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

Supplementary material for Duration of Antibiotics for Complicated UTI

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A) For all complicated UTI

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. duration*
- 9. "long course" OR "long courses"
- 10. "short course" OR "short courses"
- 11. "day course" OR "day regimen"
- 12. drug administration schedule[MeSH Terms]
- 13. time factors[MeSH Terms]
- 14. 8 OR 9 OR 10 OR 11 OR 12 OR 13
- 15. antibiotic*
- 16. antimicrobial*
- 17. antibacterial*
- 18. anti-bacterial agents[MeSH Terms]
- 19. 15 OR 16 OR 17 OR 18
- 20. 14 AND 19
- 21. 7 AND 20
- 22. "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]
- 23. 21 AND 22
- 24. "2000"[Date Publication] : "3000"[Date Publication]
- 25. 23 AND 24
- 26. "english"[Language]
- 27. 25 AND 26

Embase

- 1. 'cystitis'/exp OR cystitis
- 2. 'urinary tract infection'/exp OR 'urinary tract infection' OR 'urinary tract infections'
- 3. 'pyelonephritis'/exp OR pyelonephritis
- 4. 1 OR 2 OR 3
- 5. 'time factor'/exp
- 6. 'drug administration'/exp
- 7. duration*

- 8. 'long course' OR 'long courses'
- 9. 'short course' OR 'short courses'
- 10. 'day course' OR 'day regimen'
- 11. 'short term' OR 'long term'
- 12. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11
- 13. 'antiinfective agent'/exp
- 14. 'antiinfective agent'
- 15. antibiotic*
- 16. antimicrobial*
- 17. antibacterial*
- 18. 13 OR 14 OR 15 OR 16 OR 17
- 19. 12 AND 18
- 20. 4 AND 19
- 21. 'clinical trial'/de OR 'controlled clinical trial'/de OR 'phase 2 clinical trial'/de OR 'randomized controlled trial' OR 'clinical trial'
- 22. 20 AND 21
- 23. 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 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py
- 24. 22 AND 23
- 25. english:la
- 26. 24 AND 25

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. duration*
- 9. "long course" OR "long courses"
- 10. "short course" OR "short courses"
- 11. "day course" OR "day regimen"
- 12. MeSH descriptor: [Drug Administration Schedule] explode all trees
- 13. MeSH descriptor: [Time Factors] explode all trees
- 14. #8 OR #9 OR #10 OR #11 OR #12 OR #13
- 15. antibiotic*
- 16. antimicrobial*
- 17. antibacterial*
- 18. MeSH descriptor: [Anti-Bacterial Agents] explode all trees
- 19. #15 OR #16 OR #17 OR #18

20. #14 AND #19

21. #7 AND #20

Eligibility criteria for selection of studies

Inclusion criteria:

- Patient population: Adults patients being treated parenterally for cUTI (with or without bacteriemia)

- Intervention:

-Total duration of antibiotics between 5 to 7 days

- Comparator:
 - -Total duration of antibiotics between 10 to 14 days
- -Outcomes

-Minimally including clinical cure (at TOC)

- 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

- Total duration of antibiotics either shorter than 5 or longer than 14 days

-Outcomes

-Not including clinical cure (at 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 presenting with complicated UTI, should total duration of antibiotics be shorter (<=7 days) rather than prolonged to >7 days?

- P: In patients presenting with complicated UTII: shorter total duration of antibiotics (<=7 days)
- **C**: prolonged total duration of antibiotics (>7 days)

Setting: Inpatient and Outpatient

			Certainty as	sessment			Nº of	patients	E	Effect		
№ of studies	Study design	Risk of bias	Inconsistenc y	Indirectness	Imprecisio n	Other considerations	Shorter duration of Abx (5 to 7 days)	Prolonged duration of Abx (10 to 14 days)	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
Clinical	cure (at Te	est-of-C	ure (TOC))									
10 ¹⁻¹⁰	randomise d trials	seriousª	not serious ^b	not serious	not serious°	none	903/1014 (89.1%)	962/1096 (87.8%)	RR 1.00 (0.97 to 1.04)	0 fewer per 1,000 (from 26 fewer to 35 more)	⊕⊕⊕⊖ Moderate	CRITICAL
Microbio	ological cu	re (at Te	st-of-Cure (TO)))			I					
10 ¹⁻¹⁰	randomise d trials	serious ^d	not serious ^b	seriouse	not serious ^c	none	778/915 (85.0%)	824/975 (84.5%)	RR 0.99 (0.94 to 1.05)	8 fewer per 1,000 (from 51 fewer to 42 more)	⊕⊕⊖⊖ Low	IMPORTANT
Recurre	nce of Infe	ction (up	o to 180 days)		I		1	I		I		
6 ^{1,3,5,7,9,10}	randomise d trials	seriousª	not serious ^f	not serious	not serious ^c	none	41/535 (7.7%)	38/548 (6.9%)	RR 1.07 (0.69 to 1.65)	5 more per 1,000 (from 21 fewer to 45 more)	⊕⊕⊕⊜ Moderate	CRITICAL
Length o	of hospital	stay (me	edian days)				I					
19	randomise d trials	serious ^g	not serious	serious ^h	serious ⁱ	none	Median: 8 (IQR: 7 to 10) days (n=27)	Median: 14 (IQR 14 to 14.5) days (n=27)	-	median 6 days fewer (p<0.001)	⊕⊖⊝⊖ Very low	IMPORTANT
Readmis	ssion / Reh	ospitalis	sation (30 to 9	0 days)								
3 5,9,10	randomise d trials	serious ^g	not serious	not serious	serious	none	1/236 (0.4%)	1/246 (0.4%)	RR 0.99 (0.10 to 9.33)	0 fewer per 1,000 (from 4 fewer to 34 more)	⊕⊕⊖⊖ Low	IMPORTANT
Serious	adverse ev	/ents (up	to 180 days)	<u> </u>	1	l	I	<u> </u>	I	1		I
10 ¹⁻¹⁰	randomise d trials	seriousª	not serious	not serious	serious ^k	none	38/1370 (2.8%)	52/1478 (3.5%)	RR 0.82 (0.54 to 1.25)	6 fewer per 1,000 (from 16 fewer to 9 more)	⊕⊕⊖⊖ Low	IMPORTANT

			Certainty as	sessment			№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistenc y	Indirectness	Imprecisio n	Other considerations		Prolonged duration of Abx (10 to 14 days)	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

Non-serious adverse events (up to 180 days)

81,3,4,6-10	randomise d trials	seriousª	not serious	not serious	serious ^k	none	319/1230 (25.9%)	378/1330 (28.4%)	RR 0.92 (0.79 to 1.07)	23 fewer per 1,000 (from 60 fewer to 20 more)	⊕⊕⊖⊖ Low	IMPORTANT
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CI: confidence interval; RR: risk ratio; Abx: antibiotics; IQR: interquartile range.

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. Unblinded studies in which the measured outcomes require judgment (e.g., such as how investigators judge clinical improvement or decide to stop the treatment in patients with side effects) were judged to be at risk of high risk of bias. Multiple studies might have been influenced by incomplete outcome data (such as potential attrition bias due to early withdrawal secondary to the lack of diagnostic confirmation and/or frequent late withdrawal), but the extent of this bias was not assessable. Studies funded by industry might also have been biased due to financial conflict of interest. One study showed evidence of failed randomization potentially due to early stoppage of enrollment as well as significant and asymmetrical lost-to-follow up for recurrence of infection (Lafaurie 2023). Outcome measurement time frames varied between studies, with some studies measuring outcomes at an early specific time point after randomization rather than after end of treatment which may bias the assessment in favor of longer duration regimen. These studies were not rated down for risk of bias since this potential bias in favor of the longer course does not lower our confidence in the estimate that shorter is non-inferior to longer).

b. Talan 2000: heterogenous size of effect presented as compared to other studies and no overlapping of the 95% CI interval with at least one study. After removing this study from the analysis, Talan 2000 is clearly the main source of heterogeneity (p-value for heterogeneity: NS and the I-square: 0%). Exploration of the potential sources of heterogeneity show that the comparator was 14 days of TMP-SMX to which 18.3% of uropathogens were resistant to. This could clearly affect the clinical cure at TOC and could explain the variation in size of effect (thus, not rated down for inconsistency).

c. Based on an inferiority margin of 10%, not rated down for imprecision.

d. Multiple studies might have been influenced by incomplete outcome data (such as potential attrition bias due to early withdrawal secondary to the lack of diagnostic confirmation and/or frequent late withdrawal), but the extent of this bias was not assessable. Studies funded by industry might also have been biased due to financial conflict of interest. One study showed evidence of failed randomisation potentially due to early stoppage of enrollment (Lafaurie 2023).

e. Microbiological cure is considered a potential surrogate marker of clinical cure and recurrence of infection, but uncertainty remains around the strength of this association. f. Darouiche 2014: heterogenous size of effect presented as compared to the other studies but only contributed for 0.8% of the weight (thus, not rated down for inconsistency)

g. Unblinded study which can affect the outcome of interest that require judgment, such as how investigators judge clinical improvement and associated downstream consequences.

h. Rated down for indirectness since length of hospitalization was likely influenced by the route of administration of antimicrobials (all patients received parenteral antibiotics throughout each study for the assigned duration in the hospital, without switching to an oral option) (Rudrabhatla 2018).

i. Small sample size suggests the potential for fragility in the estimate, making the estimate uncertain.

j. Very few events and small sample size. 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the treatment with shorter duration failed to show or exclude a beneficial effect.

k. 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the treatment with shorter duration failed to show or exclude a beneficial effect.

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Desseaux,K., Empana-Barat,F., Madeleine,I., Bercot,B., Molina,J.M., Lefort,A., for the PROSTASHORT study group. Antimicrobial for 7 or 14 days for febrile urinary tract infection in men: a multicenter noninferiority double blind placebo-controlled, randomized clinical trial. CID; 2023.

Supplementary Table 2: Characteristics of the included studies (n=10, 2000-2024)

Study (Lead author, Year of publication, Name of trial, Countries) Darouiche	Population (Type UTI, Year of enrollment, N randomised, F (%), Age in Intervention vs Comparator groups) Catheter-related	Study design (Non-inferiority margin if applicable, primary outcome with its timing)	Main uro- pathogens (% of resistance) Mixed (64%)	Randomisation (timing, and criteria for clinical response if reported) Based on a	Intervention (total duration for shorter courses, IV and oral antibiotics) 5 days	Comparator (total duration for longer courses, IV and oral antibiotics)
2014 USA	UTI in hospitalised patients with SCI 2007-2011 N= 61 F: 5.5% A (mean): 61.5 vs 58.3y	Margin of 10% for CC at EOT		presumptive clinical and microbiological diagnosis of catheter-related UTI	(appropriate IV or PO systemic antibiotics, with catheter exchange)	(appropriate IV or PO systemic antibiotics, with catheter retention)
Dinh 2017 France (multicentric)	Uncomplicated AP attending ED 2009-2011 N= 88 F: 100% A (mean): 30.5 vs 33.1y	Non-inferiority trial Margin (NR) for CC at day 30 after EOT	<i>E. coli</i> (98%) R to FQ: 0%, since excluded after randomisation	Within 24h of initiation of antibiotic treatment	5 days (PO ofloxacin or levofloxacin)	10 days (PO ofloxacin or levofloxacin)
Lafaurie 2023 PROSTASHO RT France (multicentric)	Febrile UTI 2015-2019 N= 240 F: 0% Age (median): 62.3 vs 58.9y	Non-inferiority trial Margin of 10% for treatment success (CC, MC and no new antibiotics) at week 6	<i>E. coli</i> (8%) R to FQ: 0%, since exclusion criteria	Three to four days after initiation of antibiotic treatment if afebrile with empirical therapy	7 days (ofloxacin, ceftriaxone or cefotaxime for maximum of 3 days, then switch to PO ofloxacin)	14 days (ofloxacin, ceftriaxone or cefotaxime for maximum of 3 days, then switch to PO ofloxacin)
Peterson 2008 USA (multicentric)	AP/ cUTI 2005-2006 N=1,109 F: 60.9% A (mean): 54.2y (whole cohort)	Non-inferiority trial Margin of 15% for MC at day 15 to 19 after blinded EOT	<i>E. coli</i> (86%) R to ciprofloxacin: 9% and levofloxacin: 5%	Based on a clinical and microbiological diagnosis of AP/ cUTI	5 days (IV or PO levofloxacin)	10 days (IV or PO ciprofloxacin)
Ren 2017 China (multicentric)	AP/ cUTI 2012-2014 N= 317 F: 85.2% A (mean): 49.1 vs 50.2y	Non-inferiority trial Margin of 15% % for CC at EOT	<i>E. coli</i> (37%) R to FQ: NR	Based on presumptive clinical diagnosis of AP/ cUTI	5 days (IV levofloxacin)	7 to 14 days (IV x 5 days then PO levofloxacin)
Rudrabhatla 2018	AP in hospitalised patients	Non-inferiority trial	E. coli (87%)	On day 7 of effective antibiotic regimen (either	7 days	14 days

India		Margin of 15% for	R to FQ: 78%	empirical or	(effective non-	(effective non-
	2015-2016	retreatment for	(36/46)	revised), if	Ìluoroquinolone,	Ìluoroquinolone,
	N= 54	recurrent UTI at 6	· · /	sustained clinical	of which the	of which the
		weeks after EOT		improvement	great majority	great majority
	F: 58.8%			F	were	were
	A (median):				aminoglycosides	aminoglycosides
	51vs 55y				-based regimen)	-based regimen)
Sandberg	AP	Non-inferiority trial	E. coli (92%)	Based on	7 days	14 days
2012		· · · · · · · · · · · · · · · · · · ·		presumptive	· · j ·	
	2006-2008	Margin of 10% for	R to FQ: 0%,	clinical diagnosis	(initial IV as	(initial IV as
Sweden	N= 248	CC and MC 10 to	since excluded	of AP	needed, then	needed, then
(multicentric)	11 210	14 days after EOT	after	0174	PO	PO
(manoonino)	F:100%	Thay's anon Eon	randomisation		ciprofloxacin)	ciprofloxacin)
	A (median): 46		randonnoadon		olpronoxaonij	opronoxaoiny
	vs 41y					
Talan 2000	Uncomplicated	Non-inferiority trial	E. coli (68%)	Within 24h of	7 days	14 days
	AP in			initiation of		-
USA	outpatients	Margin of 10% for	R to FQ:0%	antibiotic	(IV X 1 dose if	(IV ceftriaxone X
(multicentric)		CC and MC at 4	(1/255)	treatment	needed, then	1 dose if
,	1994-1997	to 11 days after	R to TPM-SMX:		oral	needed, then
	N =378	EOT	18% (47/255)		ciprofloxacin)	oral TMP-SMX)
	F: 100%					
	A (median): 25					
	vs 23y					
van	Febrile UTI	Non-inferiority trial	E. coli (68%)	Three to four days	7 days	14 days
Nieuwkoop				after inclusion		
2017	2008-2013	Margin of 10% for	R to FQ: 0%,	(pending results of	(ciprofloxacin or	(ciprofloxacin or
	N= 200	CC at 10 to 18	since exclusion	urine culture)	b-lactams +/- IV	b-lactams +/- IV
FUTIRST		days after EOT	criteria		gentamicin, then	gentamicin, then
	F: 57.0%				early switch to	early switch to
Netherlands	A: 60 vs 61y				PO	PO
(multicentric)					ciprofloxacin)	ciprofloxacin)
Wagenlehner	AP/ cUTI in	Phase II,	E. coli (83%)	Based on	5 days	10 days
2018	hospitalised	Descriptive trial		presumptive		
	patients		R to FQ: 16%	clinical diagnosis	(IV or PO	(IV or PO
Germany and		CC and MC at	(37/225)	of AP/ cUTI	finafloxacin)	finafloxacin or
Poland	2012-2014	TOC (day 17)				ciprofloxacin)
	N = 225					
	F: 82.1%					
	A (group):					
	mostly between					
	36-65y					

UTI=Urinary Tract Infection; cUTI=Complicated UTI; AP=acute pyelonephritis; SCI=spinal cord injury; ED=Emergency department; F=female; y=years; 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; FQ=fluoroquinolone; IV=parenteral; PO=oral.

Supplementary Figure 2: Summary of the Risk of Bias of included studies (Cochrane Risk of Bias tool (n=10)





Supplementary Table 3: Assessment of the Risk of Bias of included studies (Cochrane Risk of bias Tool) (n=10)

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)
Darouiche 2014 USA	High RoB -Computer- generated randomization schedule with randomly permuted blocks -Probable failed randomization: short duration group tended to have more bacteremia at baseline and empirical / definitive choice of antibiotics varied greatly between the 2 groups (comparison most likely underpowered)	Unclear RoB -Not reported	High RoB -Open-label (especially applicable to subjective outcomes)	High RoB -Open-label (especially applicable to subjective outcomes)	High RoB -Early withdrawal after randomisation (for bacteremia) occurred exclusively in the short duration group	Low RoB	Low RoB -Not industry- funded -No financial relationship disclosed by authors
Dinh 2017 France (multicentric)	Unclear RoB -Randomization (not further detailed) -Comparable patients' characteristics at baseline, except for a trend towards higher CRP in short duration group	Unclear RoB	High RoB -Open-label (especially applicable to subjective outcomes)	High RoB -Open-label (especially applicable to subjective outcomes)	High RoB -Early withdrawal after randomisation (for absence of uropathogen or FQ-resistance uropathogen) lead to premature stoppage of the trial for safety reasons (10% FQ- resistance)	Low RoB	Low RoB -Not industry- funded -No conflict of interest declared by authors
Lafaurie 2023 PROSTA- SHORT France (multicentric)	High RoB -Stratified randomization (by age, urinary tract- related comorbidities and center) with permutation blocks of varying sizes -Probable failed randomization: short duration group had more comorbidities at baseline and more infections caused by <i>Ecoli</i>	Low RoB -Randomisation via a centralised web-based system	Low RoB -Placebo- controlled	Low RoB -Placebo- controlled	Low to Unclear RoB -No significant lost to follow up at 6 weeks (e.g. clinical failure) -Significant and asymmetrical lost to follow up after 6 weeks (27% vs 17% of lost to follow up in the short vs prolonged duration groups, respectively) (e.g. recurrence of infection) -Asymmetrical timing of outcomes measurement	Unclear RoB -Recurrence of infection at 6 weeks is not reported (but is between 6 and 12 weeks)	Low RoB -Not funded by industry

					potentially favoring longer duration		
Peterson 2008	Low RoB	Low RoB	Low RoB	Low RoB	Unclear RoB	Low RoB	High RoB
USA (multicentric)	-Computer- generated randomization schedule with randomly permuted blocks -Comparable patients' characteristics at baseline	-Randomisation via a central service	-Placebo- controlled	-Placebo- controlled	-Early withdrawal after randomisation (if NOT having an appropriate clinical diagnosis of AP or cUTI, a positive urine culture with 1 or 2 uropathogens) was frequent, but symmetrical between groups. No analysis was provided to assess the impact of early withdrawal. -Asymmetrical timing of outcomes measurement (potentially favoring longer duration)		-Industry- funded: grant related to one the studied molecules (involvement of industry not reported but authors are employees of this specific company)
Ren 2017	Low RoB	Unclear RoB	High RoB	High RoB	Low RoB	Unclear RoB	Low RoB
China (multicentric)	-Randomization (not further detailed) -Comparable patients' characteristics at baseline	-Not reported	-Open-label (especially applicable to subjective outcomes)	-Open-label (especially applicable to subjective outcomes)	-All outcomes analysed in the ITT population -No significant lost to follow up	-Clinical recurrence mentioned in abstract but not reported in manuscript	-Funding not reported but no COI disclosed by authors
Rudrabhatla	Low RoB	Low RoB	High RoB	High RoB	Low RoB	Low RoB	Low RoB
2018 India	-Computer- generated randomization with minimization method to balance prognostic variables (gender, age, comorbidities, regimen received) -Comparable patients' characteristics at baseline	-Randomization using a biased- coin method	-Open-label (especially applicable to subjective outcomes)	-Open-label (especially applicable to subjective outcomes)	-All outcomes analysed in the ITT population -No significant lost to follow up		-No funding received and no competing interests declared by authors
Sandberg 2012	Unclear RoB	Low RoB	Low RoB	Low RoB	High RoB	Low RoB	Low RoB
Sweden (multicentric)	-Computer- generated randomization sequence with randomly blocks for each study site -Comparable patients' characteristics at baseline, but comparison most likely underpowered	-Randomization via a central service	-First week was open-label while the second week was placebo- controlled (especially influencing the route of administration)	-First week was open-label while the second week was placebo- controlled (especially influencing the route of administration)	-Early withdrawal after randomisation (if NOT having an appropriate clinical diagnosis of AP or cUTI, a positive urine culture with 1 or 2 uropathogens susceptible to ciprofloxacin) in addition to lost to follow up was frequent and asymmetrical between groups (42% vs 32% in the short duration group vs the prolonged duration group,		-Not industry- funded -Sponsor not involved in study design, collection, analysis and interpretation of data, reviewing the report and the decision to submit the report for publication

					respectively). No analysis was provided to assess the impact of early withdrawal.		
Talan 2000	Unclear RoB	Unclear RoB	Low RoB	Low RoB	Unclear RoB	Low RoB	High RoB
USA (multicentric)	-Randomization (not further detailed) -Comparable patients' characteristics at baseline (in efficacy valid groups), except for a trend towards more bacteremia in the prolonged duration group	-Not reported	-Placebo- controlled	-Placebo- controlled	-Early withdrawal after randomisation (if NOT having an appropriate clinical diagnosis of uAP, a positive urine culture with uropathogens) in addition to lost to follow up was frequent and asymmetrical between groups (33% vs 32%). No analysis was provided to assess the impact of early withdrawal.		-Industry- funded: grant related to one the studied molecules (involvement of industry not reported but authors either received lecture honoraria, research support and/or are employees of this specific company)
van	Low RoB	Low RoB	Low RoB	Low RoB	Low RoB	Low RoB	Low RoB
Nieuwkoop 2017 FUTIRST Netherlands (multicentric)	-Computer- generated randomization list with permuted blocks -Comparable patients' characteristics at baseline	-Randomization via a central service	-First week was open-label while the second week was placebo- controlled (especially influencing the route of administration)	-First week was open-label while the second week was placebo- controlled (especially influencing the route of administration)	-All outcomes analysed in the ITT population -No significant lost to follow up		-Not industry- funded -Sponsor not involved in study design, data collection,analy sis and interpretation, writing of the report
Wagenlehner 2018	Unclear RoB	Unclear RoB	Low RoB	Low RoB	Low RoB	Low RoB	High RoB
Germany and Poland	-Randomization (not further detailed) -Comparable patients' characteristics at baseline, but comparison most likely underpowered	-Not reported	-Placebo- controlled	-Placebo- controlled	-Early withdrawal after randomisation (if NOT having an appropriate clinical diagnosis of AP or cUTI, a positive urine culture with a uropathogen susceptible to the studied drug) was relatively infrequent and symmetrical between groups. -Asymmetrical timing of outcomes measurement (potentially favoring longer duration) ed AP; FQ=fluoroquinolone;		-Industry- funded: grant related to one the studied molecules (involvement of industry not reported)

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

3a) Clinical cure (at Test-of-Cure (TOC))

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Darouiche 2014	28	28	27	27	11.5%	1.00 [0.93, 1.07]		
Dinh 2017	28	30	36	38	5.9%	0.99 [0.87, 1.11]		?? 🔴 🔴 🔁 🗣
Lafaurie 2023	110	115	125	125	16.1%	0.96 [0.92, 1.00]		
Peterson 2008	257	317	242	302	10.3%	1.01 [0.94, 1.09]		••••
Ren 2017	142	158	142	159	10.6%	1.01 [0.93, 1.08]		•?••••
Rudrabhatla 2018	22	22	23	23	9.4%	1.00 [0.92, 1.09]		
Sandberg 2012	71	73	80	83	13.5%	1.01 [0.95, 1.07]	_ -	? • • • • • •
Talan 2000	109	113	92	111	8.6%	1.16 [1.06, 1.28]		?? 🗣 🗣 ? 🗣 🛑
van Nieuwkoop 2017	85	94	94	99	10.0%	0.95 [0.88, 1.03]		
Wagenlehner 2018	51	64	101	129	4.1%	1.02 [0.87, 1.19]		?? 🗣 🗣 🗣 🗣
Total (95% CI)		1014		1096	100.0%	1.00 [0.97, 1.04]	. ◆	
Total events	903		962					
Heterogeneity: Tau ² = 0	0.00; Chi ² = 1	8.45, df=	= 9 (P = 0.03); l² = 51 ^o	%			
Test for overall effect: Z	= 0.22 (P = 0).83)					0.7 0.85 1 1.2	1.5
							Favours longer duration Favours shorter du	rauon

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) Clinical cure (at TOC): Sensitivity analysis after removing Talan 2000

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Darouiche 2014	28	28	27	27	11.3%	1.00 [0.93, 1.07]	_	
Dinh 2017	28	30	36	38	3.7%	0.99 [0.87, 1.11]		??●●●••
Lafaurie 2023	110	115	125	125	30.8%	0.96 [0.92, 1.00]		
Peterson 2008	257	317	242	302	9.1%	1.01 [0.94, 1.09]		
Ren 2017	142	158	142	159	9.7%	1.01 [0.93, 1.08]	_	• ? • • • ? •
Rudrabhatla 2018	22	22	23	23	7.7%	1.00 [0.92, 1.09]		
Sandberg 2012	71	73	80	83	16.9%	1.01 [0.95, 1.07]	_	?••••
Talan 2000	109	113	92	111	0.0%	1.16 [1.06, 1.28]		??••?••
van Nieuwkoop 2017	85	94	94	99	8.5%	0.95 [0.88, 1.03]		
Wagenlehner 2018	51	64	101	129	2.3%	1.02 [0.87, 1.19]		?? 🕈 🕈 🕈 🕈 🗬
Total (95% CI)		901		985	100.0%	0.99 [0.96, 1.01]	•	
Total events	794		870				-	
Heterogeneity: Tau ² = (0.00; Chi ² = 5.	15, df=	8 (P = 0.74);	I² = 0%				
Test for overall effect: Z	Z = 1.25 (P = 0).21)					0.7 0.85 1 1.2	1.5
		· ·					Favours longer duration Favours shorter du	rauon

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)

3c) Microbiological cure (at TOC)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Darouiche 2014	23	28	24	27	5.1%	0.92 [0.74, 1.15]		•?••••
Dinh 2017	20	23	16	20	3.7%	1.09 [0.83, 1.42]		?? 🔴 🖨 🖶 🛨
Lafaurie 2023	91	115	117	125	11.8%	0.85 [0.76, 0.94]		•••••
Peterson 2008	253	317	241	302	14.1%	1.00 [0.92, 1.08]	_	••••
Ren 2017	60	67	63	73	10.3%	1.04 [0.92, 1.17]	•	•?•••
Rudrabhatla 2018	18	22	21	23	4.6%	0.90 [0.71, 1.13]		
Sandberg 2012	69	73	79	83	14.6%	0.99 [0.92, 1.07]		? • • • • • •
Talan 2000	112	113	90	101	14.9%	1.11 [1.04, 1.19]	_	?? 🗣 🗣 ? 🗣 🛑
van Nieuwkoop 2017	86	93	89	92	15.0%	0.96 [0.89, 1.02]		
Wagenlehner 2018	46	64	84	129	5.9%	1.10 [0.90, 1.35]		?? ? 🕈 🕈 🕈 🖶
Total (95% CI)		915		975	100.0%	0.99 [0.94, 1.05]	•	
Total events	778		824					
Heterogeneity: Tau ² = 0	0.00; Chi ² = 2	3.47, df=	= 9 (P = 0.00	(5); I² = 6;	2%			
Test for overall effect: Z	•		,				0.7 0.85 1 1.2 Favours longer duration Favours shorter duration	1.5
	`						Favours longer duration Favours shorter durate	011

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) Microbiological cure (at TOC): Sensitivity analysis after removing Talan 2000

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Darouiche 2014	23	28	24	27	4.3%	0.92 [0.74, 1.15]		
Dinh 2017	20	23	16	20	2.9%	1.09 [0.83, 1.42]		— ??●●●••
Lafaurie 2023	91	115	117	125	13.5%	0.85 [0.76, 0.94]		
Peterson 2008	253	317	241	302	18.5%	1.00 [0.92, 1.08]		
Ren 2017	60	67	63	73	10.9%	1.04 [0.92, 1.17]		• ? • • • ? •
Rudrabhatla 2018	18	22	21	23	3.8%	0.90 [0.71, 1.13]		
Sandberg 2012	69	73	79	83	19.9%	0.99 [0.92, 1.07]		?
Talan 2000	112	113	90	101	0.0%	1.11 [1.04, 1.19]		?? 🗣 🗣 ? 🗣 🛑
van Nieuwkoop 2017	86	93	89	92	21.0%	0.96 [0.89, 1.02]		
Wagenlehner 2018	46	64	84	129	5.1%	1.10 [0.90, 1.35]		· ?? • • • • •
Total (95% CI)		802		874	100.0%	0.97 [0.93, 1.02]	•	
Total events	666		734				-	
Heterogeneity: Tau ² = (0.00; Chi ² = 13	2.02, df=	8 (P = 0.15); l ² = 33'	%			
Test for overall effect: 2	Z = 1.21 (P = 0	.23)	-				0.7 0.85 1 1.2 Favours longer duration Favours shorter d	1.5 uration

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)

3e) Recurrence of infection (up to 180 days)

	Shorter duration		Longer duration Risk Rati				Risk Ratio	Risk of Bias		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG		
Darouiche 2014	9	28	3	27	13.1%	2.89 [0.88, 9.56]				
Lafaurie 2023	2	84	5	104	7.2%	0.50 [0.10, 2.49]				
Peterson 2008	20	229	18	213	50.5%	1.03 [0.56, 1.90]	-+-	••••		
Rudrabhatla 2018	0	27	1	27	1.9%	0.33 [0.01, 7.84]				
Sandberg 2012	3	73	3	83	7.6%	1.14 [0.24, 5.46]		? • • • • • •		
van Nieuwkoop 2017	7	94	8	94	19.8%	0.88 [0.33, 2.32]				
Total (95% CI)		535		548	100.0%	1.07 [0.69, 1.65]	•			
Total events	41		38							
Heterogeneity: Tau ² = 0	.00; Chi ² = 4.	24, df = :	5 (P = 0.51);	I ² = 0%						
Test for overall effect: Z	= 0.31 (P = 0	.76)					0.01 0.1 1 10 Favours shorter duration Favours longer dur	100 ration		

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) Rehospitalisation / Readmission (30 to 90 days)

	Shorter du	ration	Longer duration			Risk Ratio	Risk I	Ratio	Risk of Bias
Study or Subgroup	Events Total		Events Total Weigh		Weight	M-H, Random, 95% Cl	M-H, Rando	m, 95% Cl	ABCDEFG
Lafaurie 2023	0	115	0	125		Not estimable			
Rudrabhatla 2018	0	27	1	27	50.5%	0.33 [0.01, 7.84]	_		
van Nieuwkoop 2017	1	94	0	94	49.5%	3.00 [0.12, 72.72]		-	
Total (95% CI)		236		246	100.0%	0.99 [0.10, 9.33]			
Total events	1		1						
Heterogeneity: Tau ² = 0	0.00; Chi ² = 0.	92, df = 1	1 (P = 0.34)	; I² = 0%				t	
Test for overall effect: Z							0.01 0.1 1 Favours shorter duration	10 Favours longer d	100 Juration

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)

3g) Serious Adverse events (up to 180 days)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Darouiche 2014	2	28	1	27	3.2%	1.93 [0.19, 20.05]		
Dinh 2017	0	43	0	45		Not estimable		?? 🗭 🖨 🖶 🛨
Lafaurie 2023	0	115	0	125		Not estimable		•••••
Peterson 2008	17	543	15	559	37.6%	1.17 [0.59, 2.31]	— — —	••••
Ren 2017	1	164	2	165	3.1%	0.50 [0.05, 5.49]		•?••••
Rudrabhatla 2018	0	27	0	27		Not estimable		
Sandberg 2012	1	86	1	93	2.3%	1.08 [0.07, 17.02]		? • • • • • •
Talan 2000	11	191	21	187	35.8%	0.51 [0.25, 1.03]		??••?•
van Nieuwkoop 2017	1	97	5	103	3.9%	0.21 [0.03, 1.79]		
Wagenlehner 2018	5	76	7	147	14.2%	1.38 [0.45, 4.21]	-	?? 🕈 🛨 🖶 🖶
Total (95% CI)		1370		1478	100.0%	0.82 [0.54, 1.25]	•	
Total events	38		52				-	
Heterogeneity: Tau ² = 0	0.00; Chi ² = 5.	86. df=	6 (P = 0.44);	I² = 0%				
Test for overall effect: Z							0.01 0.1 1 10 Favours shorter duration Favours longer du	100 uration

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

3h) Non-Serious adverse events (up to 180 days)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEFG
Darouiche 2014	2	28	2	27	0.6%	0.96 [0.15, 6.37]		
Lafaurie 2023	4	115	7	125	1.6%	0.62 [0.19, 2.07]		
Peterson 2008	192	543	185	559	45.3%	1.07 [0.91, 1.26]	+	••••
Ren 2017	36	164	38	165	12.5%	0.95 [0.64, 1.42]		• ? • • • ? •
Rudrabhatla 2018	2	27	7	27	1.0%	0.29 [0.07, 1.25]	+	
Sandberg 2012	4	86	6	93	1.5%	0.72 [0.21, 2.47]		? • • • • • •
Talan 2000	46	191	62	187	17.9%	0.73 [0.53, 1.00]		?? 🗣 🗣 ? 🗣 🗬
Wagenlehner 2018	33	76	71	147	19.6%	0.90 [0.66, 1.22]		??••••
Total (95% CI)		1230		1330	100.0%	0.92 [0.79, 1.07]	•	
Total events	319		378					
Heterogeneity: Tau ² =	0.01; Chi ² =	7.99, df:	= 7 (P = 0.33	3); I ² = 12	%			
Test for overall effect:	Z = 1.03 (P =	0.30)					0.01 0.1 1 10 Favours shorter duration Favours longer d	100 luration

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)



Supplementary Figure 4: Funnel plot for clinical cure Clinical cure (at Test-of-Cure (TOC))

Supplementary Tabl	e 4: GRADE Evidence to Decision framework for all cUTI
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Summary of Ju	udgments							
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 favor the intervention	S 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 favor the intervention	S 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	
ype of Recon	nmendation							
Strong recommend against the interve		al recommendatior the intervention	Conditional recom for either the inter the compar	vention or rec	Conditional ommendation for he intervention	-	mendation for th rvention	
0		0	0		0	0		

B) Stratification for choice of antibiotics

Supplementary Table 5: GRADE Evidence Profile

Question: In patients presenting with complicated UTI **treated with fluoroquinolones**, should total duration of antibiotics be **shorter (<=7 days)** rather than **prolonged to >7 days**?

P: In patients presenting with complicated UTI treated with fluoroquinolones (FQ)

I: shorter total duration of antibiotics (<=7 days)

C: prolonged total duration of antibiotics (>7 days)

Setting: Inpatient and Outpatient

Certainty assessment							№ of patients		Effect			
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Shorter duration of FQ (5 to 7 days)	Prolonged duration of FQ (10 to 14 days)	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

Clinical cure (at Test-of-Cure (TOC))

/1-/ serious not serious not serious not serious none	744/851 820/935 (87.4%) (87.7%) RR 0.98 (0.96 to 1.01)	1000 ()	CRITICAL
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Microbiological cure (at TOC)

71-7	randomised trials	serious℃	not serious	serious ^d	not serious ^b	none	625/752 (83.1%)	689/824 (83.6%)	RR 0.98 (0.93 to 1.03)	17 fewer per 1,000 (from 59 fewer to 25 more)	⊕⊕⊖⊖ Low	IMPORTANT	
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Recurrence of Infection (up to 90 days)

41,3,5,7	randomised trials serious	a not serious	not serious	not serious ^b	none	32/480 (6.7%)	34/494 (6.9%)	RR 0.94 (0.59 to 1.51)	4 fewer per 1,000 (from 28 fewer to 35 more)	⊕⊕⊕⊖ Moderate	CRITICAL	
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Readmission / Rehospitalisation (30 to 90 days)

23,7	randomised trials	serious ^e	not serious	not serious	serious ^f	none	1/209 (0.5%)	0/219 (0.0%)	RR 3.00 (0.12 to 72.72)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	⊕⊕⊖⊖ Low	IMPORTANT	
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Serious adverse events (up to 180 days)

71-7	randomised trials	seriousª	not serious	not serious	serious ^g	none	25/1124 (2.2%)	30/1237 (2.4%)	RR 1.04 (0.61 to 1.78)	1 more per 1,000 (from 9 fewer to 19 more)	⊕⊕⊖⊖ Low	IMPORTANT	
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Non-serious adverse events (up to 180 days)

			Certainty as	sessment			№ of patients			Effect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Shorter duration of FQ (5 to 7 days)	Prolonged duration of FQ (10 to 14 days)	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
51,4,5,6,7	randomised trials	seriousª	not serious	not serious	serious ^g	none	269/964 (27.9%)	307/1089 (28.2%)	RR 1.01 (0.88 to 1.15)	3 more per 1,000 (from 34 fewer to 42 more)	⊕⊕⊖⊖ Low	IMPORTANT

Notes:

Length of hospital stay - this outcome (judged important for decision-making) was not reported.

CI: confidence interval; RR: risk ratio; FQ: fluoroguinolone

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. Unblinded studies in which the measured outcomes require judgment (e.g., such as how investigators judge clinical improvement or decide to stop the treatment in patients with side effects) were judged to be at risk of high risk of bias. Multiple studies might have been influenced by incomplete outcome data (such as potential attrition bias due to early withdrawal secondary to the lack of diagnostic confirmation and/or frequent late withdrawal), but the extent of this bias was not assessable. Studies funded by industry might also have been biased due to financial conflict of interest. One study showed evidence of failed randomization potentially due to early stoppage of enrollment as well as significant and asymmetrical lost-to-follow up for recurrence of infection (Lafaurie 2023). Outcome measurement time frames varied between studies, with some studies measuring outcomes at an early specific time point after randomization rather than after end of treatment which may bias the assessment in favor of longer duration regimen. These studies were not rated down for risk of bias since this potential bias in favor of the longer course does not lower our confidence in the estimate that shorter is non-inferior to longer).

b. Based on an inferiority margin of 10%, not rated down for imprecision.

c. Multiple studies might have been influenced by incomplete outcome data (such as potential attrition bias due to early withdrawal secondary to the lack of diagnostic confirmation and/or frequent late withdrawal), but the extent of this bias was not assessable. Studies funded by industry might also have been biased due to financial conflict of interest. One study showed evidence of failed randomization potentially due to early stoppage of enrollment as well as significant and asymmetrical lost-to-follow up for recurrence of infection (Lafaurie 2023).

d. Microbiological cure is considered a potential surrogate marker of clinical cure and recurrence of infection, but major uncertainty remains around the strength of this association.

e. Unblinded study which can affect the outcome of interest that require judgment, such as how investigators judge clinical improvement and associated downstream consequences.

f. Very few events and small sample size. 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the treatment with shorter duration failed to show or exclude a beneficial effect.

g. 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the treatment with shorter duration failed to show or exclude a beneficial effect.

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Supplementary Figures 5: Forest plots for each patient-important outcome

Subgroup analysis: Fluoroquinolones (not including Darouiche 2014, Rudrabhatla 2018 and Talan 2000)

5a) Clinical cure (at 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

5b) Microbiological cure (at TOC)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI	ABCDEFG
Dinh 2017	20	23	16	20	3.7%	1.09 [0.83, 1.42]		- ??●●●••
Lafaurie 2023	91	115	117	125	15.1%	0.85 [0.76, 0.94]		
Peterson 2008	253	317	241	302	19.7%	1.00 [0.92, 1.08]	+	••••
Ren 2017	60	67	63	73	12.5%	1.04 [0.92, 1.17]	-	•?•••
Sandberg 2012	69	73	79	83	20.9%	0.99 [0.92, 1.07]	_	? • • • • • •
van Nieuwkoop 2017	86	93	89	92	21.8%	0.96 [0.89, 1.02]		
Wagenlehner 2018	46	64	84	129	6.2%	1.10 [0.90, 1.35]		?? 🕈 🖶 🖶 🖶 🛑
Total (95% CI)		752		824	100.0%	0.98 [0.93, 1.03]	-	
Total events	625		689				_	
Heterogeneity: Tau ² = 0	0.00; Chi ² = 1	1.39, df=	= 6 (P = 0.08); $ ^2 = 47^{\circ}$	%			
Test for overall effect: Z	. = 0.81 (P = 0	.42)					0.7 0.85 1 1.2 Favours longer duration Favours shorter duration	1.5 ation
		ŕ					Favours longer duration Favours shorter dura	auon

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)

5c) Recurrence of infection (up to 90 days)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Lafaurie 2023	2	84	5	104	8.4%	0.50 [0.10, 2.49]		
Peterson 2008	20	229	18	213	59.4%	1.03 [0.56, 1.90]		••••
Sandberg 2012	3	73	3	83	8.9%	1.14 [0.24, 5.46]		? • • • • • •
van Nieuwkoop 2017	7	94	8	94	23.2%	0.88 [0.33, 2.32]		
Total (95% CI)		480		494	100.0%	0.94 [0.59, 1.51]	+	
Total events	32		34					
Heterogeneity: Tau ² = 0	.00; Chi ² = 0.	78, df = 3	3 (P = 0.85);	I² = 0%				
Test for overall effect: Z	= 0.25 (P = 0	.80)					0.01 0.1 1 10 Favours shorter duration Favours longer d	100 uration

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

5d) Rehospitalisation / Readmission (30 to 90 days)

	Shorter du	ration	Longer du	ration		Odds Ratio	Odds	Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixe	d, 95% Cl	ABCDEFG
Lafaurie 2023	0	115	0	125		Not estimable			
van Nieuwkoop 2017	1	94	0	94	100.0%	3.03 [0.12, 75.38]			
Total (95% CI)		209		219	100.0%	3.03 [0.12, 75.38]			
Total events	1		0						
Heterogeneity: Not app	licable						0.01 0.1 1		100
Test for overall effect: Z	= 0.68 (P = 0	.50)					0.01 0.1 1 Favours shorter duration		

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)

5e) Serious Adverse events (up to 180 days)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI	ABCDEFG
Dinh 2017	0	43	0	45		Not estimable		?? 🗧 🗧 🗧 🛨
_afaurie 2023	0	115	0	125		Not estimable		
Peterson 2008	17	543	15	559	61.6%	1.17 [0.59, 2.31]	— — —	•••••
Ren 2017	1	164	2	165	5.0%	0.50 [0.05, 5.49]		• ? • • • ? •
Sandberg 2012	1	86	1	93	3.8%	1.08 [0.07, 17.02]		? • • • • • •
/an Nieuwkoop 2017	1	97	5	103	6.4%	0.21 [0.03, 1.79]		
Wagenlehner 2018	5	76	7	147	23.2%	1.38 [0.45, 4.21]		?? 🕈 🕈 🖶 🗬
Fotal (95% CI)		1124		1237	100.0%	1.04 [0.61, 1.78]	+	
Total events	25		30					
Heterogeneity: Tau ² = 0).00; Chi ² = 2.	89. df=	4 (P = 0.58);	I ² = 0%				
Fest for overall effect: Z	•		、/i				0.01 0.1 1 10 Favours shorter duration Favours longer du	100 uration

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

5f) Non-Serious adverse events (up to 180 days)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl	ABCDEFG
Lafaurie 2023	4	115	7	125	1.2%	0.62 [0.19, 2.07]		
Peterson 2008	192	543	185	559	67.2%	1.07 [0.91, 1.26]	•	••••
Ren 2017	36	164	38	165	11.2%	0.95 [0.64, 1.42]	-+-	•?•••
Sandberg 2012	4	86	6	93	1.2%	0.72 [0.21, 2.47]		? • • • • • •
Wagenlehner 2018	33	76	71	147	19.2%	0.90 [0.66, 1.22]		?? 🕈 🛨 🛨 🖶 🛑
Total (95% CI)		984		1089	100.0%	1.01 [0.88, 1.15]	•	
Total events	269		307					
Heterogeneity: Tau ² =	0.00; Chi ² =	2.01, df=	= 4 (P = 0.73	3); I ^z = 09	6			
Test for overall effect:		•					0.01 0.1 1 10 Favours shorter duration Favours longer of	100 duration

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)

Subgroup analysis: Non-Fluoroquinolones (including Rudrabhatla 2018)

5g) Clinical cure (at Test-of-Cure (TOC))



5h) Microbiological cure (at 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

5i) Recurrence of infection (at 6-8 weeks)

	Shorter du	ration	Longer du	ration		Risk Ratio		Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95% CI	ABCDEFG
Rudrabhatla 2018	0	27	1	27	100.0%	0.33 [0.01, 7.84]	2018		
Total (95% CI)		27		27	100.0%	0.33 [0.01, 7.84]			
Total events	0		1						
Heterogeneity: Not ap	plicable							0.01 0.1 1 10	100
Test for overall effect:	Z = 0.68 (P =	0.50)						Favours shorter duration Favours longer d	

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)

5j) Rehospitalisation / Readmission (up to 6 weeks)



(F) Selective reporting (reporting bias)

(r) Selective report

(G) Other bias

5k) Serious Adverse events (up 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

5l) Non-Serious adverse events (up to 6 weeks)

	Shorter du	ration	Longer du	ration		Risk Ratio		Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% CI	ABCDEFG
Rudrabhatla 2018	2	27	7	27	100.0%	0.29 [0.07, 1.25]	2018		
Total (95% CI)		27		27	100.0%	0.29 [0.07, 1.25]			
Total events	2		7						
Heterogeneity: Not ap	oplicable								
Test for overall effect	Z=1.66 (P=	: 0.10)						0.01 0.1 1 10 Favours shorter duration Favours longer of	100 duration
Risk of bias legend									
(A) Random sequent	ce generation	ı (selecti	on bias)						

(A) Random sequence generation (selection t

(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)

C) Stratification for gender

Subgroup analysis: Males (including Lafaurie 2023 and post hoc analysis of Niewkoop 2017)

Supplementary Figures 6: Forest plots for each patient-important outcome

6a) Clinical cure (at Test-of-Cure (TOC))



(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

6b) Microbiological cure (at 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)

6c) Recurrence of infection (at 6-12 weeks)



6d) Readmission/ Rehospitalisation (up to 6-12 weeks) *Data from personal communication with authors

	Shorter du		Longer du			Risk Ratio		Risk Rati		Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 9	95% CI	ABCDEFG
Lafaurie 2023	0	115	0	125		Not estimable	2023			
Total (95% CI)		115		125		Not estimable				
Total events	0		0							
Heterogeneity: Not ap	plicable									1
Test for overall effect:	Not applicab	le						0.01 0.1 1 Favours shorter duration Fav	10 100 avours longer duration	
Risk of bias legend										
(A) Random sequence	ce generation	i (selecti	on bias)							
(B) Allocation concea	Iment (select	tion bias)							
(C) Blinding of partici	pants and pe	rsonnel	(performand	ce bias)						
(D) Blinding of outcom	ne assessm	ent (dete	ction bias)							
(E) Incomplete outcom	me data (attri	tion bias)							
(F) Selective reporting	(reporting bi	ias)								

(G) Other bias

6e) Serious adverse events (up to 6 weeks)

	Shorter du	ration	Longer du	ration		Risk Ratio	Risk F	Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed	l, 95% Cl	ABCDEFG
Lafaurie 2023	0	115	0	125		Not estimable			
Total (95% CI)		115		125		Not estimable			
Total events	0		0						
Heterogeneity: Not ap	plicable						0.01 0.1 1		
Test for overall effect:	Not applicab	le					Favours shorter duration	Favours longer	100 duration

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)

6f) Non-serious adverse events (up to 6 weeks)



(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)

Subgroup analysis: Eligibility criteria of each individual study for enrolling men (presence/absence of acute bacterial prostatitis)

Supplementary Table 6: Studies of duration of treatment for cUTI including men showing impact of prostatitis on treatment effectiveness (n=7, 2000-2024) (see main text for Forest plot of these 7 trials)

Study (Lead author, Year of publication, Name of trial, Countries)	Males included (No, %)	Exclusion / Inclusion criteria-based on presence/ absence of involvement of prostate/ epididymis	Stratified analysis for male with/without prostatitis	Relative estimate of clinical cure in the whole population	Relative estimate of clinical cure in men	Relative estimate of clinical cure in men with suspected acute bacterial prostatitis
Peterson 2008 USA (multicentric)	427 (39%)	Excluded if presence of acute bacterial prostatitis or epididymitis	NR	RR 1.05 (0.97- 1.14)	NA	NA
Rudrabhatla 2018 India	24 (41%)	Excluded if evidence of prostatitis or prostatic abscess	NR	RR 1.00 (0.92 to 1.09)	NA	NA
Darouiche 2014 USA	52 (95%)	NR	NR	RR 1.00 (0.93 to 1.07)	Likely very similar to the whole population	NA
Ren 2017 China (multicentric)	40 (15%)	NR	NR	RR 1.01 (0.93 to 1.08)	NA	NA
Wagenlehner 2018 Germany and Poland	40 (18%)	NR	NR	RR 1.09 (0.96 to 1.23)	NA	NA
Lafaurie 2023 PROSTA- SHORT France (multicentric)	240 (100%)	Males with acute prostatitis included. Acute prostatitis was diagnosed based on pain on rectal examination, which was not systematically performed	Post-hoc analysis presence / absence of pain on rectal examination	RR 0.96 (0.92 to 1.00)	RR 0.96 (0.92 to 1.00)	In a subset of 27 men with pain on rectal examination, RR 0.77 (0.49 to 1.20) *
van Nieuwkoop 2017 FUTIRST Netherlands (multicentric)	86 (43%)	Males with acute prostatitis included	Randomized stratification for gender	RR 0.95 (0.88 to 1.03)	RR 0.88 (0.78 to 1.00)	NR

Interpretation: These studies suggest that the minimum effective duration of therapy in male UTI is driven by the presence or absence of acute prostatitis. As the proportion of men with potential prostatitis increases from top to bottom of this table, the effective duration of antibiotic therapy shifts from shorter course to longer course.

NR=not reported; NA=not applicable

*Personal communication with authors: 27 out of 91 men had pain on rectal examination.

Color key:

Green means: men with known prostatitis were specifically excluded, although it was unclear if all male participants were tested for prostatitis

Yellow means: whether or not the male participants had prostatitis was not reported

Orange means: men with prostatitis were included, but male participants were not systematically tested for prostatitis

D) Stratification for complicated UTI with associated gram-negative bacteremia

Subgroup analysis: complicated UTI with associated gram-negative bacteremia

Supplementary Figure 7: Forest plots for Clinical cure (at Test-of-Cure (TOC)) (including Sandberg 2012, Talan 2000, and van Nieuwkoop 2017)



*van Nieuwkoop 2017: Clinical cure rate (10 to 18 days post-treatment) in patients with bacteremia: risk difference (RD) was approximatively -10% with 90% CI (-21% to 2%), thus 7-day was not non-inferior to 14-days in bacteremia (Total number of bacteremic patients was 35, but no stratified data was reported in order to add it to the pooled analysis).

Supporting evidence: cUTI with associated gram-negative bacteremia

Supplementary Table 7: GRADE Evidence Profile

Question: In patients presenting with complicated UTI with associated gram-negative bacteremia, should total duration of antibiotics be shorter (<=7 days) rather than prolonged to >7 days?

P: In patients presenting with cUTI with associated gram-negative bacteremia

I: shorter total duration of antibiotics (<=7 days)

C: prolonged total duration of antibiotics (>7 days)

Setting: Inpatient and Outpatient

	The second se			№ of patients Effect				
№ of Study Risk of studies design bias	Inconsiste Indirectn ncy ess	Imprecision	Other considerations	Shorter duration of Abx (≤7 days)	Prolonged duration of Abx (> 7 days)	Relative (95% Cl)	Absolute (95% Cl)	

iysj

3 ¹⁻³	RCTs	seriousª	not serious	not serious	serious ^b	none	13/391 (3.3%)	9/367 (2.5%)	RR 1.31 (0.57 to 3.02)	8 more per 1,000 (from 11 fewer to 50 more)	⊕⊕⊖⊖ Low	CRITICAL	
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Mortality (at 30 days)

Mortality (at 90 days)

3 1-3	RCTs	seriousª	serious ^d	not serious	serious ^e	none	36/390 (9.2%)	36/367 (9.8%)	RR 0.94 (0.37 to 2.37)	6 fewer per 1,000 (from 62 fewer to 134 more)	⊕⊖⊖⊖ Very Low	IMPORTANT
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Readmission (at 30 days)

3 ¹⁻³	RCTs	very serious ^{a,g}	not serious	not serious	serious ^f	none	63/391 (16.1%)	70/369 (19.0%)	RR 0.80 (0.59 to 1.08)	38 fewer per 1,000 (from 78 fewer to 15 more)	⊕⊖⊖⊖ Very Low	IMPORTANT

Notes:

Clinical failure (i.e. composite outcome of the included main outcomes reported here) was not included in this EP table due to redundancy and lack of granularity.

CI: confidence interval; RR: risk ratio; Abx: antibiotics

	Certainty assessment							oatients		Effect	Certainty	Importance	
Nº of studies	Study design												
GRAD	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												
											ect		

Explanations

- a. All included data consists of post-hoc analyses of 3 different RCTs, thus considered at high risk of bias due to potential failure of randomization and serious attrition bias (between 55% and 68% of the patients had a cUTI as the primary source of bacteremia). Outcome measurement time frames varied between studies, with some studies measuring outcomes at an early specific time point after randomization rather than after end of treatment which may bias the assessment in favor of longer duration regimen. These studies were not rated down for risk of bias since this potential bias in favor of the longer course does not lower our confidence in the estimate that shorter is non-inferior to longer).
- b. Based on an inferiority margin of 10% (judged clinically significant by the panelists), not rated down for imprecision. Very few events were reported in both groups. Optimal information size criteria not met, and the wide 95% CI suggests fragility of the estimate.
- c. Very few events were reported in both groups. Optimal information size criteria not met and wide 95%CI. 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the shorter course failed to show or exclude a beneficial effect as compared to longer course.
- d. von Dach 2020 seems to be the main source of heterogeneity. After removing this study from the analysis, the I-square decreases from 59% to 29%.
- e. Optimal information size criteria not met and wide 95% CI (which might have been partially influenced by the observed inconsistency). 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the shorter course failed to show or exclude a beneficial effect as compared to longer course.
- f. 95% CI may not include a meaningful difference (i.e. crossing the null value), thus the shorter course failed to show or exclude a beneficial effect as compared to longer course
- g. Unblinded studies most likely did not affect most outcomes for their assessment or for decision-making that could influence them (except for readmission).

References

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- von Dach and al. Effect of C-Reactive Protein–Guided Antibiotic Treatment Duration, 7-Day Treatment, or 14-Day Treatment on 30-Day Clinical Failure Rate in Patients With Uncomplicated Gram-Negative Bacteremia A Randomized Clinical Trial. JAMA. 2020;323(21):2160-2169.
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Supplementary Table 8: Characteristics of the included studies on complicated UTI with associated gram-negative bacteremia (n=3, up to 2022)

Fact of publication, vame of trial, randomised, panlomised, P (%), Age)margin if applicable, primary outcome with its timing)(% of resistance, resistance, resistance, resoluter, resoluter, resoluter, resoluter, resoluter, resoluter, which 55% had culticentric Spain)criteria for clinical and oral and oral and oral antibiotics)duration, IV and oral antibiotics)Molina 2022 Molina 2022 Molina 2022 trialHospitalized and outpatients with Enterobacterales, of which 55% had culticentric Spain)Non-inferiority trial culticentric Spain)Non-inferiority trial culticentric Spain)Non-inferiority trial culticentric Spain)Non-inferiority trial culticentric Spain)Non-inferiority trial culticentric Spain)Takes the whole control. culticentric Spain)7 days14 daysVon Dach Outpatienter Switzerland)Hospitalized with uncomplicated Gram-negative bacteremia, of which 67% had culticentric Switzerland)Non-inferiority trial monificated Gram-negative bacteremia, of weight of curre or complicated for clinical work or current bactering, of wage 78 to 80yoNon-inferiority trial margin of 10% for complication, distant complication, of source of infection restarting antibiotics for clinical work organisms at 30 daysE.coli: 74% Margin of 10% for complicated failure was assessedOn day 5 (±1 d) of microbiologically efficacious antibiotic for clinical work attributed to initial organisms at 30 daysIn the whole complicated failure was assessedIntatient physicians followed choice and administrati	Study	Population	Study design	Main	Randomisation	Intervention	Comparator
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Isarel and bacteremia, of composite outcome of stable and afebrile step-down	(Isarel and			IEAT. 470/			
	Italy)			IEAI: 17%			
readmission at 90 focus of infection) physician in							
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No stratifiedday 7The type of empirical or directed antibiotic treatment and the		In the whole			uay I		
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F: 53% (post hoc analysis for oral antibiotic therapy was also							
Age: 71 yo cUTI) left to the discretion of the							
treating physician.							
JTI=Urinary Tract Infection; cUTI=complicated UTI; N=number; F=female, y=years; NR=not reported.	UTI=Urinary Tra	ct Infection: cUTI=cor	nplicated UTI: N=number	: : F=female, v=v	ears: NR=not reported	<u> </u>	

IEAT: inappropriate empiric antibiotic therapy; AEAT: appropriate empiric antibiotic therapy; MDR: multidrug resistant; ESBL= Extended spectrum Beta-Lactamase; AmpC= AmpC beta-lactamase; IV= parenteral.

Supplementary Figure 8: Summary of the Risk of Bias of included studies (Cochrane Risk of bias Tool) (n=3)





Supplementary Table 9: Assessment of the Risk of Bias of included studies (Cochrane Risk of bias Tool) (n=3)

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)
Molina 2022	High RoB	Low RoB	High RoB	High RoB	Low RoB	Low RoB	Low RoB
SHORTEN trial Multicentric (Spain)	-Randomization (not further detailed) -Post-hoc analysis for source of infection. No baseline comparison of patients' characteristics reported for this subpopulation.	-Centralised automatic system integrated in the electronic case report form	-Open-label (especially applicable to subjective outcomes)	-Open-label (especially applicable to subjective outcomes) -Analyst-blinded	-All outcomes analysed in the ITT population -No significant lost to follow up		-Not industry- funded
Von Dach 2020	High RoB	Low RoB	UnclearRoB	Low RoB	Low RoB	Low RoB	Low RoB
Multicentric (Switzerland)	-Computer- generated randomization with stratification by site -Post-hoc analysis for source of infection. No baseline comparison of patients' characteristics reported for this subpopulation.	-Concealment using sealed opaque envelopes	-Blinding performed from randomization to antibiotic discontinuation -Open-label after antibiotic discontinuation (especially applicable to subjective outcomes)	-Blinding performed throughout for outcomes assessors and data analysts	-All outcomes analysed in the ITT population -No significant lost to follow up		-Not industry- funded -The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review and approval of the manuscript; and decision to submit the manuscript for publication
Yahav 2019	High RoB	Low RoB	High RoB	High RoB	LowRoB	Low RoB	Low RoB
Multicentric (Isarel and Italy) RoB=Risk of Bias; IT	-Computer- generated randomization -Post-hoc analysis for source of infection. No baseline comparison of patients' characteristics reported for this subpopulation.	-Concealment using sealed opaque envelopes	-Open-label (especially applicable to subjective outcomes)	-Open-label (especially applicable to subjective outcomes)	-All outcomes analysed in the ITT population -No significant lost to follow up		-Not industry- funded

Supplementary Figures 9: Forest plots for each patient-important outcome

9a) Relapse of bacteremia (at 30 days)

	7 days	Abx	14 days	Abx		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Molina 2022	5	70	3	64	36.2%	1.52 [0.38, 6.12]		
von Dach 2020	1	101	1	112	9.2%	1.11 [0.07, 17.50]	_	
Yahav 2019	7	220	5	191	54.7%	1.22 [0.39, 3.77]		
Total (95% CI)		391		367	100.0%	1.31 [0.57, 3.02]	-	
Total events	13		9					
Heterogeneity: Tau ² :	= 0.00; Chi	² = 0.08	3, df = 2 (F	e = 0.96); I ^z = 0%			
Test for overall effect	: Z = 0.63 (P = 0.5	3)				0.01 0.1 1 10 Favours 7-day course Favours 14-day cou	100 rse

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

9b) Mortality (at 30 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

9c) Mortality (at 90 days)

	7 days	Abx	14 days	Abx		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Molina 2022	2	69	6	64	21.6%	0.31 [0.06, 1.48]		
von Dach 2020	9	101	4	112	30.3%	2.50 [0.79, 7.85]		
Yahav 2019	25	220	26	191	48.1%	0.83 [0.50, 1.40]		
Total (95% CI)		390		367	100.0%	0.94 [0.37, 2.37]	-	
Total events	36		36					
Heterogeneity: Tau ² =	0.40; Chi	² = 4.91	, df = 2 (P	= 0.09)); I ^z = 59%			7
Test for overall effect:	Z=0.14 (P = 0.8	9)				0.01 0.1 1 10 10 Favours 7-day course Favours 14-day cours	*

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)

9d) Mortality (at 90 days): Sensitivity analysis after removing von Dach 2020

	7 days	Abx	14 days	Abx		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Molina 2022	2	69	6	64	21.4%	0.31 [0.06, 1.48]		
von Dach 2020	9	101	4	112	0.0%	2.50 [0.79, 7.85]		
Yahav 2019	25	220	26	191	78.6%	0.83 [0.50, 1.40]		
Total (95% CI)		289		255	100.0%	0.67 [0.30, 1.50]	-	
Total events	27		32					
Heterogeneity: Tau ² =	0.14; Chi	² = 1.41	, df = 1 (P	= 0.24)); I ² = 29%			100
Test for overall effect:	Z=0.96 (P = 0.3	4)				0.01 0.1 1 10 Favours 7-day course Favours 14-day co	100 urse

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

9e) Readmission (at 30 days)

	7 days	Abx	14 days	Abx		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEFG
Molina 2022	7	70	9	66	10.3%	0.73 [0.29, 1.86]		
von Dach 2020	5	101	5	112	6.1%	1.11 [0.33, 3.72]		
Yahav 2019	51	220	56	191	83.6%	0.79 [0.57, 1.10]		
Total (95% CI)		391		369	100.0%	0.80 [0.59, 1.08]	•	
Total events	63		70					
Heterogeneity: Tau ² = Test for overall effect:			• •	= 0.85)); I ^z = 0%		0.01 0.1 1 10 Favours 7-day course Favours 14-day course	100 urse

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)

Supplementary Table 10: GRADE Evidence to Decision framework for cUTI with associated gram-negative bacteremia

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
CCEPTABILITY /	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
ype of Recon	nmendation						
		al recommendatior the intervention	Conditional recom for either the inter the compar	vention or reco	Conditional mmendation for e intervention	Strong recommendation for th intervention	
0		0	0		°	0	