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# Infections urinaires masculines big bang ou koik ?

13/06/2024

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# Déclaration de liens d'intérêt avec les industriels de santé en rapport avec le thème de la présentation (loi du 04/03/2002)

- Consultant ou membre d'un conseil scientifique : NON
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents : NON
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations : NON
- Investigateur principal d'une recherche ou d'une étude clinique: NON

# En pratique, qui fait quoi?

Mr P. 79 ans, brulures urinaires, urgenturie depuis 5 jours. Pas de fièvre.

ECBU: *E. coli* $10^5$ cfu/mL, sauvage, GB 95000/mL.

ATCD: IDM, hypercholestérolémie, PTH, Hypertrophie bénigne de prostate

Quel traitement oral, quelle durée?

- Furadantine 7 jours
- Ofloxacine 14 jours
- Fosfomycine J1-J3-J5
- Cotrimoxazole 7 jours
- Amoxicilline 10 jours
- Ciprofloxacine 21 jours
- Pivmécillinam 5 jours

# En pratique, qui fait quoi?

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ATCD: IDM, hypercholestérolémie, PTH, hypertrophie benigne de prostate

## Avant de répondre: quelle infection traite t'on?

- Ofloxacine 14 jours
- Fosfomycine J1-J3-J5
- Cotrimoxazole 7 jours
- Amoxicilline 10 jours
- Ciprofloxacine 21 jours
- Pivmécillinam 5 jours

# De quelle maladie s'agit t'il?

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- HBP associée à une bactériurie asymptomatique
- Cystite aigue
- Prostatite aigue
- Peur de vieillir
- Urétrite

# De quelle maladie s'agit t'il?

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ATCD: IDM, hypercholestérolémie, PTH, **prostatectomie radicale pour ADK**

- Hyperactivité vésicale et bactériurie asymptomatique
- Cystite aigue
- Prostatite aigue
- Hystérie de l'homme au bout de sa vie
- Urétrite

# Questions qu'on se pose encore

- Terminologie, entités cliniques : prostatite aiguë, cystite aiguë, pyélonéphrite aiguë,
- orchi-épididimyte

- Diffusion antibiotiques dans la prostate

- Durée, doses de traitement
  - Selon diagnostic
  - Selon germes
  - Selon diffusion antibiotiques

- Bilan urologique à proposer

# Groupe de travail SPILF, mise à jour recommandations infections urinaires de l'homme

W. Boutfol, F. Bruyère, Y. Caspar, V. Cattoir , A. Dinh, M. Etienne, E. Forestier, A. Hamon, M. Jonchier,

V. Jullien, M. Lafaurie (coordonnateur), A. Lefort, F. Lemaitre, H. Milacic, V. Orcel, A. Putot, C. Roubaud,

B. Soussais, M. Vallée.

**Généralistes, urgentistes, urologues, gériatres, pharmacologues, infectiologues, microb**

# Groupe de travail SPILF, mise à jour [illegible] commandations infections urinaires de l'homm[illegible]

W. Boutfol, F. Bruyère, Y. Cas[illegible]stier, A. Hamon, M. Jonchier,

V. Jullien, M. Lafa[illegible] Orcel, A. Putot, C. Roubaud,

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**Généralistes, urgenti[illegible]fectiologues, microb**

# TERMINOLOGIE

- **Cystite masculine**

SPILF: entité non individualisée dans les recommandations françaises

EAU (Urologie Europe) (2024): Cystitis in men without involvement of the prostate is uncommon and should be classed as a complicated infection. Therefore, treatment with antimicrobials penetrating into the prostate tissue is needed in males with symptoms of UTI. A treatment duration of at least seven days is recommended, preferably with trimethoprim-sulphamethoxazole or a fluoroquinolone if in accordance with susceptibility testing.

- **Infection urinaire de l'homme**

SPILF: infection urinaire masculine fébrile/non fébrile

EAU: classification du National Institute of Health (NIH) distinguant la prostatite aiguë de la prostatite chronique

D'après F. Bruyère

| Nombre | Catégorie | Caractéristiques | Signes présents dans l'urine | Prémassage | Post-massage |
|---|---|---|---|---|---|
| I | Prostatite bactérienne aiguë | Symptômes aigus d'infection urinaire | Globules blancs | +/− | + |
| | | | Bactéries | +/− | + |
| II | Prostatite bactérienne chronique | Infection urinaire récidivante par un même microrganisme | Globules blancs | +/− | + |
| | | | Bactéries | +/− | + |
| III | Prostatite chronique/syndrome de douleur pelvienne chronique | Principalement des douleurs, des troubles mictionnels et une dysfonction sexuelle | | | |
| IIIa | Inflammatoires | | Globules blancs | − | + |
| | | | Bactéries | − | − |
| IIIb | Non inflammatoire* | | Globules blancs | − | − |
| | | | Bactéries | − | − |
| IV | Prostatite inflammatoire asymptomatique | Découverte fortuite lors de l'évaluation urologique (p. ex., biopsie de la prostate, analyse du liquide séminal) pour d'autres pathologies | Globules blancs | − | + |
| | | | Bactéries | − | − |

*Précédemment appelé prostatodynie.

+/− signifie éventuellement présents; + signifie présents; − signifie absent.

# Signes cliniques de prostatite aigüe

PROSTASHORT

| Characteristic | 7-Day Therapy (n = 115) | 14-Day Therapy (n = 125) | Total |
|---|---|---|---|
| Clinical presentation | | | |
| Body temperature, °C, median (IQR) | 38.3 (37.7–38.9) | 38.2 (37.3–38.8) | |
| Urinary burning | 92 (80.0) | 104 (83.2) | |
| Dysuria | 75 (65.2) | 86 (68.8) | |
| Frequency of urination | 77 (66.9) | 89 (71.2) | |
| Urgency of urination | 48 (41.7) | 54 (43.2) | |
| Pelvic pain | 13 (11) | 10 (8) | |
| **Rectal examination done** | **47 (41)** | **44 (35)** | **91 (38)** |
| Prostatic pain on rectal examination | 15 (32) | 12 (27) | 27 (30) |

Lafaurie *et al*. CID 2023

# Acute bacterial prostatitis: heterogeneity in diagnostic criteria and management. Retrospective multicentric analysis of 371 patients diagnosed with acute prostatitis

M. Etienne *et al.*, BMC Infec Dis 2008

| | Total patients | Department of admission | | | |
|---|---|---|---|---|---|
| | n = 371 | Urology n = 178 | Infectious Diseases n = 115 | Internal Medicine n = 48 | Geriatrics n = 30 |
| **Cause of admission** | | | | | |
| Fever | 297 (80%) | 142 (80%) | 97 (84%) | 37 (78%) | 19 (63%) |
| Urinary symptoms | | | | | |
| Functional symptoms | 266 (72%) | 153 (86%) | 69 (60%) | 27 (57%) | 15 (50%) |
| Bladder outlet obstruction | 61 (23%) | 52 (29%) | 9 (8%) | 12 (25%) | 6 (20%) |
| Cognitive disorder | 14 (4%) | 0 (0%) | 5 (4%) | 4 (8%) | 10((33%) |
| Miscellaneous symptoms | 28 (8%) | 0 (0%) | 2 (2%) | 21 (44%) | 7 (23%) |
| **Main clinical symptoms during the course of AP** | | | | | |
| Fever | 297 (80%) | 154 (84%) | 86 (80%) | 38 (78%) | 19 (63%) |
| Chills | 135 (35%) | 47 (25%) | 60 (56%) | 14 (28%) | 7 (23%) |
| Urinary symptoms | 266 (72%) | 158 (86%) | 65 (60%) | 28 (57%) | 15 (50%) |
| - burning micturition | 143 (54%) | 79 (50%) | 36 (55%) | 23 (82%) | 5 (33%) |
| - pollakiuria | 200 (52%) | 77 (49%) | 35 (54%) | 18 (64%) | 9 (60%) |
| - dysuria | 79 (30%) | 53 (34%) | 15 (23%) | 7 (25%) | 4 (27%) |
| - bladder outlet obstruction | 61 (23%) | 46 (29%) | 5 (8%) | 7 (25%) | 3 (20%) |
| - macroscopic haematuria | 46 (17%) | 33 (21%) | 9 (14%) | 2 (7%) | 2 (13%) |
| Pelvic pain | 144 (43%) | 98 (58%) | 27 (28%) | 18 (42%) | 1 (4%) |
| Abnormal digital rectal examination | 235 (83%) | 135 (89%) | 55 (70%) | 25 (83%) | 20 (91%) |
| - painful prostate palpation | 175 (63%) | 115 (77%) | 31 (39%) | 15 (50%) | 14 (64%) |
| - prostatic hypertrophy | 152 (54%) | 86 (57%) | 36 (46%) | 16 (53%) | 14 (63%) |
| - prostate irregularity | 66 (24%) | 44 (30%) | 10 (13%) | 4 (13%) | 8 (22%) |

# Signes « microbiologiques » de prostatite aigüe

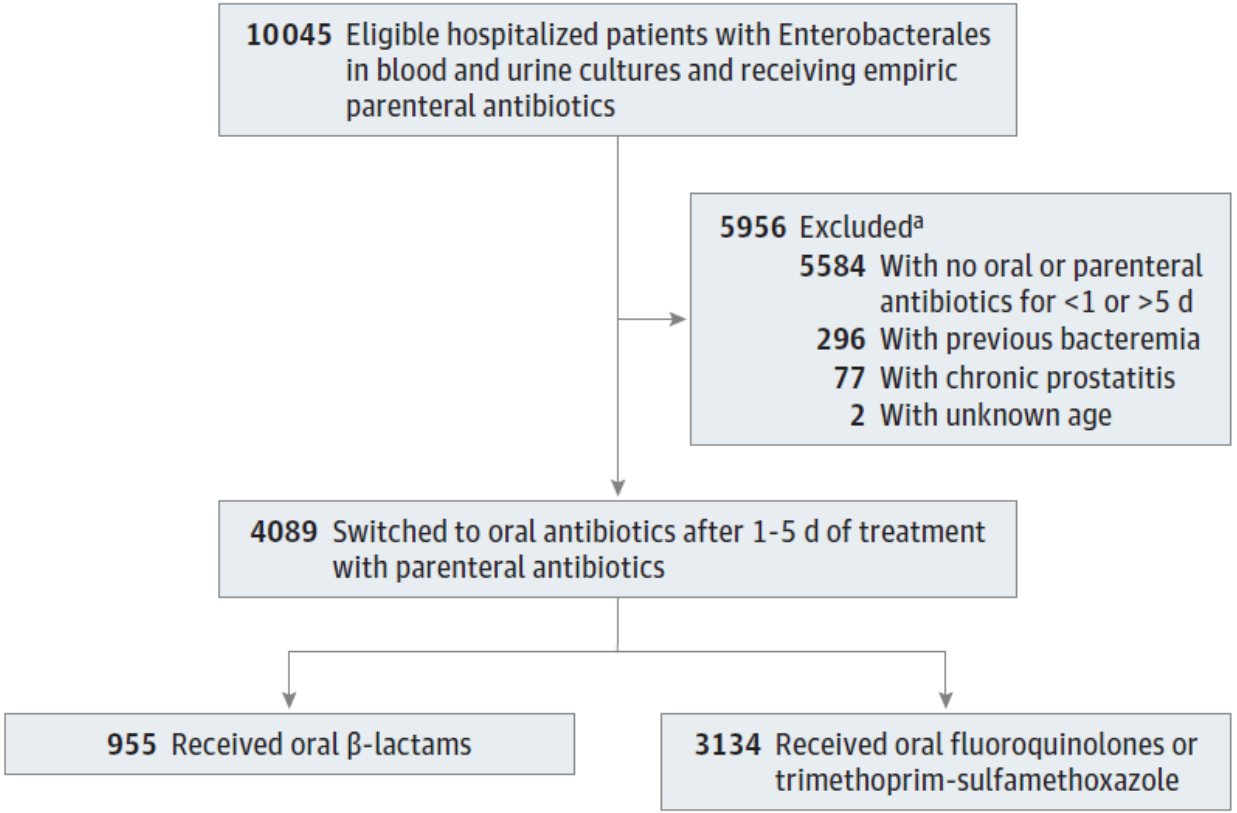
JAMA Network Open

Original Investigation | Infectious Diseases

## Oral β-Lactam Antibiotics vs Fluoroquinolones or Trimethoprim-Sulfamethoxazole for Definitive Treatment of Enterobacterales Bacteremia From a Urine Source

Jesse D. Sutton, PharmD, MS; Vanessa W. Stevens, PhD; Nai-Chung N. Chang, PhD; Karim Khader, PhD; Tristan T. Timbrook, PharmD, MBA; Emily S. Spivak, MD, MHS

October 8, 2020


10045 Eligible hospitalized patients with Enterobacterales in blood and urine cultures and receiving empiric parenteral antibiotics
5956 Excluded[a]
5584 With no oral or parenteral antibiotics for <1 or >5 d
296 With previous bacteremia
77 With chronic prostatitis
2 With unknown age
4089 Switched to oral antibiotics after 1-5 d of treatment with parenteral antibiotics
955 Received oral β-lactams
3134 Received oral fluoroquinolones or trimethoprim-sulfamethoxazole

| Characteristic | Patients, No. (%) | |
|---|---|---|
| | Fluoroquinolone or trimethoprim-sulfamethoxazole (n = 3134) | β-Lactam antibiotics (n = 955) |
| Age, median (IQR), y | 69 (62-80) | 73 (64-83) |
| Male | 2847 (90.8) | 884 (92.6) |
| Preexisting conditions[a] | | |
| Combined comorbidity score, median (IQR) | 1 (0-2) | 1 (0-3) |
| Chronic kidney disease | 564 (18.0) | 227 (23.8) |
| Chronic pulmonary disease | 681 (21.7) | 220 (23.0) |
| Heart failure | 480 (15.3) | 170 (17.8) |
| Diabetes with complication | 402 (12.8) | 130 (13.6) |
| Dementia | 180 (5.7) | 69 (7.2) |
| Immunosuppression | 182 (5.8) | 61 (6.4) |
| History of organ or stem cell transplant | 72 (2.3) | 22 (2.3) |
| Transplant antirejection medications within 90 d | 64 (2.0) | 20 (2.1) |
| High-dose corticosteroids within 30 d | 39 (1.2) | 17 (1.8) |
| Other immunosuppressive medication within 90 d | 68 (2.2) | 23 (2.4) |
| Leukopenia, leukocyte ≤1000 cells/μL | 5 (0.2) | 1 (0.1) |
| Metastatic cancer | 144 (4.6) | 47 (4.9) |
| Cirrhosis | 88 (2.8) | 20 (2.1) |
| HIV | 40 (1.3) | 10 (1.0) |

| | FQ and cotrimoxazole | B-lactams |
|---|---|---|
| Preexisting urologic conditions[a] | | |
| History of urinary tract infection | 886 (28.3) | 401 (42.0) |
| Previous antibiotics active against gram-negative organisms within 30 d | 398 (12.7) | 222 (23.2) |
| Prostate hypertrophy | 887 (28.3) | 324 (33.9) |
| Urinary retention, obstruction, or other structural urologic abnormality | 723 (23.1) | 288 (30.2) |
| Urologic procedure within 90 d before oral step-down therapy | 562 (17.9) | 212 (22.2) |
| Prostate cancer | 408 (13.0) | 143 (15.0) |
| Spinal cord injury, paraplegia, quadriplegia, or multiple sclerosis | 129 (4.1) | 52 (5.4) |
| Urinary calculi within 30 d | 138 (4.4) | 35 (3.7) |
| Acute prostatitis within 30 d | 15 (0.5) | 7 (0.7) |
| Enterobacterales isolated from bloodstream | | |
| *Escherichia coli* | 2254 (71.9) | 711 (74.5) |
| *Proteus mirabilis* | 189 (6.0) | 116 (12.1) |
| *Klebsiella pneumoniae* | 589 (18.8) | 104 (10.9) |
| *Klebsiella oxytoca* | 75 (2.4) | 14 (1.5) |
| Other or unspecified *Klebsiella* spp | 14 (0.4) | 5 (0.5) |
| Other or unspecified *Proteus* spp | 13 (0.4) | 5 (0.5) |

| | FQ and cotrimoxazole | B-lactams |
|---|---|---|
| Acute characteristics[b] | | |
| Time from hospitalization to bacteremia ≥48 h | 159 (5.1) | 28 (2.9) |
| Antibiotic initiation | | |
| Intensive care unit | 543 (17.3) | 165 (17.3) |
| Vasopressors | 122 (3.9) | 30 (3.1) |
| Serum leukocyte ≥12 000 cells/μL | 2145 (68.4) | 615 (64.4) |
| Temperature ≥38.3 °C | 1799 (57.4) | 542 (56.8) |
| Oral step-down therapy | | |
| Intensive care unit | 84 (2.7) | 22 (2.3) |
| Serum leukocyte ≥12 000 cells/μL | 480 (15.3) | 130 (13.6) |
| Temperature ≥38.3 °C | 81 (2.6) | 15 (1.6) |
| Weight, median (IQR), kg | 85 (73-100) | 86 (74-102) |
| Creatinine clearance while receiving oral step-down therapy, median (IQR), mL/min[c] | 62 (44-81) | 58 (41-76) |
| Treatment characteristics | | |
| Time to in vitro active antibiotics, median (IQR), h | 12 (6-20) | 13 (7-21) |
| 1st day of oral antibiotics alone, median (IQR), d | 4 (4-5) | 5 (4-5) |
| Day 2 | 138 (4.4) | 32 (3.4) |
| Day 3 | 474 (15.1) | 121 (12.7) |
| Day 4 | 1027 (32.8) | 303 (31.7) |
| Day 5 | 893 (28.5) | 302 (31.6) |
| Day 6 | 602 (19.2) | 197 (20.6) |
| Oral antibiotic with in vitro activity | 3077 (98.2) | 937 (98.1) |
| Unknown | 34 (1.1) | 12 (1.3) |
| Antibiotic duration, median (IQR), d | | |
| Total | 14 (12-16) | 14 (12-16) |
| Oral | 10 (9-13) | 10 (8-12) |

| Outcome | Patients, No. (%) | | aRD, % (95% CI)[a] | aRR (95% CI)[a] |
|---|---|---|---|---|
| | Fluoroquinolones or trimethoprim-sulfamethoxazole (n = 3134) | β-Lactam antibiotics (n = 955) | | |
| 30-d Mortality and recurrent bacteremia | 94 (3.0) | 42 (4.4) | 0.99 (−0.42 to 2.40) | 1.31 (0.87 to 1.95) |
| Mortality | 82 (2.6) | 29 (3.0) | 0.06 (−1.13 to 1.26) | 1.02 (0.67 to 1.56) |
| Recurrent bacteremia | 12 (0.4) | 14 (1.5) | 1.03 (0.24 to 1.82) | 3.43 (0.42 to 27.90) |
| 90-d Mortality and recurrent bacteremia | 238 (7.6) | 96 (10.1) | 1.81 (−0.24 to 3.87) | 1.23 (0.96 to 1.56) |
| Mortality | 208 (6.6) | 75 (7.9) | 0.68 (−1.16 to 2.52) | 1.10 (0.85 to 1.42) |
| Recurrent bacteremia | 34 (1.1) | 25 (2.6) | 1.38 (0.30 to 2.47) | 2.15 (0.92 to 5.01) |
| Repeated hospitalization with UTI | | | | |
| At 30 d | 22 (0.7) | 14 (1.5) | 0.81 (−0.06 to 1.67) | 2.08 (0.72 to 5.99) |
| At 90 d | 46 (1.5) | 29 (3.0) | 1.46 (0.28 to 2.64) | 1.94 (0.97 to 3.85) |

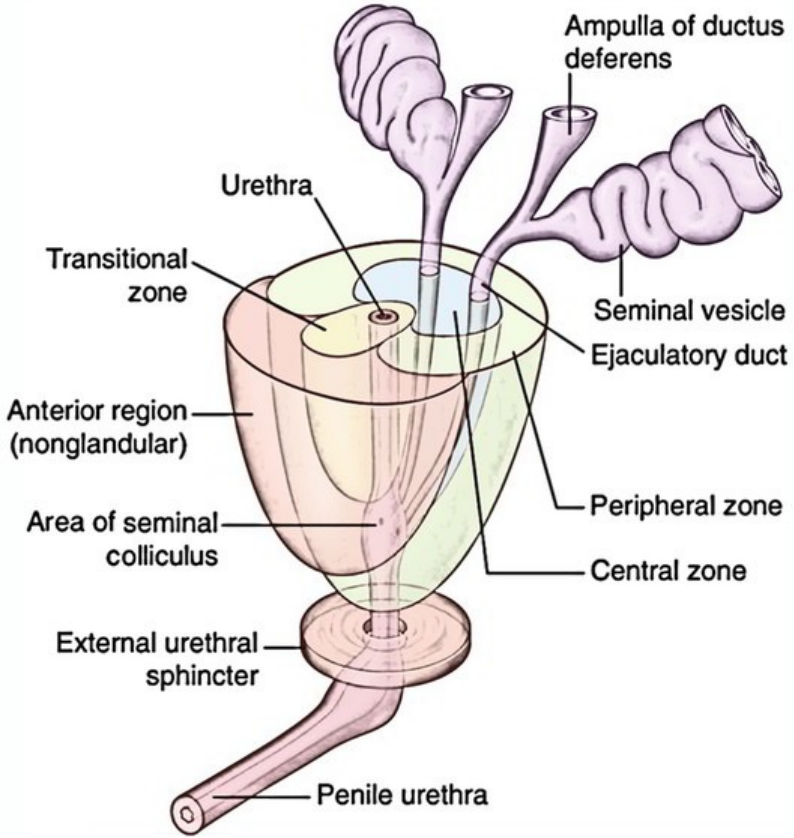
Abbreviation: aRD, adjusted risk difference; aRR, adjusted relative risk; UTI, urinary tract infection.

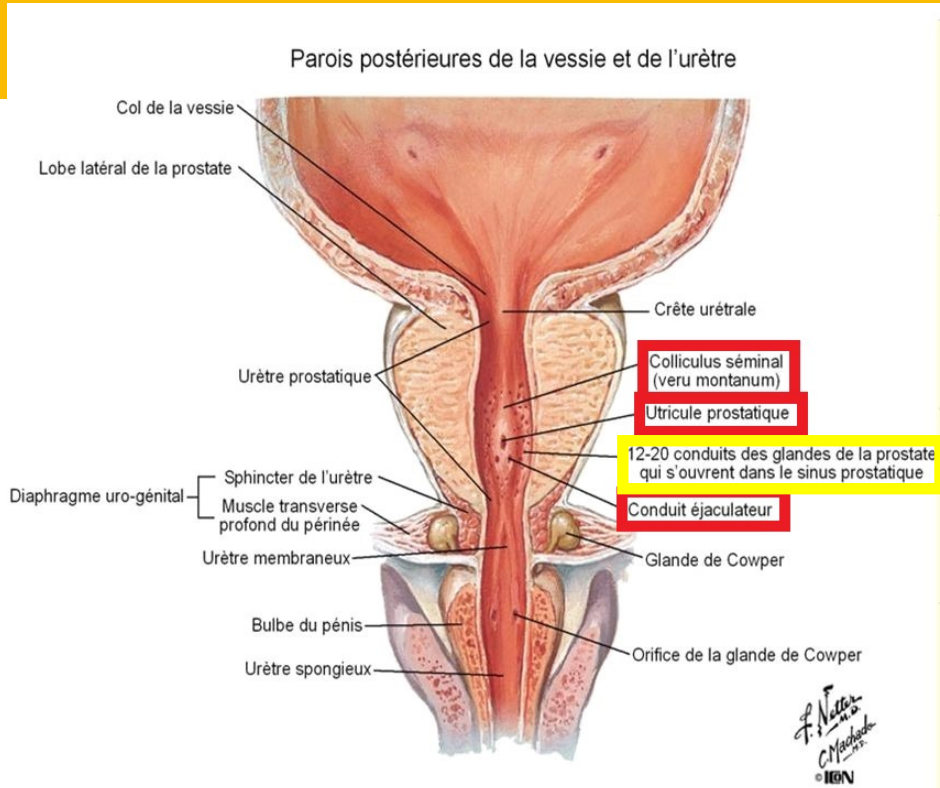
| Drug | Patients, No. (%) | 30-d Recurrent bacteremia, No./total No. (%) | 30-d Mortality, No./total No. (%) | Dose, mg/dose[a] | Doses per day, No. | Patients, No./total No. (%) |
|---|---|---|---|---|---|---|
| β-Lactam antibiotics (n = 955) | | | | | | |
| Amoxicillin-clavulanate potassium | 251 (26.3) | 4/251 (1.6) | 13/251 (5.2) | 875-125 | 2 | 161/251 (64.1) |
| | | | | 500-125 | 2 | 46/251 (18.3) |
| | | | | 500-125 | 3 | 28/251 (11.2) |
| Cephalexin | 245 (25.7) | 0 | 5/245 (2.0) | 500 | 4 | 115/245 (46.9) |
| | | | | 500 | 2 | 57/245 (23.3) |
| | | | | 500 | 3 | 47/245 (19.2) |
| Cefpodoxime proxetil | 243 (25.4) | 4/243 (1.6) | 8/243 (3.3) | 200 | 2 | 154/243 (63.4) |
| | | | | 400 | 2 | 47/243 (19.3) |
| Cefuroxime sodium | 97 (10.2) | 2/97 (2.1) | 0 | 500 | 2 | 83/97 (85.6) |
| | | | | 250 | 2 | 12/97 (12.4) |
| Amoxicillin | 63 (6.6) | 3/63 (4.8) | 1/63 (1.6) | 500 | 3 | 44/63 (69.8) |
| | | | | 500 | 2 | 9/63 (14.3) |
| Cefdinir | 35 (3.7) | 1/35 (2.9) | 0 | 300 | 2 | 33/35 (94.3) |
| Cefixime | 14 (1.5) | 0 | 0 | 400 | 1 | 11/14 (78.6) |
| | | | | 400 | 2 | 3/14 (21.4) |
| Ampicillin sodium | 6 (0.6) | 0 | 2/6 (33.3) | 500 | 4 | 2/6 (33.3) |
| | | | | 500 | 2 | 2/6 (33.3) |
| Cefadroxil | 1 (0.1) | 0 | 0 | 1000 | 1 | 1 (100) |
| Fluoroquinolones or trimethoprim-sulfamethoxazole (n = 3134) | | | | | | |
| Ciprofloxacin | 2447 (78.1) | 9/2447 (0.4) | 61/2447 (2.5) | 500 | 2 | 2003/2447 (81.9) |
| | | | | 500 | 1 | 172/2447 (7.0) |
| | | | | 250 | 2 | 130/2447 (5.3) |
| | | | | 750 | 2 | 122/2447 (5.0) |
| Levofloxacin | 374 (11.9) | 0 | 13/374 (3.5) | 750 | 1 | 156/374 (41.7) |
| | | | | 500 | 1 | 154/374 (41.2) |
| | | | | 250 | 1 | 43/374 (11.5) |
| Trimethoprim-sulfamethoxazole | 295 (9.4) | 3/295 (1.0) | 7/295 (2.4) | 800-160 | 2 | 259/295 (87.8) |
| Moxifloxacin hydrochloride | 18 (0.6) | 0 | 1/18 (5.6) | 400 | 1 | 18 (100) |

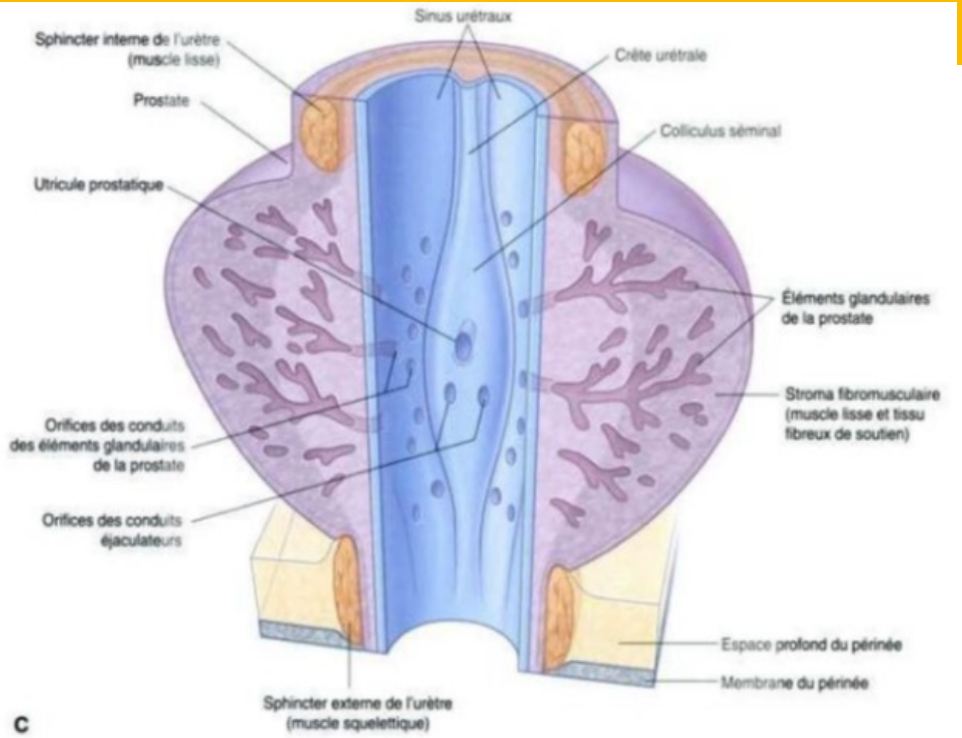
# La cystite de l'homme existe officiellement dans plusierus recommandations nationales

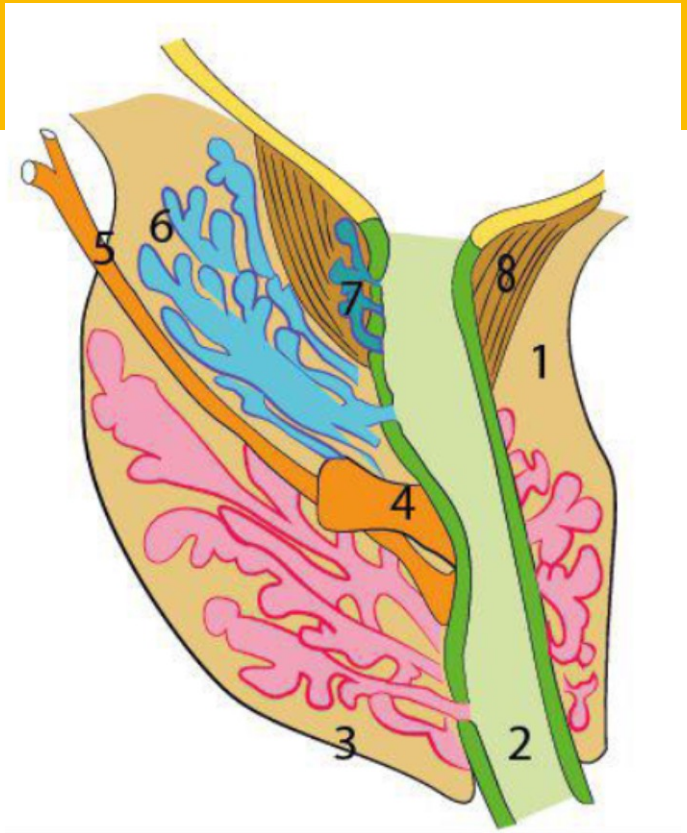
- Grande Bretagne: The National Institute for Health and Care Excellence (NICE) guideline. Urinary Tract Infection (Lower): Antimicrobial Prescribing. 2018. www.nice.org.uk/guidance/ng109
- Pays-Bas: Nederlands Huisartsen Genootshap. Urineweginfecties | NHG (Dutch).2013.https://richtlijnen.nhg.org/standaarden/urineweginfecties
- Suède: Läkemedelsverket. Läkemedelsbehandling av urinvägsinfektioner i oppenvård-behandlingsrekommendation. 2017. Available from: https://lakemedelsverket.se/malgrupp/Halso—sjukvard/Behandlings–rekommendationer/Behandlingsrekommendation—listan/UVIurinvagsinfektioner-i-oppenvard/
- …

D'après B. Soudais Family Practice, 2021, 432–440


Ampulla of ductus deferens
Urethra
Transitional zone
Seminal vesicle
Ejaculatory duct
Anterior region (nonglandular)
Peripheral zone
Area of seminal colliculus
Central zone
External urethral sphincter
Penile urethra


Parois postérieures de la vessie et de l'urètre
Col de la vessie
Lobe latéral de la prostate
Crête urétrale
Urètre prostatique
Colliculus séminal (veru montanum)
Utricule prostatique
12-20 conduits des glandes de la prostate qui s'ouvrent dans le sinus prostatique
Diaphragme uro-génital
Sphincter de l'urètre
Muscle transverse profond du périnée
Conduit éjaculateur
Urètre membraneux
Glande de Cowper
Bulbe du pénis
Orifice de la glande de Cowper
Urètre spongieux


Sinus urétraux
Sphincter interne de l'urètre (muscle lisse)
Crête urétrale
Prostate
Colliculus séminal
Utricule prostatique
Éléments glandulaires de la prostate
Stroma fibromusculaire (muscle lisse et tissu fibreux de soutien)
Orifices des conduits des éléments glandulaires de la prostate
Orifices des conduits éjaculateurs
Espace profond du périnée
Membrane du périnée
Sphincter externe de l'urètre (muscle squelettique)
C


5
6
7
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1
4
3
2

# Infection systématique de la prostate si bactéries dans les urines?

- Je ne crois vraiment pas
- Risque plus élevé après RTUP? (rupture barrière urothéliale)

- Pour simplifier:

- **Infection tissulaire=fièvre**=prostatite aigue (ou PNA)
- **Pas d'infection tissulaire=pas de fièvre**=infection vésicale=cystite
- Pas de fièvre mais bactériémie= prostatite aigue/PNA?

- Intérêt de cette distinction: durée (nature) du traitement

# Diffusion des antibiotiques dans la prostate

## Tissue concentrations: do we ever learn?

Mouton *et al*. JAC 2008.

- Attention à interpretation concentration tissulaire et lien avec activité antibiotique
- Concentration tissulaire= généralement concentration broyat tissulaire
- Hors: plusieurs compartiments tissulaires: intracellulaire (80% du volume), organites intra cellulaires, extracellulaire: liquide interstitiel (16% du volume) et intravasculaire (4%).
- Diffusion des antibiotiques variable selon le compartiment
- Bactéries généralement dans espace extracellulaire
- Compartiment extracellulaire: B-lactamines et aminosides. Donc dilution concentration si broyat et sous estimation: multiplier par 5 la concentration pour avoir la concentration réelle dans l'espace extra-cellulaire.
- Résultat inverse si concentration intracellulaire (FQ, macrolides) et surestimation concentration.

# Diffusion des antibiotiques dans la prostate

- Pièges pour interprétation PK sérum/tissu
- Les ratios de concentration tissu/plasma change avec le temps en raison

  - du décalage entre les cinétiques plasmatiques et tissulaires

  - du décalage de l'équilibre de concentration selon les compartiments

- Donc attention au  moment mesure concentration tissulaire (souvent une seule mesure), intérêt plusieurs mesures (mais pas possible pour un seul individu).
- Lien concentration un seul point et CMI: non sens

# TRAITEMENT

## SPILF

La notion de fièvre disparait pour le choix et la durée des antibiotiques

- *Apyrexie et infection « bien » tolérée* : ttt différé selon documentation microbiologique si possible

- Durée :

  - 14 j si fluoroquinolone, triméthoprime-sulfaméthoxazole, β-lactamines injectables

  - 21 j pour les autres molécules **OU** si uropathie sous jacente non corrigée (= troubles mictionnels préexistants, lithiase…)

# En pratique, qui fait quoi?

Mr P. 83 ans, brulures urinaires, urgenturie depuis 5 jours. Pas de fièvre. ECBU: *E. coli* $10^5$ cfu/mL, sauvage, GB 95000/mL.

ATCD: IDM, hypercholestérolémie, PTH, HBP

Quel traitement, quelle durée?

- Furandantine 7 jours
- Ofloxacine 14 jours
- Fosfomycine: J1-J3-J5
- Cotrimoxazole 7 jours
- Amoxicilline 10 jours
- Ciprofloxacine: 21 jours
- Pivmécillinam: 5 jours

# Traitement: Cystite de l'homme

- Hommes souvent inclus dans les études de traitement des cystites compliquées, mais de façon variable et minoritaire (jusqu'à 10%), résultats de ce sous-groupe non donnés.

- Données spécifiques chez l'homme, essentiellement cohortes rétrospectives
  - pivmécillinam
  - triméthoprime
  - cotrimoxazole
  - nitrofurantoine
  - fosfomycine

- Doses et durées variables mais ≤ 7 jours (5-7 jours)

# Recommandations internationales, cystite de l'homme

## Pays bas

- 1er choix : Nitrofurantoïne, 7 jours, 100 mg x2/j ou 50 mg x4/j.
- 2ème choix : Triméthoprime, 7 jours, 300 mg/j.

## GB

- Trimethoprime: 7 jours, 200 mg x2/j
- Nitrofurantoïne: 7 jours (si DFG estimé≥45 mL/min): 100 mg x2/j (ou 50 mg x4/j)

# Recommandations internationales, cystite de l’homme

## ❖ Suède

On cherche à obtenir une forte concentration d'antibiotiques dans les urines

- Nitrofurantoïne
- Pivmécillinam

Durée recommandée du traitement : 7 jours

# Effect of 7 vs 14 Days of Antibiotic Therapy on Resolution of Symptoms Among Afebrile Men With Urinary Tract Infection (Drenkonja *et al*. JAMA 07/2021)

- Etude **randomisée en double aveugle, contre placebo**
- 2 centres médicaux (Minnesota et Texas)
- **Patients**: hommes, > 18 ans, ttt prescrit pour 7 à 14 jours par Cipro ou cotrimoxazole pour infection urinaire non febrile, en ambulatoire, par leur médecin.
- Et au moins un signe parmi: dysuria, pollakiurie, urgenturie, hématurie, douleur angle costo-vertebral ou périnée ou flanc ou sus pubienne.
- **Non inclusion**: infection urinaire dans les 14 jours précédents, t°>38° C, germe urinaire resistant au ttt prescrit.
- **ECBU pas necessaire**
- Traitement prescrit pendant 7 jours
- Tirage au sort pour traitement à partir de J8
    - soit continuer le même ttt (mais cp différents), pdt 7 jours
    - soit prendre un placebo pdt 7 jours

Suivi téléphonique: J14, puis +7, +14 et +28.

Table 1. Baseline Demographics and Comorbid Conditions[a]

| Variable | 7-Day antimicrobial + 7-day placebo group (n = 136)[b,c] | 14-Day antimicrobial group (n = 136)[c] |
|---|---|---|
| Age, median (IQR), y | 70 (62-73) | 70 (62-75) |
| Race[d,e] | (n = 135) | (n = 135) |
| White | 107 (79) | 105 (78) |
| Black | 26 (19) | 23 (17) |
| Native American | 1 (1) | 5 (4) |
| Multiple races | 1 (1) | 2 (1) |
| Hispanic/Latino ethnicity[d,f] | 5/132 (4) | 8/134 (6) |
| Charlson comorbidity index, median (IQR)[g] | 1 (0-2) | 1 (0-2) |
| Urinary tract-related comorbidities | (n = 136) | (n = 136) |
| Any prior UTI | 84 (62) | 78 (57) |
| Prostatic hypertrophy | 56 (41) | 47 (35) |
| Urinary incontinence | 44 (32) | 52 (38) |
| Intermittent catheter use | 24 (18) | 23 (17) |
| Prostate cancer | 21 (15) | 23 (17) |
| Urethral stricture | 17 (13) | 16 (12) |
| Prior prostatitis | 16 (12) | 18 (13) |
| Indwelling catheter use | 8 (6) | 8 (6) |
| Nonurinary comorbidities | (n = 136) | (n = 136) |
| Diabetes | 46 (34) | 60 (44) |
| Cerebrovascular accident | 13 (10) | 5 (4) |
| Chronic kidney disease | 8 (6) | 14 (10) |
| Spinal cord injury | 5 (4) | 6 (4) |
| HIV | 2 (1) | 2 (1) |
| Most common symptoms associated with UTI diagnosis | (n = 136) | (n = 136) |
| Dysuria | 93 (68) | 88 (65) |
| Frequency | 80 (59) | 70 (51) |
| Urgency | 52 (39) | 39 (29) |

Table 2. Distribution of Organisms Isolated From 145 Urine Cultures With Growth at Greater Than 100 000 Colony-Forming Units/mL[a]

| Organism isolated | No. (%) | |
|---|---|---|
| | 7-Day antimicrobial + 7-day placebo group (n=70) | 14-Day antimicrobial group (n-75) |
| *Escherichia coli* | 30 (43) | 29 (39) |
| Klebsiella species | 11 (16) | 12 (16) |
| Enterococcus species | 7 (10) | 6 (8) |
| Coagulase-negative staphylococci | 6 (9) | 8 (11) |
| Citrobacter species | 3 (4) | 3 (4) |
| *Morganella morganii* | 3 (4) | 1 (1) |
| Streptococcus species | 3 (4) | 2 (3) |
| Enterobacter species | 2 (3) | 2 (3) |
| *Proteus mirabilis* | 2 (3) | 2 (3) |
| *Serratia marcescens* | 2 (3) | 1 (1) |
| *Staphylococcus aureus* | 1 (1) | 2 (3) |
| Aerococcus urinae | 1 (1) | 1 (1) |
| Gram-positive bacilli, not further identified | 1 (1) | 1 (1) |
| *Pseudomonas aeruginosa* | 0 | 2 (3) |
| Salmonella species | 0 | 1 (1) |

ECBU positif: n=145, 53%; dont 14 à SCN...

Table 3. Primary and Secondary Outcomes

| Characteristic | No./total No. (%) | | |
|---|---|---|---|
| Resolution of UTI symptoms 14 days after stopping active antimicrobials | 7-Day antimicrobial + 7-day placebo group | 14-Day antimicrobial group | Absolute difference, % (1-sided 97.5% CI)[a] |
| As-treated population (primary analysis) | 122/131 (93.1) | 111/123 (90.2) | 2.9 (-5.2 to ∞) |
| As-randomized population | 125/136 (91.9) | 123/136 (90.4) | 1.5 (-5.8 to ∞) |
| Recurrence of UTI symptoms within 28 days of stopping study medication (secondary outcome) | 7-Day antimicrobial + 7-day placebo group | 14-Day antimicrobial group | Absolute difference, % (2-sided 95% CI)[b] |
| As-treated population | 13/131 (9.9) | 15/123 (12.9) | -3.0 (-10.8 to 6.2) |
| As-randomized population | 14/136 (10.3) | 23/136 (16.9) | -6.6 (-15.5 to 2.2) |

Abbreviation: UTI, urinary tract infection.

[a] The primary analysis used a 1-sided 97.5% CI for noninferiority, which was established if the lower bound of the 1-sided 97.5% CI did not cross the noninferiority margin of −10% difference in symptom resolution.

[b] The secondary outcome was analyzed using a 2-tailed superiority hypothesis test of differences in proportions (2-sample test for equality of proportions with continuity correction) with α = .05 and with 2-sided 95% CIs.

Among afebrile men with suspected UTI, treatment with ciprofloxacin or trimethoprim/sulfamethoxazole for 7 days was non inferior to 14 days of treatment with regard to resolution of UTI symptoms by 14 days after antibiotic therapy.

# Acute cystitis in men– a nationwide study from primary care: antibiotic prescriptions, risk factors, and complications Håkon Sætre *et al*. BJGP Open 2024

- 2012-2019, Norvège
- Données médecine générale
  - registre national remboursement assurance maladie (KUHR))
  - prescriptions médicaments nationales (NorPD)
  - 3 jours de délai entre diagnostic et prescription antibiotique
- Hommes> 18 ans
- Diagnostic de cystite (ICPC-2), 1er épisode
- Prescription antibiotique « compatible » traitement d'une cystite
  - spectre étroit: pivmécillinam, triméthoprime, nitrofurantoine
  - spectre large: amoxicilline, amoxicilline-a. clavulanique, triméthoprime–sulfaméthoxazole, ciprofloxacine, ofloxacine, moxifloxacine, fosfomycine, azithromycine, doxycycline et céfalexine.
- Si antibiotique relevant dans les 90 jours: exclusion
- Durée de traitement? Doses? ECBU? Résultat?

**Table 1** First-choice treatment changes over time

| | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | Total | Confidence interval of linear regression |
|---|---|---|---|---|---|---|---|---|---|---|
| | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | |
| Pivmecillinam | 9583 (50.9%) | 9687 (53.6%) | 9579 (51.9%) | 9881 (52.9%) | 9923 (53.3%) | 9706 (53.6%) | 9712 (51.9%) | 10 074 (52.6%) | 78 145 (52.5%) | -0.1% (-0.2% to 0.5%) |
| Trimethoprim | 2871 (15.3%) | 2554 (14.0%) | 2608 (14.2%) | 2473 (13.2%) | 2570 (13.8%) | 2490 (13.7%) | 2128 (11.4%) | 2124 (11.1%) | 19 818 (13.2%) | -0.5% (-0.7% to 0.2%) |
| Nitrofurantoin | 1019 (5.4%) | 895 (5.0%) | 872 (4.7%) | 940 (5.0%) | 968 (5.2%) | 998 (5.5%) | 841 (4.5%) | 1046 (5.5%) | 7579 (5.1%) | 0.0% (-0.1% to 0.1%) |
| Trimethoprim–sulfamethoxazole | 1717 (9.1%) | 1695 (9.4%) | 2163 (11.8%) | 2307 (12.4%) | 2497 (13.5%) | 2659 (14.7%) | 3823 (20.4%) | 4019 (21.0%) | 20 880 (14.0%) | 1.8% (1.2% to 2.3%) |
| Fluoroquinolones | 2614 (13.9%) | 2403 (13.3%) | 2399 (13.0%) | 2218 (11.9%) | 1917 (10.3%) | 1559 (8.6%) | 1458 (7.8%) | 1136 (5.9%) | 15 704 (10.9%) | -1.1% (-1.4% to 0.9%) |
| Other | 1021 (5.4%) | 844 (4.7%) | 817 (4.4%) | 859 (4.6%) | 725 (3.9%) | 710 (3.9%) | 739 (4.0%) | 750 (3.9%) | 6465 (4.3%) | -0.2% (-0.3% to 0.1%) |
| Total | 18 869 (100%) | 18 078 (100%) | 18 438 (100%) | 18 678 (100%) | 18 600 (100%) | 18 122 (100%) | 18 701 (100%) | 19 149 (100%) | 148 635 | 0.003% (-0.005% to 0.01%) |
| Narrow-spectrum antibiotics | 13 517 (71.6%) | 13 136 (72.7%) | 13 059 (70.8%) | 13 294 (71.2%) | 13 461 (72.3%) | 13 194 (72.8%) | 12 681 (67.8%) | 13 244 (69.2%) | 105 586 (71.0%) | -0.2% (-1.0% to 0.2%) |
| Broad-spectrum antibiotics | 5352 (28.4%) | 4942 (27.3%) | 5379 (29.2%) | 5384 (28.8%) | 5139 (27.7%) | 4928 (27.2%) | 6020 (32.2%) | 5905 (30.8%) | 41 597 (28.0%) | 0.4% (-0.2% to 1.0%) |

**Table 2** Number of episodes and their outcome in different strata

| | | Successfully treated | | Re-prescriptions | | Complications[a] | | Hospitalisations | |
|---|---|---|---|---|---|---|---|---|---|
| | Acute cystitis episodes | *n* | (%) | *n* | (%) | *n* | (%) | *n* | (%) |
| **Total** | 148 635 | 114 697 | (77.2) | 33 328 | (22.4) | 2700 | (1.8) | 1042 | 0.7 |
| **Calendar year** | | | | | | | | | |
| 2012 | 18 869 | 14 361 | (76.1) | 4430 | (23.5) | 328 | (1.7) | 120 | 0.6 |
| 2013 | 18 078 | 13 908 | (76.9) | 4110 | (22.7) | 302 | (1.7) | 112 | 0.6 |
| 2014 | 18 438 | 14 227 | (77.2) | 4143 | (22.5) | 347 | (1.9) | 116 | 0.6 |
| 2015 | 18 678 | 14 470 | (77.5) | 4146 | (22.2) | 325 | (1.7) | 117 | 0.6 |
| 2016 | 18 600 | 14 338 | (77.1) | 4189 | (22.5) | 344 | (1.8) | 128 | 0.7 |
| 2017 | 18 122 | 14 057 | (77.6) | 3996 | (22.1) | 300 | (1.7) | 116 | 0.6 |
| 2018 | 18 701 | 14 439 | (77.2) | 4169 | (22.3) | 380 | (2.0) | 159 | 0.9 |
| 2019 | 19 149 | 14 897 | (77.8) | 4145 | (21.6) | 374 | (2.0) | 174 | 0.9 |
| **Age group, years** | | | | | | | | | |
| 18–49 | 28 680 | 23 596 | (82.3) | 5052 | (17.6) | 482 | (1.7) | 74 | 0.3 |
| 50–66 | 39 519 | 29 601 | (74.9) | 9752 | (24.7) | 1042 | (2.6) | 334 | 0.8 |
| 67–79 | 47 368 | 35 579 | (75.1) | 11 584 | (24.5) | 767 | (1.6) | 356 | 0.8 |
| 80–89 | 26 839 | 20 858 | (77.7) | 5822 | (21.7) | 334 | (1.2) | 216 | 0.8 |
| ≥90 | 6229 | 5063 | (81.3) | 1118 | (17.9) | 75 | (1.2) | 62 | 1.0 |

a Complications defined as pyelonephritis, prostatitis or admission to hospital.

| | Acute cystitis episodes | Successfully treated | | Re-prescriptions | | Complications[a] | | Hospitalisations | |
|---|---|---|---|---|---|---|---|---|---|
| | | *n* | (%) | *n* | (%) | *n* | (%) | *n* | (%) |
| **Risk factors** | | | | | | | | | |
| Diabetes | 21 505 | 16 716 | (77.7) | 4674 | (21.7) | 378 | (1.8) | 185 | 0.9 |
| Urinary retention | 17 018 | 13 193 | (77.5) | 3740 | (22.0) | 235 | (1.4) | 127 | 0.7 |
| BPH | 17 380 | 13 024 | (74.9) | 4275 | (24.6) | 332 | (1.9) | 137 | 0.8 |
| Prostate cancer | 11 199 | 8697 | (77.7) | 2446 | (21.8) | 140 | (1.3) | 80 | 0.7 |
| Other cancer | 15 338 | 11 650 | (76.0) | 3601 | (23.5) | 245 | (1.6) | 138 | 0.9 |
| **First-choice antibiotics** | | | | | | | | | |
| Pivmecillinam | 78 145 | 58 397 | (74.7) | 19 461 | (24.9) | 1415 | (1.8) | 527 | 0.7 |
| Trimethoprim | 19 862 | 15 326 | (77.2) | 4484 | (22.6) | 269 | (1.4) | 97 | 0.5 |
| Trimethoprim–sulfamethoxazole | 20 880 | 16 220 | (77.7) | 4539 | (21.7) | 522 | (2.5) | 192 | 0.9 |
| Fluoroquinolones | 15 704 | 13 506 | (86.0) | 2102 | (13.4) | 296 | (1.9) | 139 | 0.9 |
| Nitrofurantoin | 7579 | 5834 | (77.0) | 1724 | (22.7) | 104 | (1.4) | 39 | 0.5 |
| Other | 6465 | 5414 | (83.7) | 1018 | (15.7) | 94 | (1.5) | 48 | 0.7 |
| Narrow-spectrum antibiotics | 105 586 | 79 557 | (75.3) | 25 669 | (24.3) | 1788 | (1.7) | 663 | 0.6 |
| Broad-spectrum antibiotics | 43 049 | 35 140 | (81.6) | 7659 | (17.8) | 912 | (2.1) | 379 | 0.9 |

a Complications defined as pyelonephritis, prostatitis or admission to hospital.

**Table 3** Re-prescriptions with and without antibiotic switch

| Antibiotic | Total | No re-prescriptions | All re-prescriptions | Without switch | With switch |
|---|---|---|---|---|---|
| Pivmecillinam | 78 145 (100%) | 58 684 (75.1%) | 19 461 (24.9%) | 4865 (6.2%) | 14 596 (18.7%) |
| Trimethoprim | 19 862 (100%) | 15 378 (77.4%) | 4484 (22.6%) | 795 (4.0%) | 3689 (18.6%) |
| Trimetorprim–sulfamethoxazole | 20 880 (100%) | 16 341 (78.3%) | 4539 (21.7%) | 1485 (7.1%) | 3054 (14.6%) |
| Nitrofurantoin | 7579 (100%) | 5855 (77.3%) | 1724 (22.7%) | 330 (4.4%) | 1394 (18.4%) |
| Fluoroquinolones | 15 704 (100%) | 13 602 (86.6%) | 2102 (13.4%) | 782 (5.0%) | 1320 (8.4%) |
| Others | 6465 (100%) | 5447 (84.3%) | 1018 (15.7%) | 207 (3.2%) | 811 (12.5%) |
| Total | 148 635 (100%) | 115 307 (77.6%) | 33 328 (22.4%) | 8464 (5.7%) | 24 864 (16.7%) |

Rechute
Entre J15 et J30

Échec
(avant J14)

**Table 4** Different first-choice antibiotic treatment and risk of re-prescriptions and complications

| | Univariate OR (95% CI) | Age-adjusted OR (95% CI) | Age and risk factor adjusted OR (95% CI) |
|---|---|---|---|
| **Re-prescriptions** | | | |
| Pivmecillinam | 1 | 1 | 1 |
| Trimethoprim | **0.88 (0.85 to 0.91)*** | **0.88 (0.84 to 0.91)*** | **0.88 (0.85 to 0.91)*** |
| Trimethoprim–sulfamethoxazole | **0.84 (0.81 to 0.87)*** | **0.82 (0.79 to 0.85)*** | **0.82 (0.79 to 0.85)*** |
| Fluoroquinolones | **0.47 (0.44 to 0.49)*** | **0.45 (0.43 to 0.48)*** | **0.45 (0.43 to 0.47)*** |
| Nitrofurantoin | **0.89 (0.84 to 0.94)*** | **0.87 (0.82 to 0.92)*** | **0.87 (0.82 to 0.92)*** |
| Other antibiotic | **0.56 (0.52 to 0.60)*** | **0.60 (0.56 to 0.64)*** | **0.60 (0.55 to 0.64)*** |
| **Complications[a]** | | | |
| Pivmecillinam | 1 | 1 | 1 |
| Trimethoprim | **0.74 (0.65 to 0.85)*** | **0.75 (0.66 to 0.85)*** | **0.75 (0.66 to 0.85)*** |
| Trimethoprim–sulfamethoxazole | **1.39 (1.26 to 1.54)*** | **1.35 (1.22 to 1.49)*** | **1.35 (1.22 to 1.49)*** |
| Fluoroquinolones | 1.04 (0.92 to 1.18) | 1.00 (0.88 to 1.14) | 1.00 (0.88 to 1.14) |
| Nitrofurantoin | **0.75 (0.62 to 0.92)*** | **0.76 (0.62 to 0.93)*** | **0.76 (0.62 to 0.93)*** |
| Other antibiotic | **0.80 (0.65 to 0.99)*** | 0.83 (0.67 to 1.02) | 0.83 (0.67 to 1.02) |

[a]Complications defined as pyelonephritis, prostatitis, or admission to hospital. Bold and asterisked = statistically significant.

CI = confidence interval. OR = odds ratio

## **Table 5** Re-prescription and complications

| | | Re-prescription | | | | Complications[a] | | | |
|---|---|---|---|---|---|---|---|---|---|
| Risk factor | Percentage narrow-spectrum prescription | Unadjusted OR (95% CI) | Age-adjusted OR (95% CI) | Age + other risk factors OR (95% CI) | Age + risk factors + antibiotic OR (95% CI) | Unadjusted OR (95% CI) | Age-adjusted OR (95% CI) | Age + other risk factors OR (95% CI) | Age + risk factors + antibiotic OR (95% CI) |
| Diabetes | 72.4% | **0.95 (0.92 to 0.99)*** | **0.90 (0.87 to 0.93)*** | **0.90 (0.87 to 0.93)*** | **0.89 (0.86 to 0.92)*** | 0.96 (0.86 to 1.07) | 0.96 (0.86 to 1.08) | 0.97 (0.86 to 1.08) | 0.97 (0.87 to 1.08) |
| Urinary retention | 70.7% | 0.97 (0.93 to 1.01) | **0.96 (0.92 to 0.99)*** | **0.95 (0.91 to 0.99)*** | **0.95 (0.91 to 0.99)*** | **0.73 (0.64 to 0.84)*** | **0.84 (0.74 to 0.97)*** | **0.83 (0.73 to 0.96)*** | **0.83 (0.72 to 0.95)*** |
| Prostate cancer | 71.5% | 0.96 (0.92 to 1.01) | **0.93 (0.88 to 0.97)*** | **0.93 (0.88 to 0.97)*** | **0.93 (0.88 to 0.97)*** | **0.67 (0.56 to 0.79)*** | **0.75 (0.63 to 0.89)*** | **0.76 (0.64 to 0.90)*** | **0.75 (0.63 to 0.90)*** |
| Benign prostate hyperplasia | 70.3% | **1.14 (1.10 to 1.19)*** | **1.09 (1.05 to 1.13)*** | **1.10 (1.05 to 1.14)*** | **1.10 (1.06 to 1.15)*** | 1.06 (0.94 to 1.19) | **1.14 (1.01 to 1.28)*** | **1.17 1.03 to 1.31)*** | **1.16 (1.03 to 1.31)*** |
| Cancer | 70.3% | **1.07 (1.03 to 1.11)*** | 1.03 (0.99 to 1.07) | 1.03 (0.99 to 1.07) | 1.04 (0.99 to 1.08) | **0.87 (0.77 to 0.99)*** | 0.95 (0.83 to 1.09) | 0.96 (0.84 to 1.10) | 0.95 (0.83 to 1.09) |

[a]Complications defined as pyelonephritis, prostatitis, or admission to hospital. Bold and asterisked = statistically significant.

# Durée de traitement cystite de l'homme

- Quelques propositions avant recommandations …

| Antibiotique par voie orale | Dose journalière | Durée |
|---|---|---|
| **Pivmécillinam** | **400 mg** x2 (ou **x3**) | (5-) 7 jours |
| **Nitrofurantoïne** | 100 mg x (2-3) (**50 mg x4**) | 7 jours |
| **Fosfomycine trométamol** | **3 g** | J1, J3, J5 |
| **Trimethoprime** | **300 mg** | |
| **TMP-SMZ** | **800 mg x2** | 7 jours |
| **Fluoroquinolones** | | 7 jours |
| - **ofloxacine** | **200 mg x2** | |
| - **lévofloxacine** | **500 mg x1** | |
| - **ciprofloxacine** | **500 mg x2** | |

# Infection urinaire masculine fébrile?

Ciprofloxacin for 2 or 4 Weeks in the Treatment of Febrile Urinary Tract Infection in Men A Randomized Trial with a 1 Year Follow-up. Ulleryd et Sandber, Scand J Infect Dis, 2003.

Table I. *Characteristics of study patients*

| | Ciprofloxacin 500 mg b.i.d. | |
|---|---|---|
| | 2 weeks | 4 weeks |
| Patients randomized | 57 | 57 |
| Patients valid for efficacy analysis | 38 | 34 |
| Median age (y) | 61 (18–85) | 62 (30–77) |
| History of UTI | 20 (53) | 14 (41) |
| Median initial temperature (°C)[a] | 39.3 (38.0–40.7) | 39.6 (38.0–41.4) |
| Median initial CRP (mg/l) | 135 (15–420) | 130 (9–370) |
| Median initial WBC ($\times 10^9$/l) | 13.2 (4.0–25.6) | 13.6 (5.1–29.8) |
| Pyuria | 28/35 (80) | 28/33 (85) |
| Positive blood culture | 7 (18) | 3 (9) |
| Flank pain and/or costovertebral angle | 12 (32) | 15 (44) |

Pas de différence significative guérison clinique ni guérison microbiologique 2 semaines ou 12 mois post ttt

Table V. *Cumulative clinical cure rate (%) and type of recurrent urinary tract infection (UTI)*

| | Ciprofloxacin 500 mg b.i.d. | |
|---|---|---|
| | 2 weeks ($n = 38$) | 4 weeks ($n = 34$) |
| 2 weeks post-treatment | $n = 38$ | $n = 34$ |
| Cure | 35 (92) | 33 (97) |
| Lower urinary tract symptoms with bacteriuria | 2 | 0 |
| Febrile UTI | 1 | 0 |
| Lower urinary tract symptoms without bacteriuria | 0 | 1 |
| After 3 months | $n = 36$ | $n = 34$ |
| Cure | 30 (83) | 30 (88) |
| Lower urinary tract symptoms with bacteriuria | 3 | 2 |
| Febrile UTI | 2 | 0 |
| Lower urinary tract symptoms without bacteriuria | 1 | 2 |
| After 6 months | $n = 33$ | $n = 33$ |
| Cure | 25 (76) | 29 (88) |
| Lower urinary tract symptoms with bacteriuria | 3 | 2 |
| Febrile UTI | 4 | 0 |
| Lower urinary tract symptoms without bacteriuria | 1 | 2 |
| After 12 months | $n = 32$ | $n = 33$ |
| Cure | 23 (72) | 27 (82) |
| Lower urinary tract symptoms with bacteriuria | 3 | 2 |
| Febrile UTI | 5 | 1 |
| Lower urinary tract symptoms without bacteriuria | 1 | 3 |

Table IV. *Cumulative bacteriological cure rate (%)*

| | Ciprofloxacin 500 mg b.i.d. | |
|---|---|---|
| | 2 weeks ($n = 38$) | 4 weeks ($n = 34$) |
| 2 weeks post-treatment | $n = 38$ | $n = 34$ |
| Bacteriological cure | 34 (89) | 33 (97) |
| Relapse | 2 | 1 |
| Reinfection | 2 | 0 |
| After 3 months | $n = 36$ | $n = 34$ |
| Bacteriological cure | 27 (75) | 29 (85) |
| Relapse | 3 | 4 |
| Reinfection | 6 | 1 |
| After 6 months | $n = 33$ | $n = 33$ |
| Bacteriological cure | 21 (64) | 27 (82) |
| Relapse | 4 | 4 |
| Reinfection | 7 | 2 |
| Unspecified recurrence | 1 | 0 |
| After 12 months | $n = 32$ | $n = 33$ |
| Bacteriological cure | 19 (59) | 25 (76) |
| Relapse | 4 | 4 |
| Reinfection | 8 | 4 |
| Unspecified recurrence | 1 | 0 |

Pas de différence significative guérison clinique ni guérison microbiologique 2 semaines ou 12 mois post ttt

# Treatment duration of febrile urinary tract infection: a pragmatic randomized, double-blind placebo-controlled non inferiority trial in men and women NieuwKoop *et al*. BMC medicine 2017.

- Etude randomisée, double aveugle contre placebo, non infériorité
- Adultes, hommes et femmes, infection urinaire fébrile
- 7 jours vs 14 jours
- Ciprofloxacine 500 mg ou placebo 2 fois/jour la 2ème semaine.
- *Critère de jugement principal*:

guérison clinique 10-18 jours après traitement

- *Critères secondaires*:

guérison bactériologique, 10-18 jours après traitement et guérison clinique 70–84 jours post-traitement.

- Effectif nécessaire: 200/bras, marge non infériorité de 10%

**Table 1** Baseline characteristics of 357 patients with febrile urinary tract infection

| | Randomized (n = 200) | | Not randomized (n = 157) | *P* value[c] |
|---|---|---|---|---|
| | Antibiotic treatment for 7 days (n = 97) | Antibiotic treatment for 14 days (n = 103) | | |
| Age (years) | 60 (48–72) | 61 (40–73) | 63 (49–75) | 0.277 |
| Male sex | 44 (45%) | 42 (41%) | 58 (37%) | 0.247 |
| Urologic history | | | | |
| Indwelling urinary catheter | 3 (3%) | 2 (2%) | 12 (8%) | 0.024 |
| Urinary tract disorder[a] | 28 (29%) | 28 (27%) | 52 (33%) | 0.296 |
| Recurrent UTI[b] | 19 (20%) | 19/100 (19%) | 47/147 (32%) | 0.007 |
| Comorbidity | | | | |
| Diabetes mellitus | 12 (12%) | 17 (17%) | 25 (16%) | 0.709 |
| Malignancy | 3 (3%) | 5 (5%) | 17 (11%) | 0.012 |
| Heart failure | 12 (12%) | 6 (6%) | 19 (12%) | 0.340 |
| Cerebrovascular disease | 5 (5%) | 5 (5%) | 13 (8%) | 0.210 |
| Chronic renal insufficiency | 3 (3%) | 2 (2%) | 10 (6%) | 0.070 |
| COPD | 10 (10%) | 11 (11%) | 23 (15%) | 0.236 |
| Immunocompromised | 3 (3%) | 8 (8%) | 14 (9%) | 0.209 |
| Signs and symptoms at presentation | | | | |
| Presentation at emergency department | 59 (61%) | 68 (66%) | 145 (92%) | <0.001 |
| Antibiotic pretreatment | 23 (24%) | 29 (28%) | 56 (36%) | 0.048 |
| Fever duration, hours | 30 (15–48) | 36 (20–60) | 48 (19–96) | 0.081 |
| Dysuria | 82/95 (86%) | 78/102 (77%) | 102/145 (70%) | 0.019 |
| Flank pain | 57/96 (59%) | 67/102 (66%) | 91/144 (63%) | 0.914 |
| Suprapubic pain | 51/96 (53%) | 48/100 (48%) | 72/145 (50%) | 0.876 |
| Perineal pain | 4/96 (4%) | 7/98 (7%) | 8/140 (6%) | 0.986 |
| Shaking chills within previous 24 hours | 63/97 (65%) | 60/101 (59%) | 102/149 (70%) | 0.256 |
| Temperature > 38 °C | 66 (68%) | 76 (74%) | 121 (77%) | 0.226 |
| Systolic blood pressure (mm Hg, mean, SD) | 132 (19) | 132 (22) | 129 (20) | 0.324 |
| Pulse rate (beats/minute) | 93 (17) | 94 (19) | 97 (19) | 0.360 |
| Outpatient treatment | 45 (46%) | 45 (44%) | 23 (15%) | <0.001 |
| Positive urine culture | 69 (71%) | 68 (66%) | 107 (68%) | 0.944 |
| Positive blood culture | 20/88 (23%) | 15/98 (15%) | 45/153 (29%) | 0.012 |
| Positive urine and/or blood culture | 75 (77%) | 70 (68%) | 118 (75%) | 0.571 |
| Initial intravenous dose(s) of antibiotics | 48 (50%) | 55 (53%) | 133 (85%) | < 0.001 |

**Table 3** Clinical and bacteriologic outcomes in the intention-to-treat and per-protocol population

| | Randomized | | Difference (90% CI) | Non-inferiority test *P* value | Not randomized population |
|---|---|---|---|---|---|
| | Antibiotic treatment for 7 days | Antibiotic treatment for 14 days | | | |
| Intention-to-treat population | (n = 94) | (n = 99) | | | |
| Short-term efficacy[a] | (n = 94) | (n = 99) | | | (n = 119) |
| Clinical cure[b] | 85 (90.4%) | 94 (94.9%) | −4.5% (−10.7 to 1.7) | 0.072 | 101 (84.9%) |
| Bacteriologic cure[c] | 86/93 (92.5%) | 89/92 (96.7%) | −4.3% (−9.7 to 1.2) | 0.041 | 94/109 (86.2%) |
| Cumulative efficacy[d] | (n = 94) | (n = 94) | | | (n = 116) |
| Clinical cure[b] | 87 (92.6%) | 86 (91.5%) | 1.1% (−5.5 to 7.6) | 0.005 | 88 (75.9%) |
| Per-protocol population | (n = 92) | (n = 92) | | | |
| Short-term efficacy[a] | (n = 92) | (n = 92) | | | NA |
| Clinical cure[b] | 83 (90.2%) | 87 (94.6%) | −4.3% (−10.8 to 2.1) | 0.073 | |
| Bacteriologic cure[c] | 84/91 (92.3%) | 83/86 (96.5%) | −4.2% (−9.9 to 1.4) | 0.045 | |
| Cumulative efficacy[d] | (n = 92) | (n = 87) | | | |
| Clinical cure[b] | 85 (92.4%) | 79 (90.8%) | 1.6% (−5.3 to 8.4) | 0.005 | |

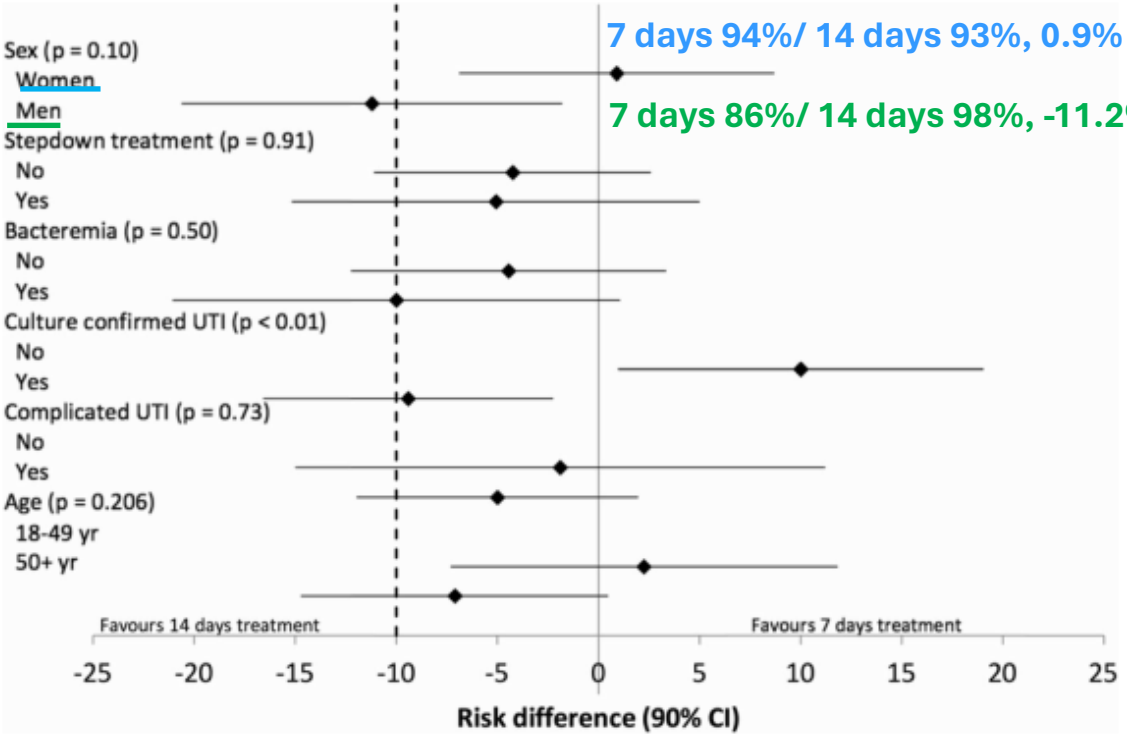
Data presented as number (%), unless otherwise indicated. NA: not applicable

[a]Short-term efficacy: endpoints assessed at 10- to 18-days post-treatment visit

[b]Clinical cure: being alive with absence of fever and resolution of UTI symptoms through post-treatment visit with no additional antimicrobial therapy for a relapse of UTI prescribed

[c]Bacteriologic cure: elimination of study entry uropathogen or pathogen growth < $10^4$ CFU/mL (women) or <$10^3$ CFU/mL (men) combined with disappearance of leucocyturia

[d]Cumulative efficacy: endpoint assessed at 70- to 84-days post-treatment visit




7 days 94%/ 14 days 93%, 0.9% (90% CI, -6.9 to 8.7, p=0.01

7 days 86%/ 14 days 98%, -11.2% (90% CI, -20.6 to -1.8, p=0

**Fig. 2** Difference in clinical cure rates (10- to 18-days post-treatment) of febrile UTI treated for 7 days versus 14 days in specific subgroups. Stepdown treatment implies initial empiric intravenous antibiotic treatment. *UTI* urinary tract infection; *CI* confidence interval. *P* values represent test for interaction. Data presented from intention to treat analysis

# Antimicrobial for 7 or 14 Days for Febrile Urinary Tract Infection in Men: A Multicenter Noninferiority Double-Blind, Placebo-Controlled, Randomized Clinical Trial

Matthieu Lafaurie,[1] Sylvie Chevret,[2] Jean-Paul Fontaine,[3] Pierre Mongiat-Artus,[4] Victoire de Lastours,[5,6] Lélia Escaut,[7] Stéphane Jaureguiberry,[7] Louis Bernard,[8] Franck Bruyere,[9] Caroline Gatey,[10] Sophie Abgrall,[11] Milagros Ferreyra,[12] Hugues Aumaitre,[12] Caroline Aparicio,[13] Valérie Garrait,[14] Vanina Meyssonnier,[15] Anne Bourgarit-Durand,[16] Amélie Chabrol,[17] Emilie Piet,[18] Jean-Philippe Talarmin,[19] Marine Morrier,[20] Etienne Canoui,[21] Caroline Charlier,[21,22] Manuel Etienne,[23] Jerome Pacanowski,[24] Nathalie Grall,[6,25] Kristell Desseaux,[26] Florence Empana-Barat,[27] Isabelle Madeleine,[28] Béatrice Bercot,[6,29] Jean-Michel Molina,[30,a] and Agnès Lefort,[5,6,a]; for the PROSTASHORT Study Group[b]

Clin Infect Dis. 2023

# Endpoints

- **Primary endpoint**: treatment success, defined as a negative urine culture, the absence of fever and of subsequent antibiotic treatment between the end of treatment and 6 weeks after day 1.

- **Secondary endpoints**: recurrent urinary tract infection within weeks 6 and 12 after day 1, rectal carriage of antimicrobial-resistant *Enterobacterales* and drug-related events.

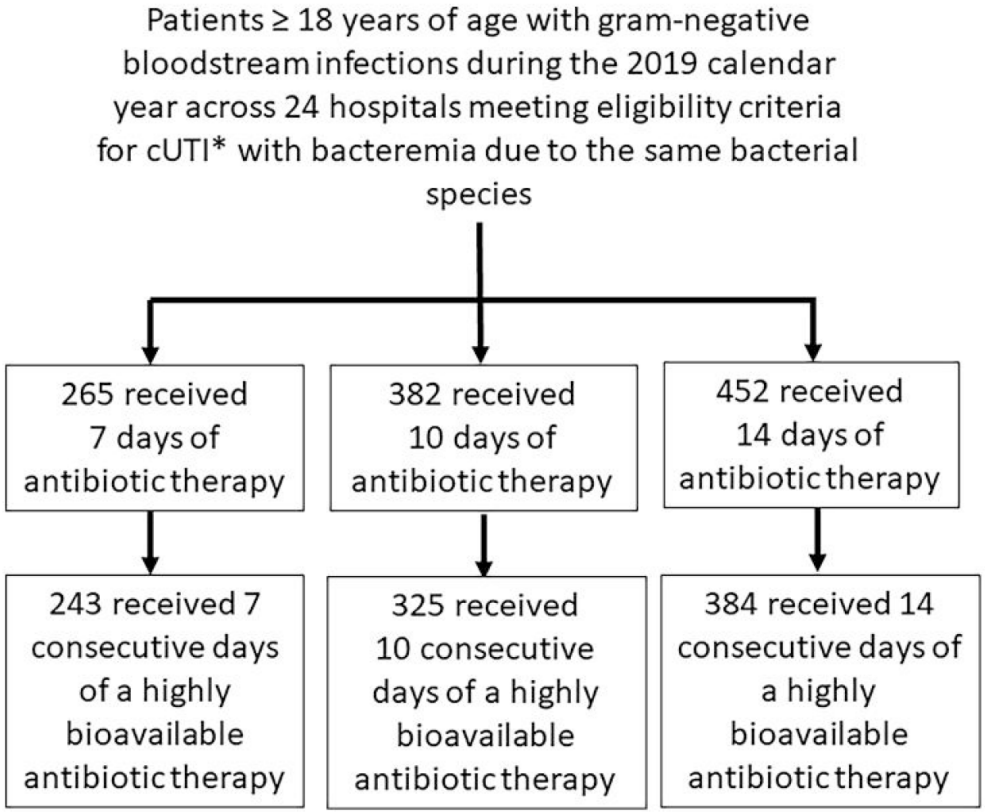
**Table 2. Difference in Risk of Treatment Success 6 Weeks After the First Day of Antibiotic Therapy (Primary Outcome) in the Intention-to-Treat and Per-Protocol Analyses**

| Analysis | 7-Day Therapy No. of Participants With Event/Total No. (%) | 14-Day Therapy No. of Participants With Event/Total No. (%) | *P* Value | Risk Difference (95% CI) |
|---|---|---|---|---|
| Intention-to-treat | (n = 115) | (n = 125) | | |
| Main analysis[a] | 64 (55.7) | 97 (77.6) | | −21.9 (−33.3 to −10.1) |
| Microbiological success[b] | 91 (79.1) | 117 (93.6) | .001 | −14.5 (−23.5 to −6.0) |
| Clinical success[c] | 110 (95.6) | 125 (100) | .02 | −4.3 (−9.8 to −1.3) |
| No new antibiotic after the end of treatment | 93 (80.9) | 116 (92.8) | .007 | −11.9 (−20.9 to −3.5) |
| Per-protocol | (n = 108) | (n = 117) | | … |
| Main analysis[a] | 64 (59.3) | 96 (82.1) | | −22.8 (−34.2 to −11.0)[d] |

**Table 3. Predictive Factors of Treatment Success**

| Factor | No. of Treatment Success/Total | Univariate Analysis OR for Treatment Success (95% CI) | Multivariable Analysis OR for Treatment Success (95% CI) | Multivariable Analysis *P* Value |
|---|---|---|---|---|
| Total | 161/240 (67.1) | | | |
| Randomization group | | | | |
| 14-d therapy | 97/125 (77.6) | 1.0 (reference) | … | |
| 7-d therapy | 64/115 (55.6) | 0.4 (.2–.6) | 0.4 (.2–.7) | .002 |
| Age >50 y | 109/177 (61.6) | 0.3 (.2–.7) | 0.4 (.2–.9) | .023 |
| Coexisting medical condition, No./total No. (%) | | | | |
| Diabetes | 25/48 (52.1) | 0.5 (.2–.9) | 0.9 (.3–2.2) | .78 |
| Obesity (BMI ≥30 kg/m$^2$) | 15/30 (50.0) | 0.4 (.2–.9) | 0.7 (.3–1.6) | .35 |
| CCI score >0 | 50/89 (56.2) | 0.5 (.2–.8) | 0.8 (.3–1.7) | .49 |
| Urinary tract–related comorbidities | | | | |
| Any urologic history | 45/76 (59.2) | 0.6 (.3–1.1) | 1.3 (.4–3.8) | .67 |
| Prostatic hypertrophy | 26/51 (51.0) | 0.4 (.2–.8) | 0.5 (.2–1.7) | .27 |
| Prostate calcifications | 30/47 (63.8) | 0.8 (.4–1.6) | … | |
| Prostate size >30 g | 90/136 (66.2) | 0.9 (.5–1.6) | … | |
| Clinical presentation | | | | |
| Fever | 98/145 (67.6) | 1.1 (.6–1.8) | … | |
| Urinary burning | 134/196 (68.4) | 1.4 (.7–2.8) | … | |
| Dysuria | 109/161 (67.7) | 1.1 (.6–1.9) | … | |
| Frequency of urination | 119/166 (71.7) | 1.9 (1.1–3.4) | … | |
| Urgency of urination | 74/102 (72.5) | 1.5 (.9–2.7) | … | |
| WBC at diagnosis >10$^9$ cells/L | 122/181 (67.4) | 1.1 (.6–2.0) | … | |
| Participants with positive blood culture | 20/33 (60.6) | 0.7 (.3–1.6) | … | |
| Pathogen identified, No./total No. (%) | | | | |
| *Escherichia coli* | 135/202 (66.8) | 0.9 (.4–2.0) | … | |
| Other pathogens | 26/38 (68.4) | 1.0 (reference) | … | |
| WBC in urine >10$^9$ cells/L | 83/131 (63.3) | 0.7 (.4–1.2) | … | |
| Initial antibiotic treatment | | | | |
| 3GC | 143/215 (66.5) | 0.8 (.3–1.9) | … | |

# Defining the optimal duration of therapy for hospitalized patients with complicated urinary tract infections and associated bacteremia. Mc Ateer *et al.* CID 2023




***Complicated UTI (cUTI) defined as growth of at least 1,000 CFU/mL of a gram-negative organism in the urine of an adult patient (same bacterial species as in the blood culture) with any of the following conditions:**

- Male sex OR
- UTI associated with one or more of the following underlying conditions at time of diagnosis:
  - Prostate hypertrophy
  - Prostate cancer
  - Nephrolithiasis
  - Intermittent or indwelling urinary catheter
  - Urethral stent
  - Nephrostomy tube
  - Intestinal conduit
  - Renal transplant

**Table 2. Baseline Characteristics of 834 Adults With Complicated Urinary Tract Infections With Associated Bloodstream Infections, Before and After Inverse Probability of Treatment Weighting, Comparing 10 Days With 14 Days of Antibiotic Therapy**

| | Full Cohort | | | Inverse Probability Weighted Cohort | | |
|---|---|---|---|---|---|---|
| Variable | 10 Days (n = 382; 46%) | 14 Days (n = 452; 54%) | *P* | 10 Days (%) | 14 Days (%) | Standardized Mean Difference |
| Age in years, median (IQR) | 70 (60–80) | 68 (56–77) | .04 | … | … | … |
| Age ≥65 years | 246 (64%) | 263 (58%) | .08 | 64.4 | 64.9 | 0.011 |
| Male sex, n (%) | 244 (64%) | 293 (65%) | .83 | 63.9 | 64.5 | 0.013 |
| Weight, median (IQR), kg | 78 (66–94) | 82 (68–96) | .09 | 78 (66–94) | 80 (68–93) | 0.007 |
| Body mass index ≥30 kg/m$^2$ | 137 (36%) | 178 (39%) | .33 | 35.9 | 35.4 | 0.011 |
| Race/ethnicity, n (%) | | | | | | |
| White | 212 (55%) | 238 (53%) | .45 | … | … | … |
| Black | 76 (20%) | 110 (24%) | .15 | … | … | … |
| Asian | 15 (3.9%) | 17 (3.8%) | .99 | … | … | … |
| Hispanic | 53 (14%) | 60 (13%) | .88 | … | … | … |
| Severe immunocompromise,[a] n (%) | 71 (19%) | 117 (26%) | .015 | 18.6 | 18.1 | 0.013 |
| Intensive care unit on day 1, n (%) | 107 (28%) | 120 (27%) | .69 | 28.0 | 27.7 | 0.007 |
| Pitt bacteremia score ≥4 on day 1, n (%) | 52 (14%) | 70 (15%) | .51 | 13.6 | 13.8 | 0.006 |
| Charlson Comorbidity Index ≥5, n (%) | 58 (15%) | 84 (19%) | .23 | 15.2 | 15.7 | 0.016 |
| Diabetes, n (%) | 116 (30%) | 172 (38%) | .02 | 30.4 | 30.6 | 0.006 |
| Cerebrovascular disease, n (%) | 61 (16%) | 63 (14%) | .47 | 16.0 | 15.3 | 0.019 |
| Chronic kidney disease, n (%) | 95 (25%) | 143 (32%) | .04 | 24.9 | 25.0 | 0.003 |
| Renal replacement therapy, n (%) | 11 (2.9%) | 14 (3.1%) | .99 | 2.9 | 3.2 | 0.020 |
| Urologic conditions/devices on day 1, n (%) | 208 (54%) | 288 (64%) | .008 | 54.5 | 54.0 | 0.009 |
| Renal transplant | 13 (3.4%) | 42 (9.3%) | .001 | … | … | … |
| Prostate hypertrophy | 45 (12%) | 55 (12%) | .95 | … | … | … |
| Nephrostomy tube | 19 (5%) | 36 (8%) | .11 | … | … | … |
| Ureteral stent | 9 (2.4%) | 6 (1.3%) | .39 | … | … | … |
| Ileostomy | 5 (1.3%) | 7 (1.5%) | .99 | … | … | … |
| Suprapubic catheter | 3 (0.8%) | 16 (3.5%) | .015 | … | … | … |
| Intermittent urinary catheterization | 19 (5%) | 25 (5.5%) | .84 | … | … | … |
| Foley catheter | 55 (14%) | 56 (12%) | .45 | … | … | … |
| Prostate cancer | 12 (3.1%) | 18 (4%) | .64 | … | … | … |
| Nephrolithiasis | 70 (18%) | 96 (21%) | .34 | … | … | … |
| Active empiric therapy, n (%) | 348 (91%) | 407 (90%) | .61 | 90 | 90 | 0.008 |
| *Pseudomonas aeruginosa*, n (%) | 20 (5.2%) | 34 (7.5%) | .23 | 5.2 | 5.4 | 0.006 |
| ESBL-producing Enterobacterales, n (%) | 51 (13%) | 55 (12%) | .68 | 13.4 | 14.0 | 0.019 |
| Carbapenem-resistant organism, n (%) | 4 (1%) | 2 (0.4%) | .54 | … | … | … |
| Source control by end of antibiotic therapy, n (%) | 65 (17%) | 50 (11%) | .03 | 11.3 | 11.5 | 0.009 |

| | Durée Antibiothérapie 10 jours | Durée Antibiothérapie 14 jours | p |
|---|---|---|---|
| Nombre de patients | 382 | 452 | |
| Rechute* à J30 | 20/382 (5,2%) | 28/452 (6,2%) | OR 0,99 (0,52-1,87) p=0,99 |
| Rechute à germe résistant** | 2/20 (10%) | 10/28 (35,7%) | p=0,10 |

*Rechute clinique et ECBU positif à la même espèce bactérienne que l'uroculture initiale,
* *Souche résistante à l'antibiotique utilisé (élévation de la CMI ≥ 4x CMI initiale).

7 jours vs 14 jours: risque rechute 2,5 fois plus élevé avec 7 j (OR ajusté 2,54 ; IC95% 1,40-4,60)
7 jours vs 14 jours et B-lactamine IV et/ou FQ ou cotrimoxazole (OR ajusté 0,76 ; IC95% 0,38-1,5

# Au total

- Infections urinaires classées en fébriles/bactérémiantes/non fébriles
- Infection non fébrile, non bactériémiante= cystite
- Cystite: durée de traitement de 7 jours maximum/antibiotiques à spectre étroit et pas de nécessité de diffusion intraprostatique
- Prostatite aiguë: traitement de 7 jours probablement insuffisant/durée 14 jours (10 jours dans certaines situations?)