin	10%	Piperacillin/ tazobactam	3.44	
	Vancomycin + meropenem	10%	Meropenem	1.79	
Pulmonary sepsis–HAP/VAP (66.7% of pulmonary)	Piperacillin/tazobactam + levofloxacin	30%	Piperacillin/ tazobactam	8.39	6.13
	Meropenem + levofloxacin	70%	Meropenem	5.16	
Pulmonary composite (re-normalized to 70.6%)					5.54
Urinary-origin sepsis (re-normalized to 29.4%)	Piperacillin/tazobactam	40%	Piperacillin/ tazobactam	6.08	11.62
	Ceftriaxone + amikacin	20%	Ceftriaxone	21.85	
	Meropenem	10%	Meropenem	2.19	
	Cefepime	30%	Cefepime	15.34	
Sepsis composite					7.33
Hospitalized patients with LRTI					
CAP (60%)	Amoxicillin	70%	Amoxicillin	4.42	6.08
	Ceftriaxone + azithromycin	20%	Ceftriaxone	7.02	
	Moxifloxacin or levofloxacin	10%	Fluoroquinolone	15.74	
HAP/VAP (40%)	Piperacillin/tazobactam or cefepime	90%	Piperacillin/ tazobactam–cefepime	8.30	7.99

Subtype (weight)[a]	Regimen	Share	Principal agent	Antibiotic resistance rate by principal agent, %[b]	Antibiotic resistance rate by subtype, %[b]
	Meropenem / imipenem	10%	Carbapenem	5.16	
LRTI composite					6.84

Abbreviations: CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; ICU, intensive care unit; LRTI, lower respiratory tract infection; VAP, ventilator-associated pneumonia

[a]For further details of weighting, refer to **Supplementary Table S3.**

[b]Regimen resistance was computed from the pathogen-specific antibiotic resistance rates shown in **Supplementary Table S1** over the pathogen distributions shown in **Supplementary Table S2**. Intra-abdominal/other sepsis was excluded from the resistance composite as no reproducible regimen-level estimate was available; the weights for pulmonary sepsis (60%) and urinary-origin sepsis (25%) were re-normalized to 70.6% and 29.4% for the calculation. A worked example for pulmonary sepsis–CAP / ceftriaxone + fluoroquinolone is as follows: the principal agent is ceftriaxone (the companion fluoroquinolone is assumed effective and not counted) and its agent-specific antibiotic resistance rate is ceftriaxone resistance-weighted across the CAP pathogen distribution shown in **Supplementary Table S2**, using the per-pathogen ceftriaxone antibiotic resistance rate shown in **Supplementary Table S1** (*S. pneumoniae* 1.7%, *K. pneumoniae* 23.8%, *E. coli* 35.2%; *S. aureus* and *P. aeruginosa* not reported, treated as susceptible = 0): (0.459 × 1.7) + (0.176 × 0) + (0.162 × 23.8) + (0.135 × 0) + (0.068 × 35.2) = 7.02%. The antibiotic resistance rate by subtype (4.35%) is then the prescribing-share-weighted mean of the agent-specific antibiotic resistance rate for the four pulmonary sepsis–CAP regimens: (0.30 × 7.02) + (0.60 × 3.44) + (0.10 × 3.44) + (0.10 × 1.79) = 4.35%. The sepsis composite is the subtype-weighted mean of the subtype values.

Table S5. Microcosting methodology to estimate the costs of antibiotic treatment per day for patients with suspected sepsis in the ICU and hospitalized patients with LRTI (as shown in **Table 1**)

Antibiotic 1	**Antibiotic 2**	**Proportion of patients using antibiotics[a]**	**Average cost of antibiotic 1 per day (total cost), AED[b]**	**Average cost of antibiotic 2 per day (total cost), AED[b]**
Pulmonary sepsis				
Ceftriaxone 1-2 g OD	Fluoroquinolone (moxifloxacin 400 mg BID or levofloxacin 750 mg OD)	CAP: 30% HAP: 0%	54.4 (380.8)	13.5 (67.7)
Piperacillin/tazobactam 4.5 g IV bolus followed by 4.5 g IV every 6 hours by extended infusion 4-6 hours	Azithromycin 500 mg OD	CAP: 50% HAP: 0%	194.4 (1361.1)	10.5 (52.6)
Piperacillin/tazobactam 4.5 g IV bolus followed by 4.5 g IV every 6 hours by extended infusion 4-6 hours	Levofloxacin 750 mg OD	CAP: 10% HAP: 30%	194.4 (1361.1)	9.5 (47.4)
Meropenem 1-2 g every 8 hours	Levofloxacin 750 mg OD	CAP: 0% HAP: 70%	336.3 (2354.1)	9.5 (47.4)
Vancomycin 1 g BID (25 mg/kg, 60 kg) + linezolid 600 mg BID	Meropenem 1-2 g every 8 hours	CAP: 10% HAP: 0%	534.3 (3739.8)	336.3 (2354.1)
Urinary-origin sepsis				
Piperacillin/tazobactam 4.5 g IV bolus followed by 4.5 g IV every 6 hours by extended infusion 4-6 hours	–	40%	194.4 (1361.1)	–
Ceftriaxone 1-2 g OD	Amikacin 15-20 mg/kg OD	20%	54.4 (380.8)	123.9 (495.6)
Meropenem 1-2 g every 8 hours	–	10%	336.3 (2354.1)	–
Cefepime 2 g every 8 hours	–	30%	173.5 (1214.6)	–

Antibiotic 1	Antibiotic 2	Proportion of patients using antibiotics[a]	Average cost of antibiotic 1 per day (total cost), AED[b]	Average cost of antibiotic 2 per day (total cost), AED[b]
LRTI				
Amoxicillin 1 g BID	–	CAP: 70% HAP: 0%	5.4 (37.6)	–
Ceftriaxone 1-2 g OD	Azithromycin 500 mg OD	CAP: 20% HAP: 0%	54.4 (380.8)	10.5 (52.6)
Moxifloxacin 400 mg BID or levofloxacin 750 mg OD	–	CAP: 10% HAP: 0%	13.5 (94.8)	–
Piperacillin/tazobactam 4.5 g IV every 6 hours OR cefepime 1-2 g every 8 hours	–	CAP: 0% HAP: 90%	184.0 (1287.9)	–
Meropenem/imipenem 1 g every 8 hours	–	CAP: 0% HAP: 10%	224.2 (1569.4)	–

Abbreviations: AED, United Arab Emirates dirham; BID, twice daily; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; ICU, intensive care unit; IV, intravenous; LRTI, lower respiratory tract infection; OD, once daily.

[a]Based on the opinion of the expert panel.

[b]Based on drug costs derived from the Department of Health Abu Dhabi 2019 price list.

Table S6. Summary of scenarios explored by the scenario analyses

Parameter varied	Base case	Scenario value	Source
Suspected sepsis in the ICU			
Rate of *C. diff* infection	4.3%	1%	Expert panel meeting
Absolute reduction in the rate of AMR (per percent reduction of days on antibiotic treatment) due to PCT-guided AMS	3.2%	0%	Assumption
Reduction in the rate of hospital-acquired *C. diff* infection due to PCT-guided AMS	32%	0%	Assumption
Reduction in the rate of hospital-acquired *C. diff* infection due to PCT-guided AMS	32%	16.5%	Expert panel meeting
Inclusion of antibiotics-related cost savings only	–	All other savings = 0	Assumption
Additional LOS on general ward for AMR	7.4 days	4 days	Expert panel meeting
Reduction in LOS on general ward due to PCT-guided AMS	0 days	3.5 days	Andriolo et al.[5]
Reduction in LOS in ICU due to PCT-guided AMS	0 days	2.05 days	Andriolo et al.[5]
Reduction in duration of antibiotic treatment due to PCT-guided AMS	1.28 days	0.99 days	Peng et al.[6]
Reduction in duration of antibiotic treatment due to PCT-guided AMS	1.28 days	1.79 days	Papp et al.[7]
Hospitalized patients with LRTI			
Reduction in the rate of antibiotic prescription due to PCT-guided AMS	15.4%	0%	Assumption

Parameter varied	**Base case**	**Scenario value**	**Source**
Absolute reduction in the rate of AMR (per percent reduction of days on antibiotic treatment) due to PCT-guided AMS	3.2%	0%	Assumption
Reduction in the rate of hospital-acquired *C. diff* infection due to PCT-guided AMS	32%	0%	Assumption
Inclusion of antibiotics-related cost savings only	–	All other savings = 0	Assumption
Antibiotic prescription rate with routine care	85.8%	100%	Assumption

Abbreviations: AMR, antimicrobial resistance; AMS, antimicrobial stewardship; *C. diff*, *Clostridioides difficile*; ICU, intensive care unit; LOS, length of stay; LRTI, lower respiratory tract infection; PCT, procalcitonin

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