Le Pielonefriti

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The Increase in Hospitalizations for Urinary Tract Infections and the Associated Costs in the United States, 1998–2011

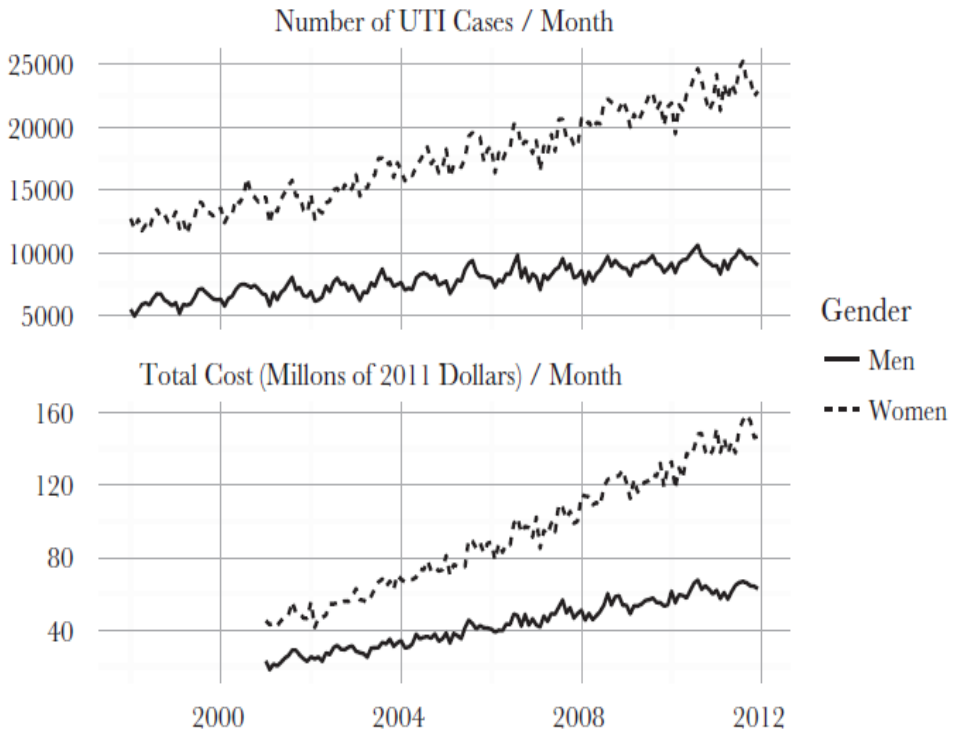

Figure 1. Urinary tract infection (UTI) incidence and total cost of hospitalizations by sex, 1998–2011. Incidence is the number of cases per 10 000 people in the community by sex, and real total costs are converted to costs using the Healthcare Cost and Utilization Project cost-to-charge ratio and are normalized to constant December 2011 dollars. Solid lines denote the male series, whereas dotted lines represent the female series.

Simmering JE, OFID 2017

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Acute Pyelonephritis in Adults

James R. Johnson, M.D., and Thomas A. Russo, M.D., C.M.

KEY CLINICAL POINTS

ACUTE PYELONEPHRITIS

- Acute pyelonephritis has the potential to cause sepsis, septic shock, and death.
- Urine culture is the cardinal confirmatory diagnostic test.
- Imaging is recommended at the time of presentation for patients with sepsis or septic shock, known or suspected urolithiasis, a urine pH of 7.0 or higher, or a new decrease in the glomerular filtration rate to 40 ml per minute or lower. Subsequent imaging is indicated in patients whose condition worsens or does not improve after 24 to 48 hours of therapy.
- The rising prevalence of *Escherichia coli* resistant to fluoroquinolones and trimethoprim–sulfamethoxazole complicates empirical oral therapy. In patients who receive oral treatment from the outset, depending on the likelihood of resistance, an initial dose of a supplemental, long-acting, parenteral antimicrobial agent (e.g., an aminoglycoside, ceftriaxone, or ertapenem) may be appropriate, and close follow-up is warranted.
- Assessment of illness severity, underlying host status, and the patient's psychosocial situation and estimation of the likelihood of pathogen resistance to relevant antimicrobial agents are critical in decisions regarding patient disposition and treatment.

Short- and long-term mortality in patients with urosepsis caused by *Escherichia coli* susceptible and resistant to 3rd generation cephalosporins

Background: The aim of this study was to compare short- and long-term mortality among patients with urosepsis caused by *Escherichia coli* susceptibile (EC-SC) and resistant (EC-RC) to 3rd generation cephalosporins.

Methods: A retrospective cohort study that included all patients with *E. coli* urosepsis admitted to a 700-bed hospital from January 2014 until December 2019. Mortality up to 30 days, 6 months and 1 year was assessed using logistic multivariate regression analysis and Cox regression analysis.

Tocut *et al. BMC Infectious Diseases* (2022) 22:571
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Table 1 Characteristics of patients with *E. coli* urosepsis

	All patients N = 313	EC-SR group N = 195 (62.3)	EC-RC group N = 118 (37.7)	P value
Age (years), mean (SD)	79 (12.0)	79 (12.8)	80 (10.7)	0.376
Sex (female) n (%)	199 (63.6)	136 (69.7)	63 (53.4)	0.004
Nursing care institution, n (%)	57 (18.2)	18 (9.2)	39 (33.1)	< 0.001
Charlson score, mean (SD)	5.24 (2.18)	4.93 (2.27)	5.74 (1.92)	0.001
DM, (%)	133 (42.5)	83 (42.6)	50 (42.4)	0.974
BPH, n (%)	43 (13.7)	21 (10.8)	22 (18.6)	0.050
CRF, n (%)	50 (16.0)	22 (11.3)	28 (23.7)	0.004
Nephrolithiasis, n (%)	26 (8.3)	15 (7.7)	11 (9.3)	0.613
Urinary malignancy, n (%)	8 (2.6)	3 (1.5)	5 (4.2)	0.159
Permanent urinary catheter, n (%)	16 (5.1)	6 (3.1)	10 (8.5)	0.036
Recent urinary tract manipulation, n (%)	4 (1.3)	2 (1.0)	2 (1.7)	0.634
History of urinary retention, n (%)	6 (1.9)	3 (1.5)	3 (2.5)	0.676
History of recurrent UTI, n (%)	23 (7.3)	9 (4.6)	14 (11.9)	0.017
Previous hospitalization with EC-SC urosepsis, n (%)	7 (2)	4 (2)	3 (3)	1.0
Previous hospitalization with RC Enterobacteriaceae urosepsis, n (%)	18 (5.8)	6 (3.1)	12 (10.2)	0.009
Outpatient antibiotic therapy for UTI in the past 3 months, n (%)	25 (8.0)	4 (2.1	21 (17.8)	< 0.001

Data is presented as mean (SD) or number (%)

EC-CS Group—patients with urosepsis caused by *E. coli* susceptible to 3rd generation cephalosporins

EC-RC Group—patients with urosepsis caused by *E. coli* resistant to 3rd generations cephalosporins

SD standard deviation, *DM* diabetes mellitus, *BPH* benign prostate hypertrophy, *CRF* chronic renal failure, *UTI* urinary tract infection, *S/P* status post

Table 4 Logistic regression of 30 days mortality

EC-SC 6.3% vs EC-RC 12.7%

	Univariate analysis			Multivariate analysis		
	P-value	OR	95% CI	P-value	OR	95% CI
Gender (female)	0.086	0.499	0.226–1.103			
Permanent Nursing Home stay	0.038	2.479	1.051–5.848			
Charlson comorbidity index score*	<0.001	1.395	1.170–1.662	<0.001	1.437	1.172–1.763
History of urinary retention	0.489	2.162	0.243–19.204	–	–	–
PBS*	<0.001	1.625	1.259–2.099	<0.001	1.644	1.151–7.29
Fever upon admission*	0.209	0.831	0.622–1.110			
CRP*	0.028	1.043	1.005–1.083	–	–	–
ARF*	0.054	2.269	0.986–5.219	–	–	–
EC-CR*	0.019	2.624	1.173–5.868	0.024	2.885	1.151–7.229
Appropriate empirical antibiotic treatment	0.131	0.520	0.222–1.216	–	–	–
Constant	–	–	–	<0.001	0.004	–

Nagelkerke R square 0.239

PBS Pitt bacteremia score, *CRP* C reactive protein, *ARF* acute renal failure, *EC-CR E. coli* resistant to 3rd generation cephalosporins, *OR* odds ratio, *CI* confidence interval

* Variables that were entered into the multivariate logistic regression

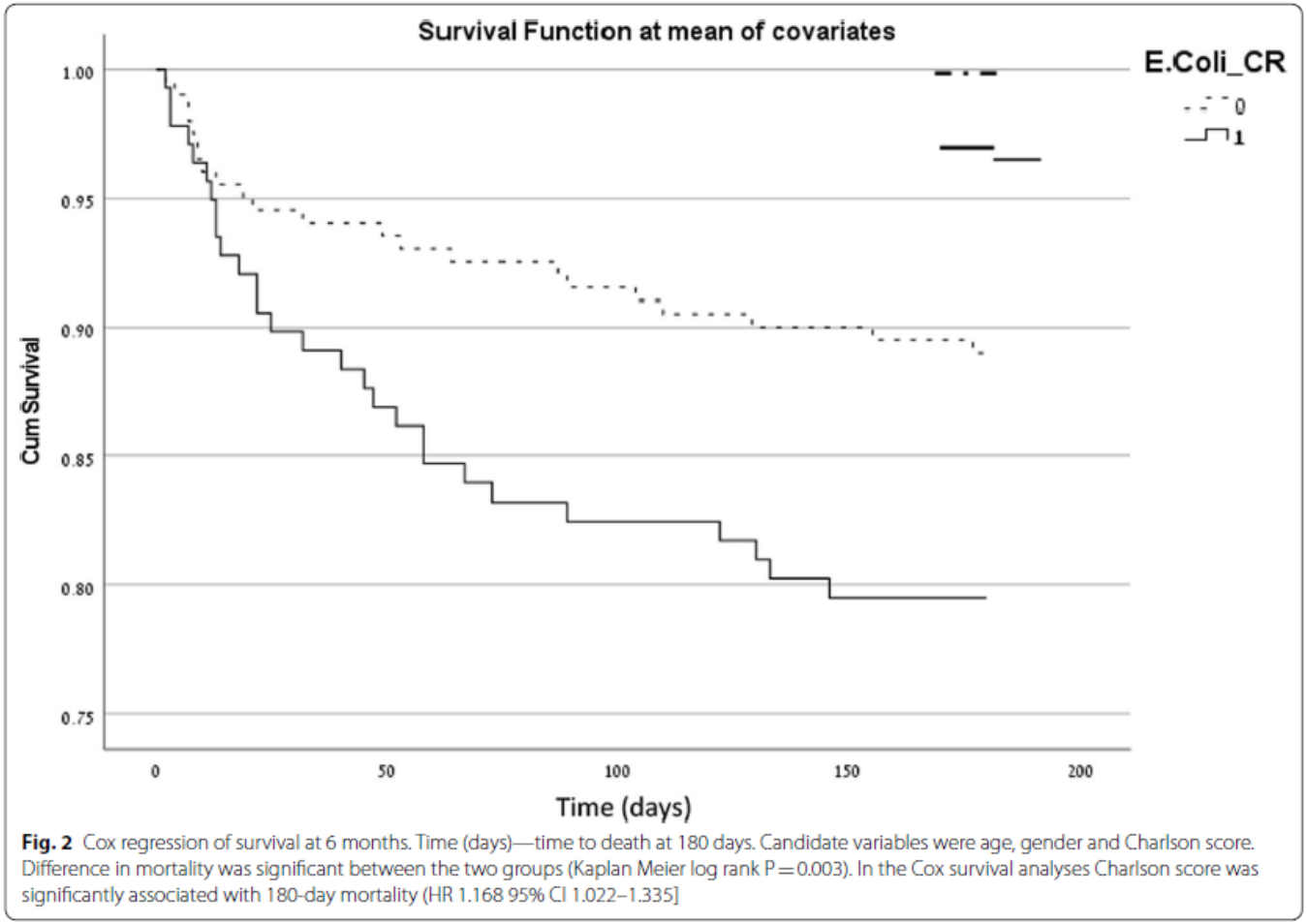


Fig. 2 Cox regression of survival at 6 months. Time (days)—time to death at 180 days. Candidate variables were age, gender and Charlson score. Difference in mortality was significant between the two groups (Kaplan Meier log rank P = 0.003). In the Cox survival analyses Charlson score was significantly associated with 180-day mortality (HR 1.168 95% CI 1.022–1.335]

Figure 2. ***Escherichia coli.*** **Percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country, EU/EEA, 2020**

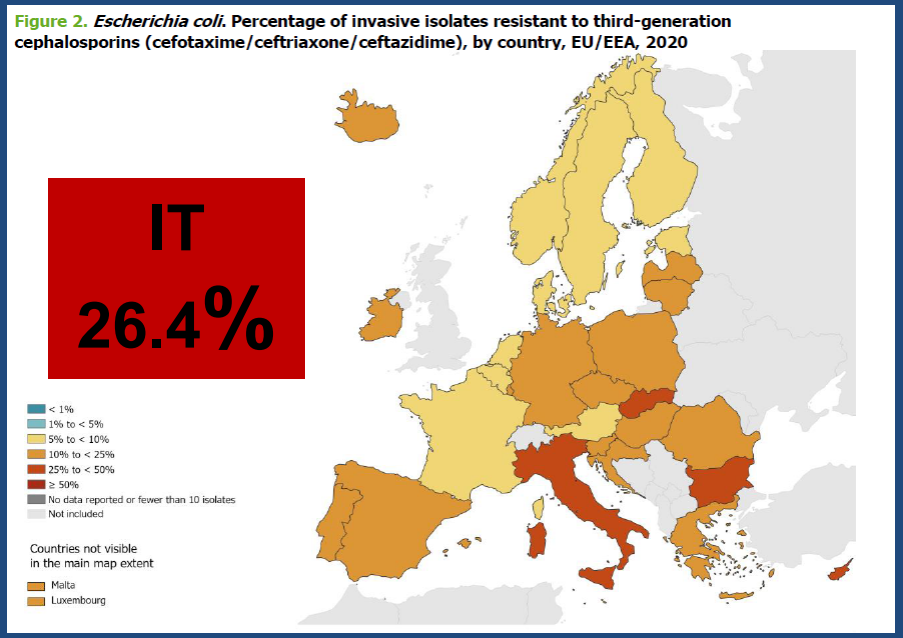
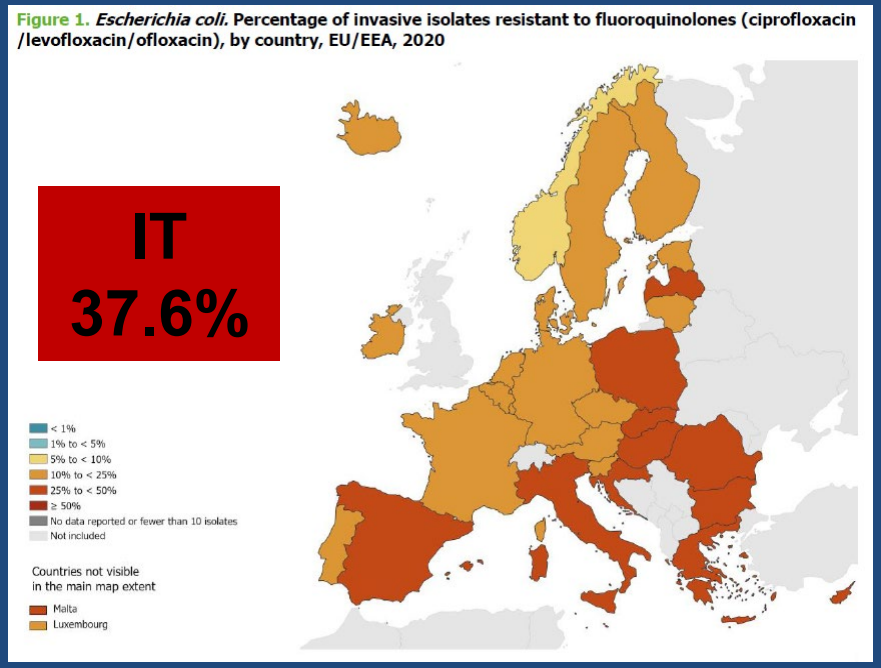


Figure 1. ***Escherichia coli.*** **Percentage of invasive isolates resistant to fluoroquinolones (ciprofloxacin /levofloxacin/ofloxacin), by country, EU/EEA, 2020**



Pielonefriti Acute: studio pilota osservazionale

Variabile	Popolazione (N=147)
Sesso femminile n (%)	134 (91)
Età (media; anni [DS])	40.4 (17.8)
Charlson comorbidity index (media; [DS])	1.6 (0.6)
Fattori di rischio per IVU	
Diabete n (%)	4 (2.7)
BMI>30 n (%)	5 (3.4)
Contracettivi medicati n (% femm)	27 (20)
estroprogestinico	19 (14.2)
IUD	6 (4.5)
Altro	2 (1.5)
Pregressi episodi di IVU n (%)	58 (39.4)
Manip. tratto urinario <3 mesi n (%)	4 (2.7)
Vescica neurologica n (%)	1 (1.7)
Ipertrofia prostatica n (%)	6 (46)
Calcolosi renale n (%)	20 (13.6)
Anomalie del tratto urinario n (%)	34 (23)
Trapianto renale n (%)	5 (3.4)
Immunosoppressione n (%)	5 (3.4)
Recente ricovero <3 mesi n (%)	22 (14.9)
Urinocoltura positiva n (%)	82 (56.9)
Escherichia coli n (%)	74 (90.2)
E. coli ESBL-positivo n (%)	20 (27)
Emocoltura positiva n (%)	32 (21.7)
Escherichia coli n (%)	27 (84.4)
E. coli ESBL-positivo n (%)	4 (14.8)

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Bad bugs: antibiotic-resistant bacteriuria in pregnancy and risk of pyelonephritis

BACKGROUND: The introduction of antibiotics has significantly reduced morbidity and mortality from microbial infections, but the rise of antibiotic-resistant and multidrug-resistant microbes is of increasing clinical concern. Few studies have examined the prevalence and impact of antibiotic resistance in common antenatal infections.

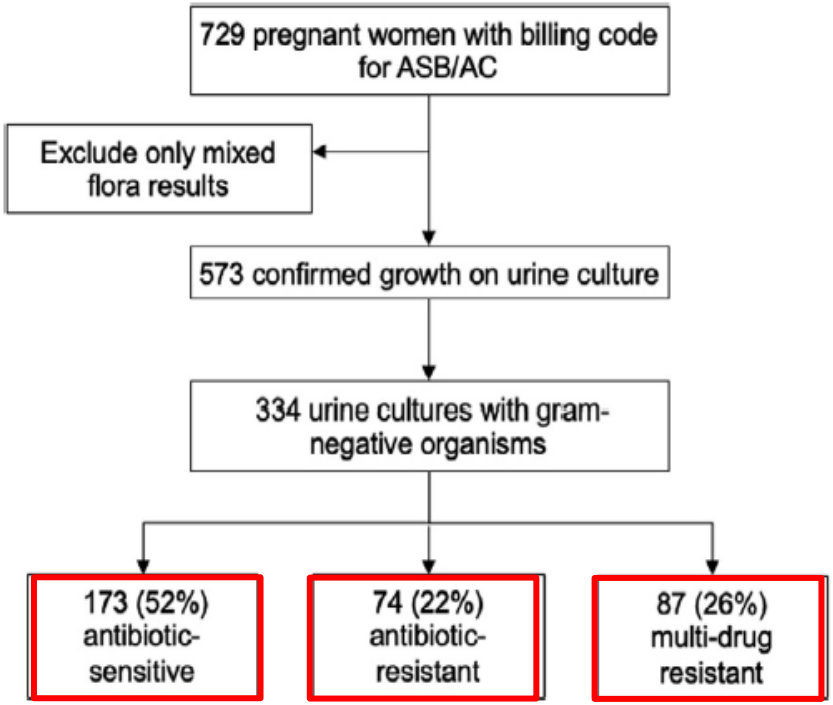
OBJECTIVE: This study aimed to determine whether pregnant women with a urine culture positive for antibiotic-resistant or multidrug-resistant gram-negative bacteria are at increased risk of developing pyelonephritis than pregnant women infected with antibiotic-susceptible organisms.

STUDY DESIGN: This was a retrospective cohort study of pregnant women with asymptomatic bacteriuria or acute cystitis from a single health system from July 2013 to May 2019. Women with gram-negative antibiotic-resistant (resistance to 1–2 antibiotic classes) and multidrug-resistant (resistance to ≥3 antibiotic classes) lower urinary tract infections were compared with women with antibiotic-susceptible urinary tract infections in terms of demographic, infectious, antepartum, and

Denoble A, Am J Obstet Gynecol 2022

FIGURE 1

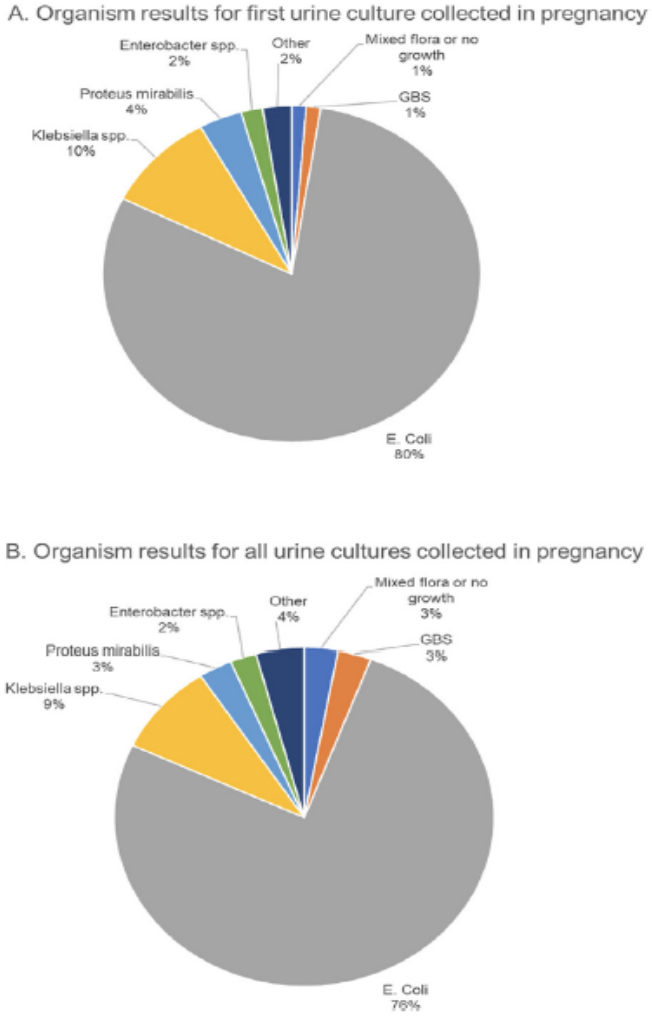
Flow diagram of the study population



AC, acute cystitis; ASB, asymptomatic bacteriuria.

Denoble. Antibiotic-resistant bacteriuria in pregnancy and risk of pyelonephritis. Am J Obstet Gynecol MFM 2021.

FIGURE 2
Distribution of organisms cultured from urine



A, The chart displays the distribution of organisms from the first urine collected in pregnancy. **B,** The chart displays the data from all primary urine samples collected (excluding samples sent for test of cure).

GBS, group B Streptococcus.

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TABLE 2

Comparison of primary and secondary outcomes by antibiotic-sensitive, antibiotic-resistant, and multidrug-resistant urinary tract infections by logistic regression

Primary outcome				
Outcome	Antibiotic-sensitive UTI n=173	Antibiotic-resistant UTI n=74	Multidrug-resistant UTI n=87	*P* value
Pyelonephritis	23 (13)	18 (24)	26 (30)	.005
Adjusted odds	Ref	2.27 (1.08–4.78) *P*=.03	3.06 (1.57–5.96) *P*=.001	
Overall secondary outcomes				
Gestational age at delivery (wk)	39.3 (38.4–40.1)	39.0 (37.6–40.1)	39.0 (37.3–39.9)	.01
Preterm delivery (<37 wk)	19 (11)	11 (15)	18 (21)	.12
Pyelonephritis secondary outcomes				
Outcome	Antibiotic-sensitive pyelonephritis n=23	Antibiotic-resistant pyelonephritis n=18	Multidrug-resistant pyelonephritis n=26	*P* value
Pyelonephritis—length of stay in the hospital	3 (1–4)	2 (2–4)	4 (3–5)	.41
Composite of pyelonephritis complications	2 (9)	0 (0)	1 (4)	—[a]

Data are presented as number (percentage) or median (interquartile range), unless otherwise indicated.

Ref, reference; *UTI*, urinary tract infection.

[a] Low outcome sample size precluded statistical comparison.

Denoble. Antibiotic-resistant bacteriuria in pregnancy and risk of pyelonephritis. Am J Obstet Gynecol MFM 2021.

JAMA | Original Investigation

Effect of Cefepime/Enmetazobactam vs Piperacillin/Tazobactam on Clinical Cure and Microbiological Eradication in Patients With Complicated Urinary Tract Infection or Acute Pyelonephritis

A Randomized Clinical Trial

IMPORTANCE Cefepime/enmetazobactam is a novel β-lactam/β-lactamase inhibitor combination and a potential empirical therapy for resistant gram-negative infections.

OBJECTIVE To evaluate whether cefepime/enmetazobactam was noninferior to piperacillin/tazobactam for the primary outcome of treatment efficacy in patients with complicated urinary tract infections (UTIs) or acute pyelonephritis.

DESIGN, SETTING, AND PARTICIPANTS A phase 3, randomized, double-blind, active-controlled, multicenter, noninferiority clinical trial conducted at 90 sites in Europe, North and Central America, South America, and South Africa. Recruitment occurred between September 24, 2018, and November 2, 2019. Final follow-up occurred November 26, 2019. Participants were adult patients aged 18 years or older with a clinical diagnosis of complicated UTI or acute pyelonephritis caused by gram-negative urinary pathogens.

INTERVENTIONS Eligible patients were randomized to receive either cefepime, 2 g/enmetazobactam, 0.5 g (n = 520), or piperacillin, 4 g/tazobactam, 0.5 g (n = 521), by 2-hour infusion every 8 hours for 7 days (up to 14 days in patients with a positive blood culture at baseline).

Kaye KS, JAMA2022

Table 1. Demographic and Baseline Characteristics of Patients Who Received at Least 1 Dose of Study Drug

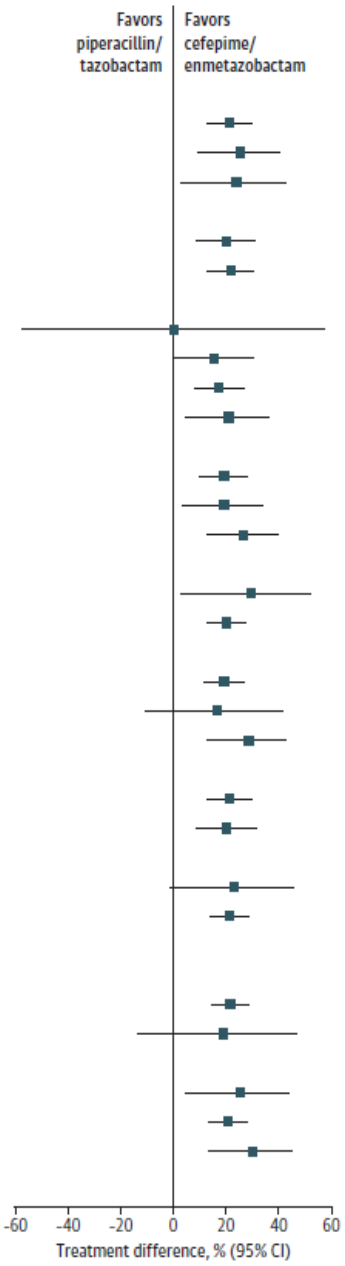
	No. (%)	
	Cefepime/ enmetazobactam (n = 516)	Piperacillin/ tazobactam (n = 518)
Age, mean (SD), y	55.0 (19.0)	54.3 (19.1)
Type of infection		
Acute pyelonephritis	251 (48.6)	247 (47.7)
Complicated UTI with removable source of infection[c]	120 (23.3)	127 (24.5)
Complicated UTI without removable source of infection but with other risk factors	145 (28.1)	144 (27.8)
Presence of concurrent bacteremia at baseline	41 (7.9)	30 (5.8)
Diabetes at baseline	79 (15.3)	78 (15.1)
Enterobacterales baseline pathogen, extended-spectrum β-lactamase producing	98 (19.0)	89 (17.2)

Table 2. Primary Outcome, Clinical Cure, and Microbial Eradication in the Primary Analysis Set

Response at visit	No. (%)		Treatment difference, % (95% CI)[a]
	Cefepime/ enmetazobactam (n = 345)	Piperacillin/ tazobactam (n = 333)	
Day 14[b]			
Overall success[c]	273 (79.1)	196 (58.9)	21.2 (14.3 to 27.9)
Clinical cure	319 (92.5)	296 (88.9)	3.5 (−1.0 to 8.0)
Microbiological eradication	286 (82.9)	216 (64.9)	19.0 (12.3 to 25.4)
Day 3 of treatment			
Overall success	318 (92.2)	293 (88.0)	4.1 (−0.6 to 8.9)
Clinical cure	18 (5.2)	16 (4.8)	0.5 (−3.1 to 4.0)
Improvement[d]	317 (91.9)	302 (90.7)	Not determined
Microbiological eradication	323 (93.6)	299 (89.8)	3.8 (−0.6 to 8.3)
End of treatment			
Overall success	318 (92.2)	311 (93.4)	−1.3 (−5.3 to 2.9)
Clinical cure	323 (93.6)	315 (94.6)	−1.1 (−4.8 to 2.7)
Microbiological eradication	332 (96.2)	322 (96.7)	−0.7 (−3.7 to 2.5)
Day 21[e]			
Overall success	236 (68.4)	196 (58.9)	10.7 (3.4 to 17.8)
Clinical cure	299 (86.7)	279 (83.8)	2.8 (−2.7 to 8.3)
Microbiological eradication	258 (74.8)	221 (66.4)	9.5 (2.6 to 16.3)

Figure 2. Subgroup Analyses in the Primary Analysis Set

Subgroup	No./total (%) Cefepime/ enmetazobactam (n = 345)	Piperacillin/ tazobactam (n = 333)	Treatment difference, % (95% CI)
Age, y			
<65	172/209 (82.3)	137/220 (62.3)	21.5 (12.9 to 29.6)
65 to <75	65/85 (76.5)	36/70 (51.4)	25.3 (9.2 to 40.2)
≥75	36/51 (70.6)	23/43 (53.5)	24.0 (2.8 to 43.0)
Sex			
Male	114/144 (79.2)	74/127 (58.3)	20.1 (8.7 to 30.8)
Female	159/201 (79.1)	122/206 (59.2)	21.9 (12.9 to 30.4)
Baseline eGFR group, mL/min/1.73 m^2			
<30	1/2 (50.0)	1/5 (20.0)	0.0 (-57.3 to 57.3)
30-59	59/79 (74.7)	43/75 (57.3)	15.6 (0.1 to 30.2)
60-89	151/187 (80.7)	107/166 (64.5)	17.5 (8.0 to 26.8)
≥90	50/63 (79.4)	39/66 (59.1)	21.1 (4.4 to 36.2)
Infection type			
Acute pyelonephritis	144/171 (84.2)	115/178 (64.6)	19.3 (10.1 to 28.0)
Complicated UTI with removable source of infection	53/75 (70.7)	39/73 (53.4)	19.3 (3.4 to 34.1)
Complicated UTI without removable source of infection	76/99 (76.8)	42/82 (51.2)	26.7 (12.6 to 39.6)
Prior antibiotic therapy			
Short-acting antibiotic up to 24 h	23/25 (92.0)	14/23 (60.9)	29.8 (3.0 to 52.1)
None	250/320 (78.1)	182/310 (58.7)	20.3 (13.1 to 27.3)
Region			
Eastern Europe	197/238 (82.8)	153/240 (63.8)	19.3 (11.4 to 26.9)
Americas	17/22 (77.3)	13/22 (59.1)	16.9 (-10.7 to 41.3)
Other countries	59/85 (69.4)	30/71 (42.3)	28.7 (12.7 to 42.8)
Baseline Charlson Comorbidity Index score			
<3	163/198 (82.3)	126/205 (61.5)	21.5 (12.6 to 29.8)
>3	109/145 (75.2)	69/125 (55.2)	20.4 (8.7 to 31.4)
Presence of concurrent bacteremia at baseline			
Yes	27/38 (71.1)	14/28 (50.0)	23.3 (-1.5 to 45.9)
No	246/307 (80.1)	182/305 (59.7)	21.5 (14.2 to 28.5)
Race			
Black or African American	0/1	0	Not determined
White	260/327 (79.5)	186/316 (58.9)	21.6 (14.5 to 28.5)
Other (not including African descent)[a]	13/17 (76.5)	10/17 (58.8)	19.2 (-13.4 to 46.9)
Diabetes at baseline			
Yes	41/55 (74.5)	19/41 (46.3)	25.6 (4.8 to 44.1)
No	232/290 (80.0)	177/292 (60.6)	20.9 (13.4 to 28.1)
Enterobacterales baseline pathogen, ESBL-producing	56/76 (73.7)	34/66 (51.5)	30.2 (13.4 to 45.1)



Sulopenem for the Treatment of Complicated Urinary Tract Infections Including Pyelonephritis: A Phase 3, Randomized Trial

Background. Sulopenem is a thiopenem antibiotic being developed for the treatment of multidrug-resistant infections. The availability of both intravenous (IV) and oral formulations will facilitate earlier hospital discharge.

Methods. Hospitalized adults with pyuria, bacteriuria, and signs and symptoms of complicated urinary tract infection (cUTI) were randomized to 5 days of IV sulopenem followed by oral sulopenem etzadroxil/probenecid or 5 days of IV ertapenem followed by oral ciprofloxacin or amoxicillin-clavulanate, depending on uropathogen susceptibility. The primary end point was overall combined clinical and microbiologic response at the test-of-cure visit (day 21).

Dunne MW, CID 2022

Table 1. Patient Demographics: Primary Analysis Population: Microbiologic Modified Intent-to-Treat

Parameter	Sulopenem (N = 444), n (%)	Ertapenem (N = 440), n (%)
Age, mean (SD), years	57.4 (18.4)	59.5 (17.9)
Type of infection		
Pyelonephritis	261 (58.8)	257 (58.4)
cUTI	183 (41.2)	183 (41.6)
Baseline pathogen from urine or blood culture[b]		
Escherichia coli	338/444 (76.1)	346/440 (78.6)
Klebsiella pneumoniae	56/444 (12.6)	47/440 (10.7)
Proteus mirabilis	26/444 (5.9)	14/440 (3.2)
Enterobacter cloacae complex	9/444 (2.0)	15/440 (3.4)
Klebsiella oxytoca	7/444 (1.6)	7/440 (1.6)
Other[c]	28/444 (6.3)	30/440 (6.8)
ESBL-positive Enterobacterales	110/444 (24.8)	125/440 (28.4)
FQ-nonsusceptible Enterobacterales	162/444 (36.5)	179/440 (40.7)
TMP-SMX–nonsusceptible Enterobacterales	154/444 (34.7)	161/440 (36.6)
ESBL-positive/FQ-nonsusceptible	91/444 (20.5)	99/440 (22.5)
ESBL-positive/FQ-nonsusceptible/TMP-SMX–nonsusceptible	58/444 (13.1)	75/440 (17.0)

Table 3. Primary and Additional Key Efficacy End Points

Outcome	Sulopenem (N = 444), n (%)	Ertapenem (N = 440), n (%)	Difference, % (95% Confidence Interval
Microbiologic modified intent-to-treat population			
Overall response at TOC (primary end point)			
Overall responder	301 (67.8)	325 (73.9)	−6.1 (−12.0 to −.1)
Overall nonresponder	126 (28.4)	93 (21.1)	
Indeterminate	17 (3.8)	22 (5.0)	
Clinical response at TOC			
Success	397 (89.4)	389 (88.4)	1.0 (−3.1 to 5.1)
Failure	33 (7.4)	34 (7.7)	
Indeterminate	14 (3.2)	17 (3.9)	
Microbiologic response per patient at TOC			
Success	316 (71.2)	343 (78.0)	−6.8 (−12.5 to −1.1)
Failure	111 (25.0)	74 (16.8)	
Indeterminate	17 (3.8)	23 (5.2)	
Overall success at TOC by baseline infection type			
Pyelonephritis	179/261 (68.6)	186/257 (72.4)	−3.8 (−11.6 to 4.1)
Complicated urinary tract infection	122/183 (66.7)	139/183 (76.0)	−9.3 (−18.5 to −.1)
Overall success at day 5			
Cure	198 (44.6)	193 (43.9)	0.7 (−5.8 to 7.3)
Cure + Improved[a]	360 (81.1)	352 (80.0)	1.1 (−4.2 to 6.3)
Clinical success			
Cure	203 (45.7)	196 (44.5)	1.2 (−5.4 to 7.7)
Cure + Improved[a]	369 (83.1)	362 (82.3)	0.8 (−4.2 to 5.9)
Microbiologic success	427 (96.2)	419 (95.2)	0.9 (−1.7 to 3.6)
Overall success at end of treatment (day 10)	385 (86.7)	391 (88.9)	−2.2 (−6.5 to 2.2)
Clinical success	399 (89.9)	399 (90.7)	−0.8 (−4.7 to 3.1)
Microbiologic success	418 (94.1)	421 (95.7)	−1.5 (−4.4 to 1.4)
Clinical success at final visit (day 28)	386 (86.9)	383 (87.0)	−0.1 (−4.5 to 4.3)
Clinical response at TOC (intention-to-treat population)	615/697 (88.2)	603/698 (86.4)	1.8 (−1.6 to 5.3)
Clinical response at TOC (modified intent-to-treat population)	615/695 (88.5)	603/697 (86.5)	2.0 (−1.5 to 5.4)

Abbreviation: TOC, test of cure.

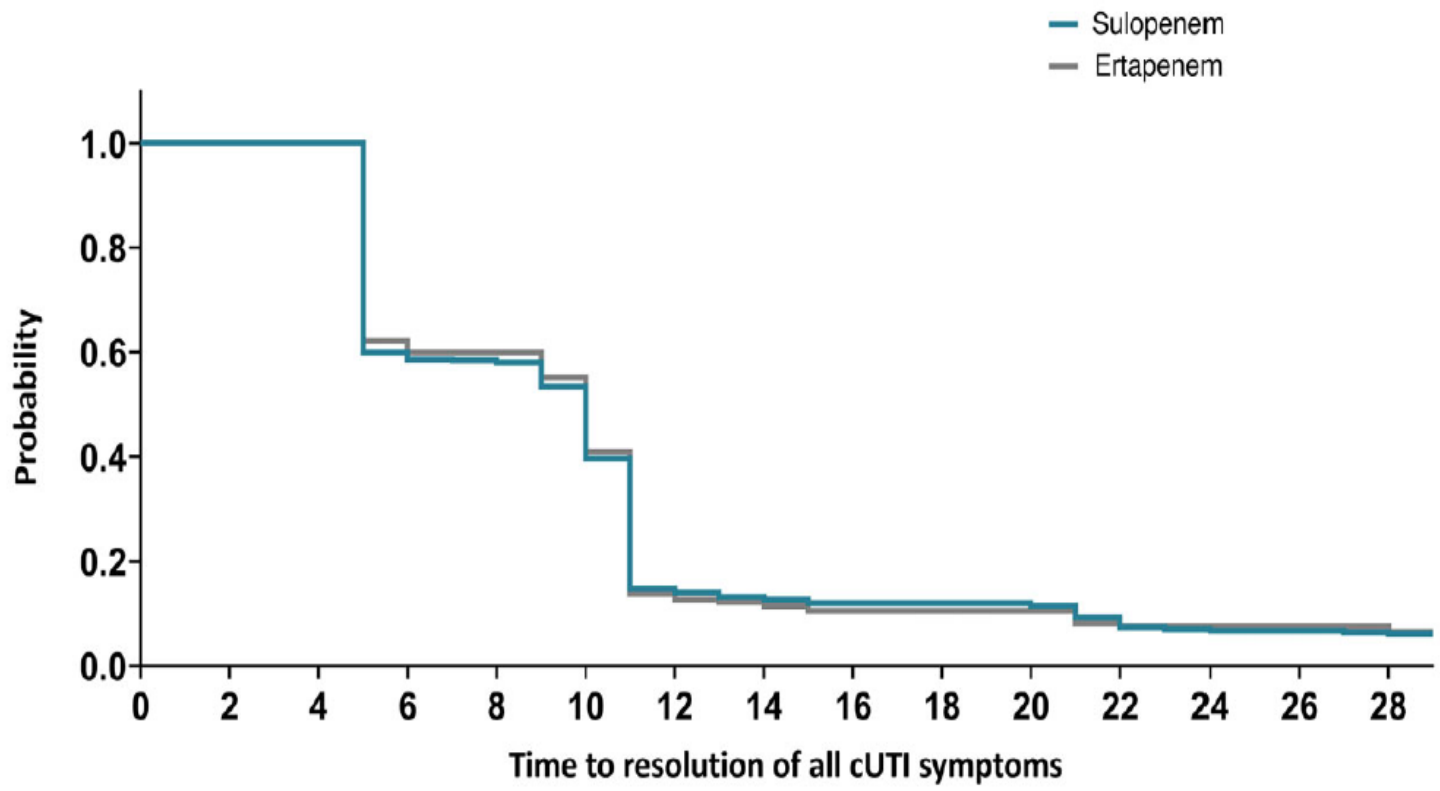


Figure 2. Time to resolution (days) of all cUTI symptoms, survival and without nonstudy antibiotic use. Patients who received rescue antibiotic prior to resolution or who died without resolution were censored at day 29. Abbreviation: cUTI, complicated urinary tract infection.

Oral Tebipenem Pivoxil Hydrobromide in Complicated Urinary Tract Infection

BACKGROUND

There is a need for oral antibiotic agents that are effective against multidrug-resistant gram-negative uropathogens. Tebipenem pivoxil hydrobromide is an orally bioavailable carbapenem with activity against uropathogenic Enterobacterales, including extended-spectrum beta-lactamase–producing and fluoroquinolone-resistant strains.

METHODS

In this phase 3, international, double-blind, double-dummy trial, we evaluated the efficacy and safety of orally administered tebipenem pivoxil hydrobromide as compared with intravenous ertapenem in patients with complicated urinary tract infection or acute pyelonephritis. Patients were randomly assigned, in a 1:1 ratio, to receive oral tebipenem pivoxil hydrobromide (at a dose of 600 mg every 8 hours) or intravenous ertapenem (at a dose of 1 g every 24 hours) for 7 to 10 days (or up to 14 days in patients with bacteremia). The primary efficacy end point was overall response (a composite of clinical cure and favorable microbiologic response) at a test-of-cure visit (on day 19, within a ±2-day window) in the microbiologic intention-to-treat population. The noninferiority margin was 12.5%.

Eckburg PB, NEJM 2022

Table 1. Characteristics of the Patients at Baseline (Microbiologic Intention-to-Treat Population).*

Characteristic	Tebipenem Pivoxil Hydrobromide (N=449)	Ertapenem (N=419)	Overall (N=868)
Age — yr	57.6±18.7	58.7±17.9	58.1±18.3
Infection type — no. (%)§			
Complicated urinary tract infection	223 (49.7)	218 (52.0)	441 (50.8)
Acute pyelonephritis	226 (50.3)	201 (48.0)	427 (49.2)
Infection with resistant Enterobacterales pathogen — no. of patients with resistant pathogen/ total no. with Enterobacterales pathogen (%)¶‖			
ESBL-positive	105/396 (26.5)	85/386 (22.0)	190/782 (24.3)
Fluoroquinolone-nonsusceptible	159/396 (40.2)	146/386 (37.8)	305/782 (39.0)
TMP-SMX–resistant	168/396 (42.4)	168/386 (43.5)	336/782 (43.0)

Table 2. Primary and Secondary Efficacy End Points (Microbiologic Intention-to-Treat Population).

End Point	Tebipenem Pivoxil Hydrobromide (N=449)	Ertapenem (N=419)	Treatment Difference (95% CI)*
	number (percent)		*percentage points*
Primary end point			
Overall response at test-of-cure visit†	264 (58.8)	258 (61.6)	−3.3 (−9.7 to 3.2)
Secondary end points			
Overall response at end-of-treatment visit†	437 (97.3)	396 (94.5)	2.8 (0.1 to 5.7)
Clinical response‡			
Clinical improvement at day 5	336 (74.8)	321 (76.6)	−1.9 (−7.6 to 3.8)
Clinical cure at end-of-treatment visit	446 (99.3)	410 (97.9)	1.4 (−0.1 to 3.4)
Clinical cure at test-of-cure visit	418 (93.1)	392 (93.6)	−0.6 (−4.0 to 2.8)
Sustained clinical cure at late follow-up	398 (88.6)	377 (90.0)	−1.5 (−5.7 to 2.6)
Microbiologic response§			
Response at day 5	427 (95.1)	397 (94.7)	0.3 (−2.7 to 3.4)
Response at end-of-treatment visit	439 (97.8)	403 (96.2)	1.5 (−0.8 to 4.1)
Response at test-of-cure visit	267 (59.5)	266 (63.5)	−4.5 (−10.8 to 1.9)
Sustained response at late follow-up	257 (57.2)	244 (58.2)	−1.5 (−7.9 to 5.0)

Subgroup	Tebipenem Pivoxil Hydrobromide	Ertapenem	Difference (95% CI)
	no. of events/total no. (%)		*percentage points*
Overall	264/449 (58.8)	258/419 (61.6)	−3.3 (−9.7 to 3.2)
Age at informed consent			
≥18 to <65 yr	164/246 (66.7)	145/222 (65.3)	1.4 (−7.2 to 9.9)
≥65 to <75 yr	60/122 (49.2)	76/132 (57.6)	−8.4 (−20.6 to 3.8)
≥75 yr	40/81 (49.4)	37/65 (56.9)	−7.5 (−23.8 to 8.7)
Sex			
Male	111/197 (56.3)	104/166 (62.7)	−6.3 (−16.4 to 3.8)
Female	153/252 (60.7)	154/253 (60.9)	−0.2 (−8.7 to 8.4)
Baseline diagnosis			
Acute pyelonephritis	149/226 (65.9)	142/201 (70.6)	−4.7 (−13.5 to 4.1)
Complicated urinary tract infection	115/223 (51.6)	116/218 (53.2)	−1.6 (−11.0 to 7.7)
Creatinine clearance			
>30 to ≤50 ml per minute	26/53 (49.1)	19/46 (41.3)	7.8 (−11.8 to 27.3)
>50 ml per minute	237/394 (60.2)	235/366 (64.2)	−4.1 (−10.9 to 2.8)
Bacteremia			
Yes	34/47 (72.3)	35/53 (66.0)	6.3 (−11.8 to 24.4)
No	230/402 (57.2)	223/366 (60.9)	−3.7 (−10.7 to 3.2)
Modified SIRS criteria met			
Yes	66/98 (67.3)	53/73 (72.6)	−5.3 (−19.1 to 8.6)
No	198/351 (56.4)	205/346 (59.2)	−2.8 (−10.2 to 4.5)
Previous antibiotic use			
Yes	12/19 (63.2)	16/22 (72.7)	−9.6 (−38.1 to 19.0)
No	252/430 (58.6)	242/397 (61.0)	−2.4 (−9.0 to 4.3)

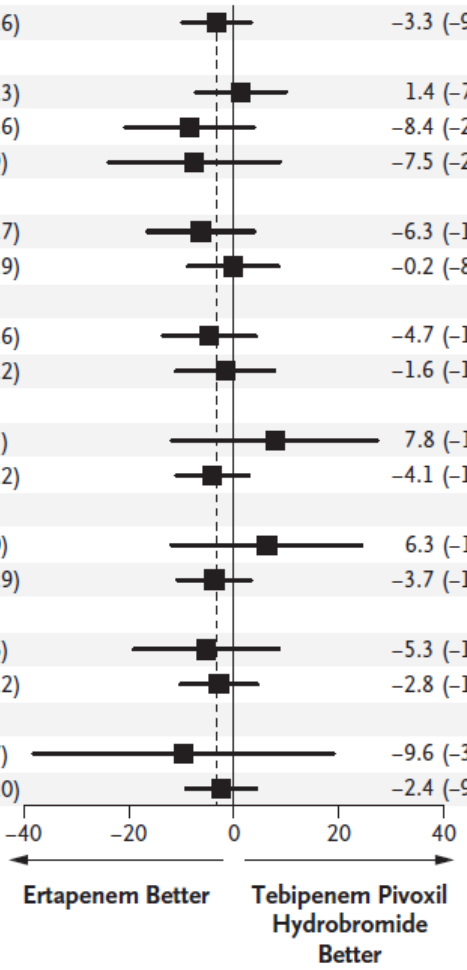


Figure 2. Overall Response at Test-of-Cure Visit According to Characteristics of the Patients at Baseline.

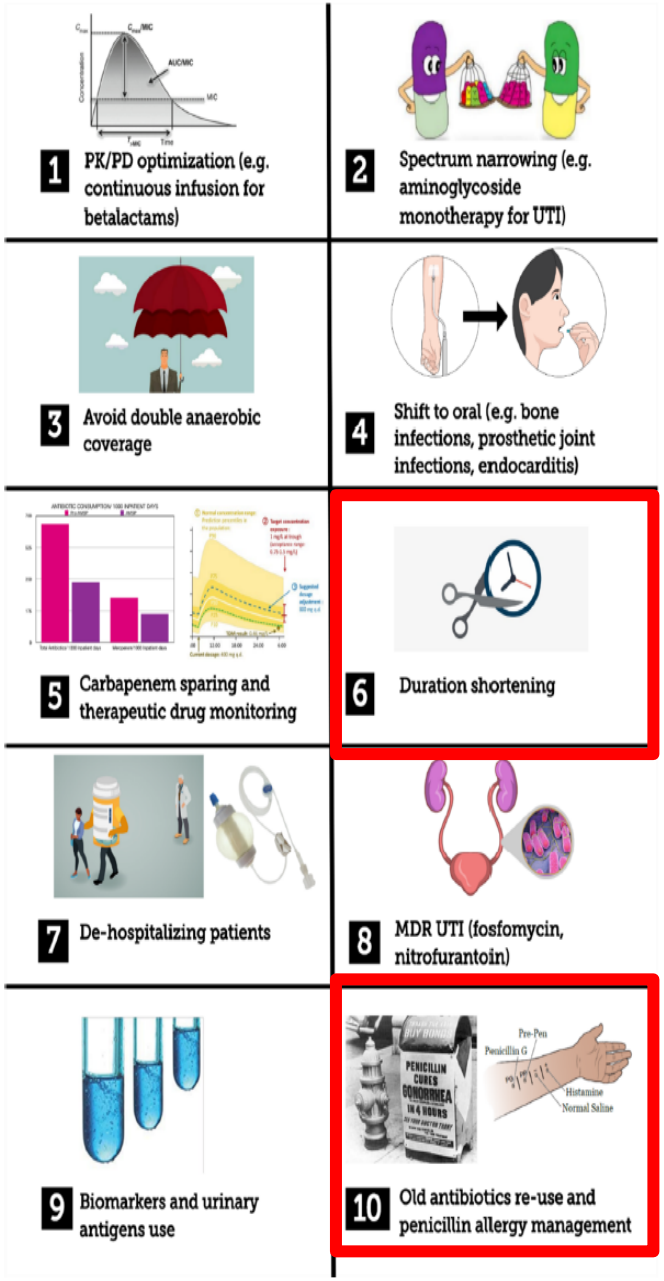


Figure 1. Graphical summary of stewardship interventions described in the manuscript. MDR: multidrug resistant; PK/PD: pharmacokinetic/pharmacodynamics; UTI: urinary tract infection

Di Bella S & Luzzati R. Antibiotics, 2020

Review

Temocillin: Applications in Antimicrobial Stewardship as a Potential Carbapenem-Sparing Antibiotic

Abstract: Temocillin is an old antibiotic, but given its particular characteristics, it may be a suitable alternative to carbapenems for treating infections due to ESBL-producing *Enterobacterales* and uncomplicated UTI due to KPC-producers. In this narrative review, the main research question was to summarize current evidence on temocillin and its uses in infectious diseases. A search was run

Other advantages in temocillin use are that it is well-tolerated; it is associated with a low rate of *C. difficile* infections; it is active against ESBL, AmpC, and KPC-producing *Enterobacterales*; and it can be used in the OPAT clinical setting.

Lupia T, Antibiotics 2022

WHERE IT IS CURRENTLY USED AND AVAILABLE IN THE MARKET

Table 7 Clinical breakpoints of temocillin according to countries where temocillin is actually marketed

Country	MIC (mg/L)	
	S	R
Belgium [15]	≤16	≥32
UK, systemic infection [60]	≤8	>8
UK, uncomplicated UTI [60]	≤32	>32
France [61]	≤8	>8

S sensible strain, *R* resistant strain, *UTI* urinary tract infection

Clin Pharmacokinet (2018) 57:287–296
https://doi.org/10.1007/s40262-017-0584-7

REVIEW ARTICLE

Pharmacokinetics and Pharmacodynamics of Temocillin

Kevin Alexandre[1] · Bruno Fantin[2,3]

TEMOCILLIN
SUMMARY OF THE PROS AND CONS

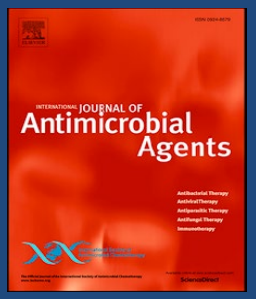
PROS

- Narrow spectrum of action
- Active against ESBL, KPC, AmpC *Enterobacteriaceae*
- Lower rates of *C. difficile* infections
- Milder side effects if compared with other β-lactams

CONS

- Clinical breakpoints and optimal dosing are still debated
- No experience of temocillin in human pregnancy
- Comparative studies are lacking
- Not marketed in Italy

Temocillin versus carbapenems for urinary tract infection due to ESBL-producing Enterobacteriaceae: a multicenter matched case-control study.



Methods: We conducted a multicenter retrospective case-control study of adults with ESBL-E UTI between January-2015 and October-2019. Cases received temocillin ≥50% of the effective antibiotic therapy duration. Control exclusively received carbapenem. They were statistically matched (1:1 ratio) on period, sex, and age. The clinical cure at the end of antibiotic therapy was analyzed using conditional logistic regression.

Deloroy T, 2021

Table 3: Occurrence of primary and secondary endpoints

Endpoints	Carbapenem *N* = 72	Temocillin *N* = 72	Total *N* = 142	OR †	95%CI	*p*-value
Clinical cure at EOT	71 / 72 (99%)	68 / 72 (94%)	139 /142 (97%)	0.24	(0.03 to 2.20)	0.206
Length of hospital-stay	8 days [5 to 18]	12 days [7 to 27]	10 days [6 to 23]	1.00	(0.99 to 1.01)	0.947
Effective antibiotic therapy duration	16 days [13 to 20]	14 days [11 to 17]	15 days [12 to 18]	0.93	(0.87 to 0.98)	0.067
Relapse of UTI	16 / 71 (23%)	17 / 68 (25%)	33 /139 (24%)	1.15	(0.52 to 2.50)	0.733
Time to relapse	9 days [6 to 34]	13 days [8 to 41]	11 days [7 to 34]	1.00	(0.99 to 1.01)	0.935
Re-hospitalization	39 / 71 (55%)	29 / 67 (43%)	68 / 138 (49%)	0.63	(0.32 to 1.23)	0.172
Time to re-hospitalization	11 days [6 to 38]	36 days [10 to 65]	20 days [9 to 51]	1.03	(1.01 to 1.05)	0.013
Clostridium difficile infection	4 / 64 (6%)	4 / 64 (6%)	8 / 128 (6%)	1.00	(0.24 to 4.17)	1.000
All-cause death	5 / 72 (7%)	6 / 71 (8%)	11 / 143 (8%)	1.02	(0.28 to 3.67)	0.981
Loss to follow-up	4 / 72 (6%)	10 / 72 (14%)	14 / 144 (10%)	2.74	(0.82 to 9.19)	0.102

†OR: Odds Ratio. For the computation of each OR, a conditional logistic regression is used, and the reference class is the carbapenem arm (control).

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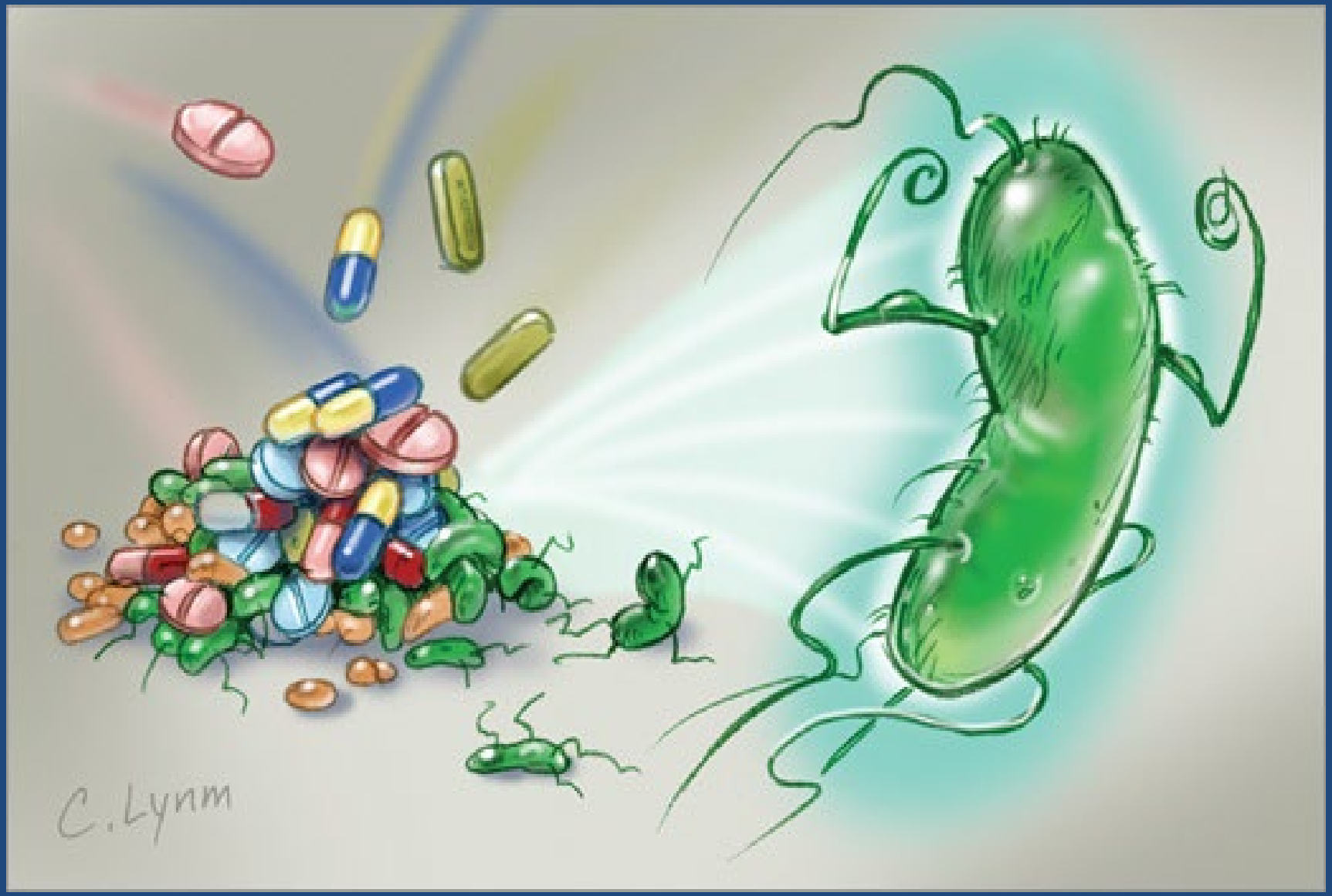
Narrative review

Short-course antibiotics for common infections: what do we know and where do we go from here?

[4,24]. Current guidelines recommend 7–14 days of antibiotic therapy for women with pyelonephritis but do not comment on men given lack of data [25].

Data consistently show that the short-duration courses are appropriate for the management of complicated UTI and pyelonephritis, with appropriate diagnosis based on clinical response. More data are needed in men to confirm that short-duration courses are as effective as long-duration courses for the treatment of complicated UTI.

Lee R, CMI 2022


C.Lynm