Clinical Practice Guideline by Infectious Diseases Society of America (IDSA): 2025 Guideline on Management and Treatment of Complicated Urinary Tract Infections

Supplementary material for Timing of Intravenous to Oral Antibiotics Transition for Complicated UTI

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Literature Search Strategies (last updated on September 15th, 2024)

Medline (PubMed)

1. urinary tract infection[MeSH Terms]
2. "urinary tract infection" OR "urinary tract infections"
3. cystitis[MeSH Terms]
4. cystitis
5. pyelonephritis[MeSH Terms]
6. pyelonephritis
7. 1 OR 2 OR 3 OR 4 OR 5 OR 6
8. administration, oral[MeSH Terms]
9. oral*
10. per os
11. switch
12. 8 OR 9 OR 10 OR 11
13. injections[MeSH Terms]
14. infusions, parenteral[MeSH Terms]
15. intra-venous OR intravenous OR intramuscular
16. 13 OR 14 OR 15
17. 12 AND 16
18. anti-bacterial agents[MeSH Terms]
19. antibiotic*
20. antimicrobial*
21. antibacterial*
22. 18 OR 19 OR 20 OR 21
23. 17 AND 22
24. 16 AND 22
25. 23 OR 24
26. 7 AND 25
27. “randomized controlled trial” OR “clinical trial” OR "randomized controlled trial"[Publication Type] OR "clinical trial"[Publication Type] OR "clinical trial, phase i"[Publication Type] OR "clinical trial, phase ii"[Publication Type] OR "clinical trial, phase iii"[Publication Type] OR "clinical trial, phase iv"[Publication Type]
28. 26 AND 27
29. "2000"[Date - Publication] : "3000"[Date - Publication]
30. 28 AND 29
31. "english"[Language]
32. 30 AND 31

Embase

1. 'cystitis'/de OR cystitis
2. 'urinary tract infection'/de OR 'urinary tract infection' OR 'urinary tract infections'
3. 'pyelonephritis'/de OR pyelonephritis
4. 1 OR 2 OR 3
5. ‘oral drug administration’/de

6. oral*
7. ‘per os’
8. switch
9. 5 OR 6 OR 7 OR 8
10. ‘injection’/de
11. ‘parenteral drug administration’/de
12. ‘intra venous’ OR intravenous OR intramuscular
13. 10 OR 11 OR 12
14. 9 AND 13
15. ‘antiinfective agent’/de
16. antibiotic*
17. antimicrobial*
18. antibacterial*
19. 15 OR 16 OR 17 OR 18
20. 14 AND 19
21. 13 AND 19
22. 20 OR 21
23. 4 AND 22
24. 'clinical trial'/de OR 'controlled clinical trial'/de OR 'phase 2 clinical trial'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial' OR 'clinical trial'
25. 23 AND 24
26. 2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py
27. 25 AND 26
28. english:la
29. 27 AND 28

Cochrane

1. MeSH descriptor: [Cystitis] explode all trees
2. MeSH descriptor: [Urinary Tract Infections] explode all trees
3. MeSH descriptor: [Pyelonephritis] explode all trees
4. cystitis
5. pyelonephritis
6. "urinary tract infection" OR "urinary tract infections"
7. #1 OR #2 OR #3 OR #4 OR #5 OR #6
8. MeSH descriptor: [Administration, Oral] explode all trees
9. oral*
10. "per os"
11. switch
12. #8 OR #9 OR #10 OR #11
13. MeSH descriptor: [Injections] explode all trees
14. MeSH descriptor: [Infusions, Parenteral] explode all trees

15. intra-venous OR intravenous OR intramuscular
16. #13 OR #14 OR #15
17. #12 AND #16
18. MeSH descriptor: [Anti-Bacterial Agents] explode all trees
19. antibiotic* OR antimicrobial* OR antibacterial*
20. #18 OR #19
21. #17 AND #20
22. #16 AND #20
23. #21 OR #22
24. #7 AND #23

Eligibility criteria for selection of studies

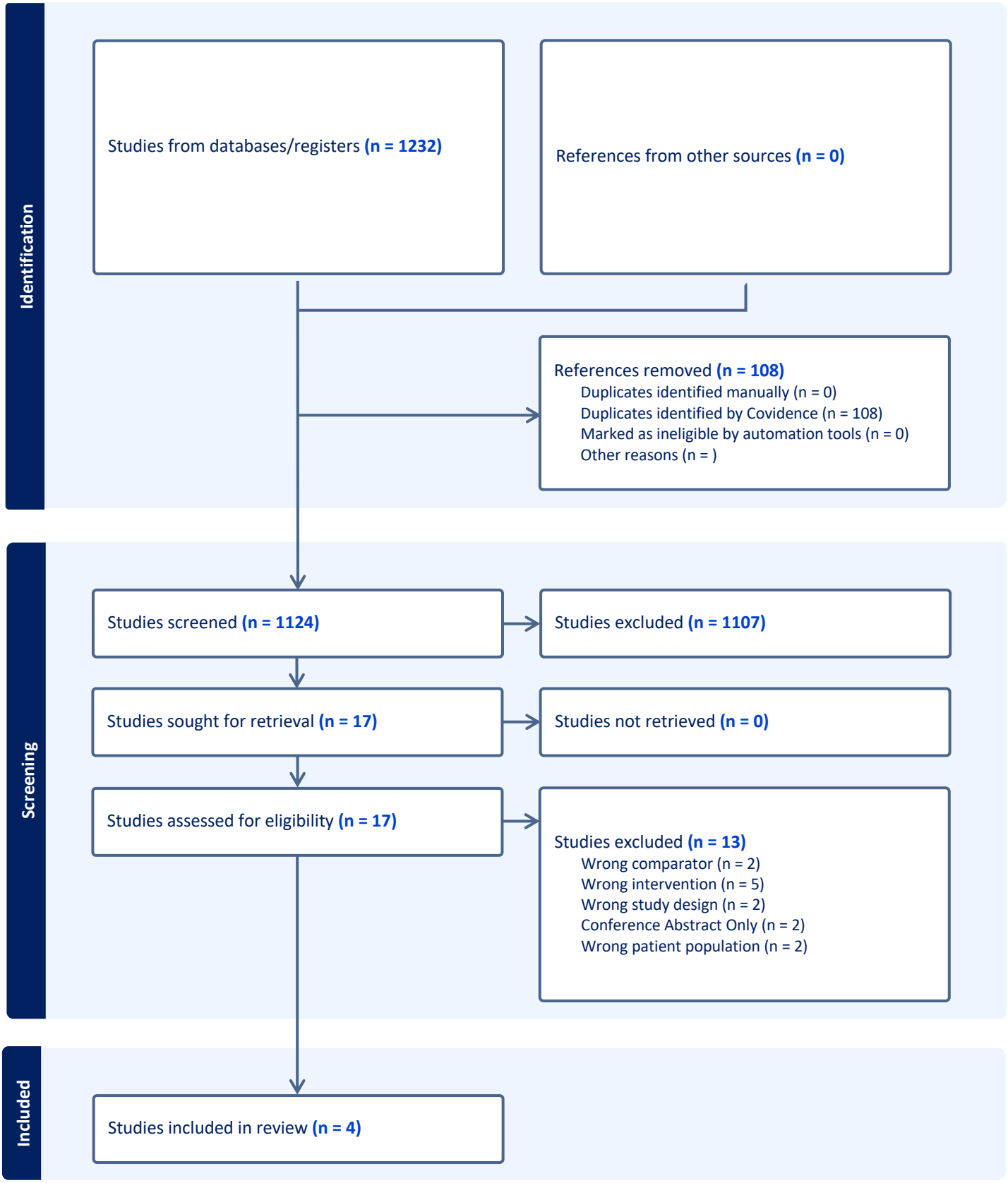
Inclusion criteria:

- Patient population: Adults patients being treated parenterally for cUTI (with or without bacteriemia)
- Intervention:
    - -Transition from parenteral to oral antibiotics
    - -Timing of transition = when patients are clinically stable, are able to take an oral medication and for whom an oral option is available
    - -No restriction based on the choice of antibiotics
- Comparator:
    - -Completing treatment with parenteral antibiotics
    - -No restriction based on the choice of antibiotics
- -Outcomes
    - -Minimally including clinical cure (at EOT)
- Study design: Randomized controlled trials (RCTs)
- Year: published from 2000 up to present
- Language: English only

Exclusion criteria:

- -Patient population:
    - -Children
    - -Renal transplant patients
    - -Neutropenic patients
    - -Pregnant women and lactating women
    - -Uncomplicated UTI
- -Intervention / Comparator = supporting indirect evidence only
    - -Single dose of IV/IM followed by oral antibiotics vs oral antibiotics (complete course)
    - -Single dose of IV/IM followed by oral antibiotics vs switch therapy
    - -Oral vs parenteral antibiotics (complete course)
    - -Oral antibiotics (complete course) vs switch therapy
- -Outcomes
    - -Not including clinical cure or success (at EOT or TOC)

Supplementary Figure 1: Prisma Flow Diagram of study identification and selection (last updated on September 15th, 2024)



Supplementary Table 1: GRADE Evidence Profile

Question: In patients being treated parenterally for complicated UTI, are clinically stable, can take an oral medication and for whom an oral option is available, should parenteral therapy be transitioned to oral rather than continued for the complete duration of therapy?

P: In patients being treated parenterally for complicated UTI, are clinically stable, can take an oral medication and for whom an oral option is available
I: parenteral therapy transitioned to oral therapy
C: parenteral therapy continued for the complete duration of therapy
Setting: Inpatient and Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Transition IV to PO*	Completion with IV*	Relative (95% CI)	Absolute (95% CI)		
Clinical cure (at End Of Therapy (EOT) or Test-Of-Cure (TOC))												
4[1-4]	randomised trials	serious[a]	not serious	not serious[b]	serious[c,d]	none	85/94 (90.4%)	83/92 (90.2%)	**RR 1.02** (0.96 to 1.08)	**18 more per 1,000** (from 36 fewer to 72 more)	⊕⊕◯◯ Low	CRITICAL
Recurrence of UTI (at 4 to 6 weeks)												
3[1,2,4]	randomised trials	serious[a]	not serious	not serious[b]	serious[d,e]	none	0/70 (0.0%)	2/67 (3.0%)	**RR 0.33** (0.04 to 3.05)	**20 fewer per 1,000** (from 29 fewer to 61 more)	⊕⊕◯◯ Low	IMPORTANT
Length of hospital stay (days)												
1[3]	randomised trials	serious[f]	not serious	serious[g]	serious[c]	none	Median 10.9 days (n=23)	Median 17.2 days (n=24)	-	MD **6.3 days fewer** (11.78 fewer to 0.82 fewer)	⊕◯◯◯ Very low	IMPORTANT
Serious Antibiotic Adverse Events												
4[1-,4]	randomised trials	serious[f]	not serious	not serious[c]	serious[e]	none	1/94 (1.1%)	2/92 (2.2%)	**RR: 0.65** (0.11 to 3.88)	**8 fewer per 1,000** (from 19 fewer to 63 more)	⊕⊕◯◯ Low	IMPORTANT
IV Catheter Related Adverse Events												
1[1]	randomised trials	serious[a]	not serious	not serious[b]	very serious[e,h]	none	0/41 (0.0%)	2/41 (4.9%)	**RR 0.20** (0.01 to 4.04)	**49 fewer per 1,000** (from 115 fewer to 17 more)	⊕◯◯◯ Very low	IMPORTANT
Non-Serious Antibiotic Adverse Events												
3[1,2,4]	randomised trials	serious[a]	not serious	not serious[b]	very serious[e,h]	none	3/71 (4.2%)	2/68 (2.9%)	**RR 1.35** (0.27 to 6.67)	**10 more per 1,000** (from 21 fewer to 167 more)	⊕◯◯◯ Very low	IMPORTANT

Notes:
*The choice of antimicrobial therapy varied between studies: IV ceftriaxone followed by oral cefditoren pivoxil versus IV ceftriaxone (Monmaturapoj 2012), IV carbapenems followed by oral sitafloxacin versus IV ertapenem (Malaisri 2017), IV levofloxacin with/without IV amikacin X 3-7 days followed by oral levofloxacin versus IV piperacillin-tazobactam +/- IV amikacin X 3-7 days (Concia 2006), and IV 3rd generation cephalosporin followed by either prulifloxacin versus IV ertapenem.
**Rehospitalisation / Readmission – this outcome (judged important for decision-making) was not reported in the 4 studies included in this table.

UTI: urinary tract infection;.**IV**: parenteral; **PO**: oral; **CI:** confidence interval; **RR:** risk ratio.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Transition IV to PO*	Completion with IV*	Relative (95% CI)	Absolute (95% CI)		

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

GRADE domains

Risk of bias: Study limitations
Inconsistency: Unexplained heterogeneity across study findings
Indirectness: Applicability or generalizability to the research question
Imprecision: The confidence in the estimate of an effect to support a particular decision
Publication bias: Selective publication of studies

Explanations

a. Monmaturapoj 2012 was judged to be at high risk of bias due to potential financial bias favoring oral switch (research grant funded by industry, which was related to the oral antibiotic). The three other trials judged at high risk of bias mainly due to the unblinded design that could have biased the occurrence, the measurement, or the interpretation of outcomes.
b. Concia 2006 included adult patients with uUTI or cUTI associated with confirmed or suspected sepsis. So-Ngern 2023, Malaisri 2017 and Monmaturapoj 2012 included hospitalized and non-hospitalized adult patients with presumptive diagnosis of acute pyelonephritis, but both So-Ngrern 2023, Malaisri 2017 restricted their inclusion to ESBL-producing organisms.
c. Not fulfilling the optimal information size (IOS).
d. Based on an inferiority margin of 10%, not further rated down for imprecision.
e. Not fulfilling the optimal information size (IOS), but low baseline risk.
f. Concia 2006 is an open label study, thus at high risk of bias due to unblinded design.
g. Rated down for indirectness since length of hospitalization was likely influenced by the route of administration of antimicrobials (all patients received parenteral antibiotics throughout the study for the assigned duration in the hospital, without transferring to OPAT) (Concia 2006)
h. Wide 95% CI which are crossing the null value, thus cannot exclude the potential for no benefit or harm.

References

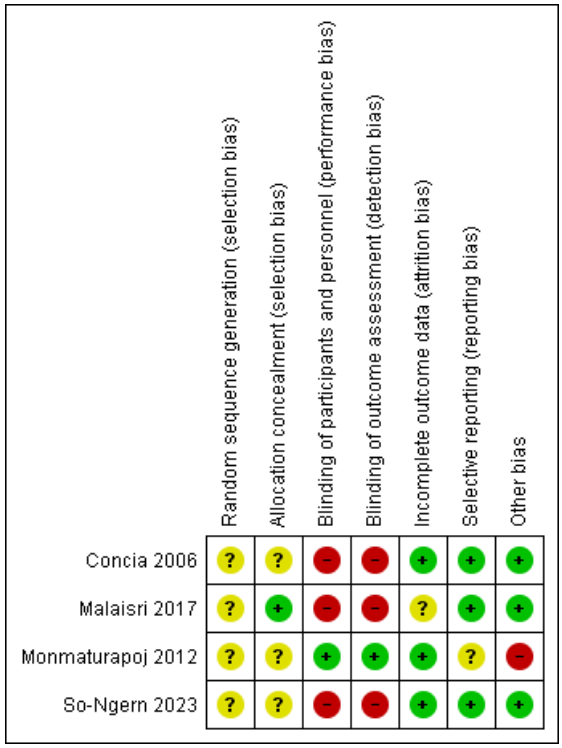
1.Monmaturapoj, T., Montakantikul, P., Mootsikapun, P., Tragulpiankit, P. A prospective, randomized, double dummy, placebo-controlled trial of oral cefditoren pivoxil 400mg once daily as switch therapy after intravenous ceftriaxone in the treatment of acute pyelonephritis. Int J Infect Dis; 2012.
2.Malaisri, C., Phuphuakrat, A., Wibulpolprasert, A., Santanirand, P., Kiertiburanakul, S. A randomized controlled trial of sitafloxacin vs. ertapenem as a switch therapy after treatment for acute pyelonephritis caused by extended-spectrum β-lactamase-producing Escherichia coli: A pilot study. Journal of Infection and Chemotherapy; 2017.
3.Concia, E., Marchetti, F.. Early discharge of hospitalised patients with community-acquired urosepsis when treated with levofloxacin in sequential therapy. Arch Ital Urol Androl; 2006.
4. So-Ngern A., Jirajariyavej S., Thuncharoon H., Khunthupat N., Chantarojanasiri T, Montakantikul P. A randomized, controlled trial of prulifloxacin as conversion therapy after intravenous carbapenem in the treatment of acute pyelonephritis caused by third generation cephalosporin resistant pathogens: A pilot study. Clin Transl Sci; 2023.

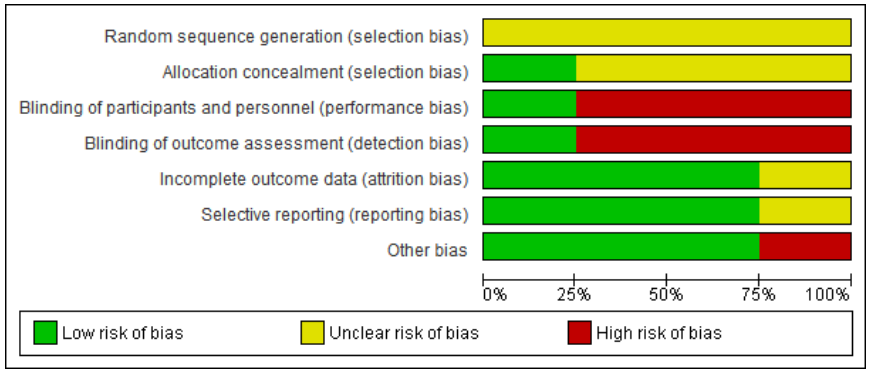
Supplementary Table 2: Characteristics of the included studies (n=4, 2000-2024)

Study *(Lead author, Year of publication, Name of trial, Countries)*	**Population** *(Type UTI, Year of enrollment, n randomised, F (%), Age in Intervention vs Comparator groups)*	**Study design** *(Non-inferiority margin if applicable, primary outcome with its timing)*	**Main uro-pathogens** (*% of resistance)*	**Timing of randomisation / Criteria for transition to PO**	**Intervention** *(IV and PO antibiotics, total duration)*	**Comparator** *(IV antibiotics, total duration)*
Concia 2006 Italy (multicentric)	cUTI or uUTI associated with confirmed/ suspected sepsis (not admitted to ICU) Year of enrollment: NR N= 47 F: NR Age (mean): 49.0 vs 59.0y	Descriptive trial CC 1 to 5 days after EOT	*E. coli* (87.5%) R: NR	Randomisation: at day 1 Criteria for transition to PO: after at least 3 days of IV if resolution of at least one of the clinical symptoms, afebrile on two consecutive measures, clinically stable with normal CNS and no GI disorders	IV levofloxacin with/without IV amikacin X 3-7 days followed by oral levofloxacin (switch occurred at a median of 5 days in 82.6% of this arm) Total duration: maximum of 14 days (median 11 days received)	IV piperacillin-tazobactam +/- IV amikacin X 3-7 days Total duration: maximum of 14 days (median of 17 days received)
Malaisri 2017 Thailand	Non-bacteremic presumptive AP caused by ESBL-*E. coli* 2012-2015 N= 36 F: 66.7% Age (median): 72.3 vs 65.0y	Descriptive trial CC at day EOT	*E. coli* (100%) R: ESBL-*E.coli* (100%), but 0% to ertapenem and 5.6% (2/36) to sitafloxacin	Randomisation: at day 3 Criteria for transition to PO: NR	IV carbapenems (meropenem, imipenem, doripenem or ertapenem) followed by oral sitafloxacin Total duration: 10 days	IV ertapenem Total duration: 10 days
Monmaturapoj 2012 Thailand	Presumptive AP 2010-2011 N= 82 F: 96.3% Age (mean): 41.7 vs 48.6y	Non-inferiority trial Margin 25% for CC at EOT	*E. coli* (83.5%) R: 31.6% to fluoroquinolones but 0% to studied drugs	Randomisation: at day 3 if criteria for transition to PO meet Criteria for transition to PO: (1) clinical improvement for at least 24 h from the initial presentation; (2) functioning GI tract; (3) afebrile; (4) trend towards normalized white blood cells and neutrophil count values	IV ceftriaxone x 3 days, followed by oral cefditoren pivoxil Total duration: 10 days	IV ceftriaxone Total duration: 10 days
So-Ngern 2023 Thailand (multicenter)	Non-bacteremic and bacteremic presumptive AP caused by ESBL producing organisms 2015-2020 N=21	Superiority trial CC at TOC	*E. coli* (85.7%) R: ESBL (100%), but no resistance to both studied drugs	Randomisation: at day 4 if criteria for transition to PO meet Criteria for transition to PO: (1) afebrile; (2) hemodynamically stable; (3) improvement in signs,	IV empiric antibiotics (most received a 3rd gen cephalosporin but 2 received ertapenem and 1 piperacillin-tazobactam),	IV empiric antibiotics (all received a 3rd gen cephalosporin), followed by IV ertapenem

	F: 90.5% Age (median): 73.0 vs 70.5y			symptoms, and leukocytosis; (4) resolution of nausea and vomiting; and (5) ability to adequately absorb oral medications or food; (6) for patients with bacteremic AP, no growth on the blood culture collected on day 4.	followed by oral prulifloxacin Total duration: 14 days	Total duration: 14 days
UTI=Urinary Tract Infection; cUTI=Complicated UTI; uUTI=Uncomplicated UTI; AP=acute pyelonephritis; ESBL=Extended-Spectrum Beta-Lactamase; N=number; F=female, y=years; ICU=intensive care unit; NR = not reported. CC=clinical cure or response; MC=microbiologic cure, eradication, or response; EOT = End of therapy; TOC = Test-Of-Cure. R=resistant, including non-susceptible; S=susceptible; IV=parenteral; PO=oral.						

Supplementary Figure 2: Summary of the Risk of Bias of included studies (Cochrane Risk of Bias tool) (n=4)





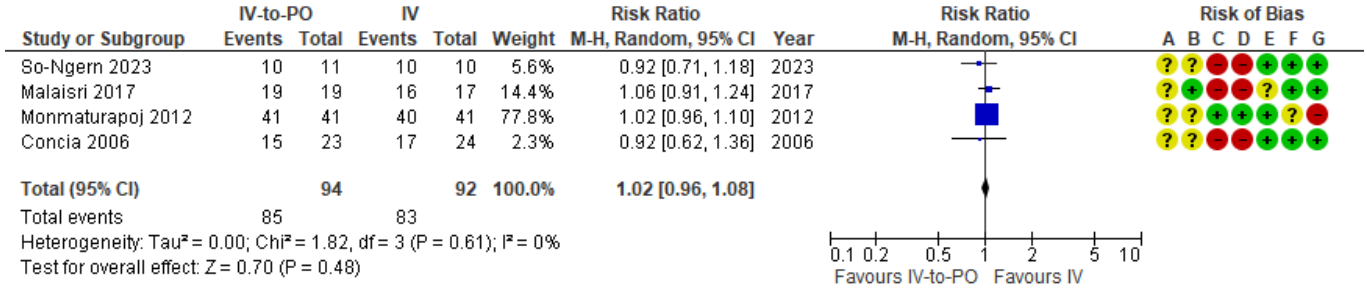
Supplementary Table 3: Assessment of the Risk of Bias of included studies (Cochrane Risk of bias Tool) (n=4)

Study *(Lead author, Year of publication, Name of trial, Countries)*	**Random sequence generation** (selection bias)	**Allocation concealment** (selection bias)	**Blinding of participants and personnel** (performance bias)	**Blinding of outcome assessment** (detection bias)	**Incomplete outcome data** (attrition bias)	**Selective reporting** (reporting bias)	**Other bias** (e.g. sources of funding)
Concia 2006 Italy (multicentric)	Unclear RoB -Randomized (no explanation) -No comparison of patients' characteristics at baseline and small sample size	Unclear RoB -Not reported	High RoB -Open-label (especially applicable to subjective outcomes)	High RoB -Open-label (especially applicable to subjective outcomes)	Low RoB -All outcomes measured in the ITT population	Low RoB	Low RoB -Industry-funded: grant unrelated to the studied molecules (involvement of industry not reported)
Malaisri 2017 Thailand	Unclear RoB -Randomized via a computer-generated random number allocation schedule with block size of four -Comparable patients' characteristics at baseline, except for higher frequency of prior urinary catheter in the IV group (comparison most likely underpowered)	Low RoB -Sealed envelope method	High RoB -Open-label (especially applicable to subjective outcomes)	High RoB -Open-label (especially applicable to subjective outcomes)	Low to Unclear RoB -All outcomes analysed in the ITT population -No significant lost to follow up at 10 days (e.g. clinical failure) -Significant lost to follow up after 30 days (lost to follow up in 4/19 (21%) in the group transitioning to oral vs 3/17 (18%) in the IV group) (e.g. recurrence of infection)	Low RoB	Low RoB -Industry-funded: grant related to one of the studied molecules, but the company had no part in the design or performance of the study, in the data analysis, in the writing or editing of the manuscript, or in the decision to submit the manuscript for publication
Monmaturapoj 2012 Thailand	Unclear RoB -Randomized via a computer-generated random number allocation schedule with block size of four -Possible failed randomization: IV group tended to be older, to be hospitalized more often and to have bacteremia more frequently than the group transitioned to oral therapy	Unclear RoB -Not reported	Low RoB -Double dummy	Low RoB -Double dummy	Low RoB -All outcomes were measured in the ITT population	Unclear RoB -Clinical response measured at 3 time points (24h after switch, at follow-up visit and at 2 weeks after the end of treatment) but only reported at the follow up visit	High RoB -Industry-funded: grant related to one of the studied molecules
So-Ngern 2023 Thailand	Unclear RoB -Randomized via a computer-generated	Unclear RoB -Not reported	High RoB -Open-label (especially	High RoB -Open-label (especially	Low RoB	Low RoB	Low RoB -Industry-funded: grant related to

(multicenter)	random number allocation schedule with block size of four -Possible failed randomization: the group transitioning to oral therapy tended to have more comorbidities such as diabetes mellitus more frequently than the IV group		applicable to subjective outcomes)	applicable to subjective outcomes)	-All outcomes analysed in the ITT population -No significant lost to follow up for clinical outcomes (clinical success or recurrence of infection)		one of the studied molecules, but the company had no part in the design of the study, in the data collection and analysis, decision to publish, or preparation of the manuscript.
RoB=Risk of Bias; IV=parenteral; ITT=intention-to-treat.							

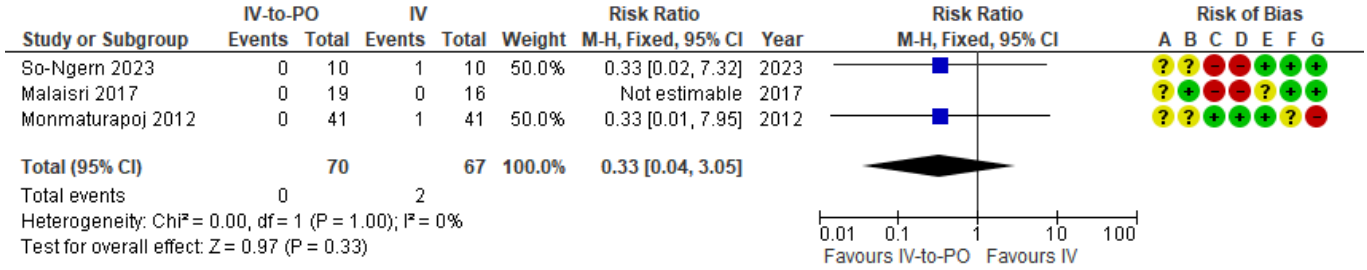
Supplementary Figures 3: Forest plots for each patient-important outcome

3a) Clinical cure (at End Of Therapy (EOT) or Test-Of-Cure (TOC))



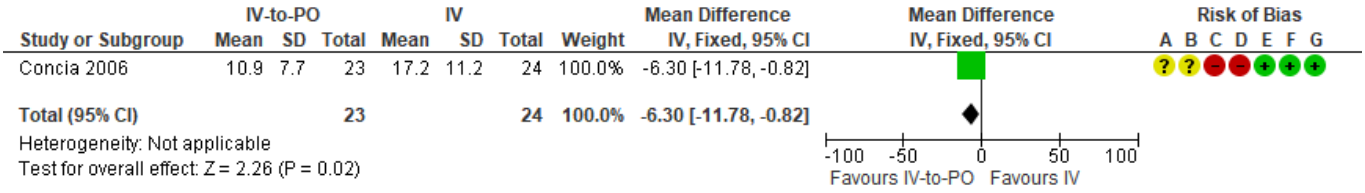
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

3b) Recurrence of UTI (at 4 to 6 weeks)



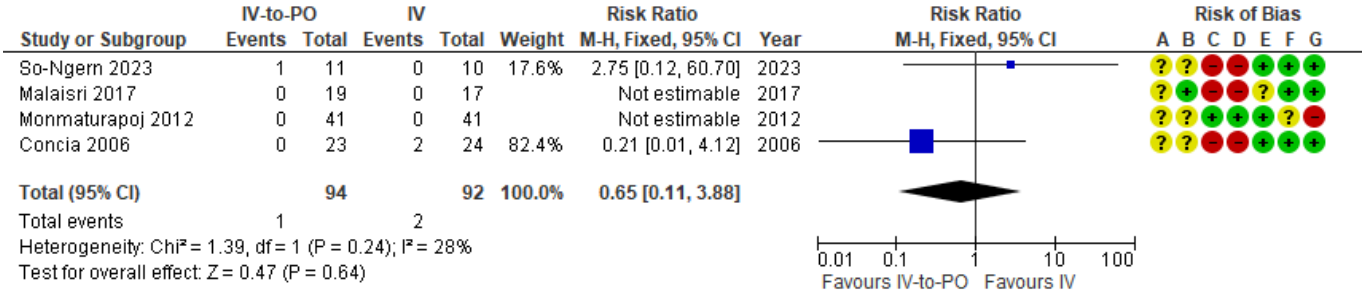
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

3c) Length of stay (days)



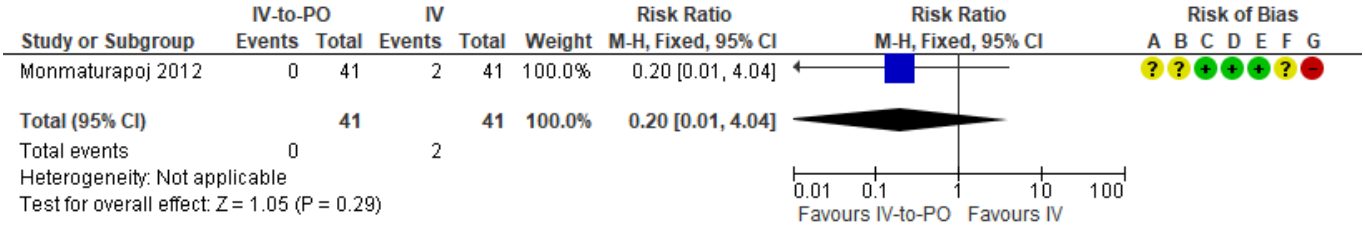
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

3d) Serious antibiotic adverse events



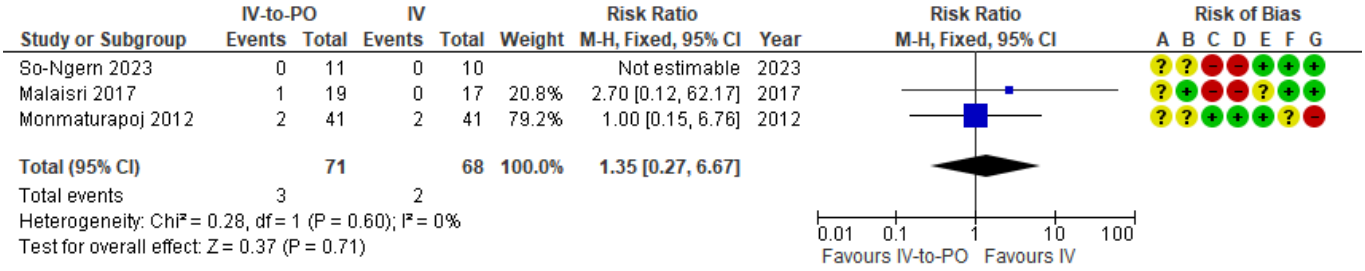
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

3e) IV catheter related adverse events



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

3f) Non-serious antibiotic adverse events



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Supplementary Table 4: GRADE Evidence to Decision framework

Summary of Judgments							
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	**Probably favors the intervention**	Favors the intervention	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	No included studies
ACCEPTABILITY / STEWARDSHIP	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	**Increased**	Varies	Don't know

Type of Recommendation				
Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	**Conditional recommendation for the intervention** ○	Strong recommendation for the intervention ○