Universitair Ziekenhuis Gent

UNIVERSITEIT GENT

BILULU Symposium "2π or not 2π"

Wat verwacht de clinicus van het microbiologisch urineonderzoek

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Verwachtingen van het microbiologisch urineonderzoek?

- Consensus en guidance in de interpretatie
- Uitwerking, ook bij lagere cfu/ml dan het “conventionele” Kass criterium?
- Snelle rapportering
- Alliantie met de infectioloog in het nastreven van congruentie met richtlijnen van rationeel antibiotica-gebruik

Indications for urinary cultures

- **In all UTI, with exception of acute uncomplicated cystitis (in women**)

  (Geerlings, Stichting Werkgroep Antibioticabeleid of SWAB, 2013)

- **Blood cultures in lower UTI?**
  - In hospitalised patients (including complicated UTI) 29 % positive
  - With previous antimicrobial treatment

    (Spoorenberg, Clin Microb Infection 2014; 20 (8): O476-9)

Quantitative and semi-quantitative urine cultures

- **"Classic" Kass criterium of 10^5 CFU/ml (studied in asymptomatic infections) probably not even originally intended to become standard for diagnosis of UTI in general**

- **Best diagnostic criterion for diagnosis of coliform infection in acutely dysuric women ≥ 10^2 per ml (sensitivity 0.95; specificity 0.85; high predictive value of 0.88) in symptomatic women**

  (Stamm et al NEJM 1982; 307: 463-8)

- **Paradigm (further) challenged by prospective analysis of 202 paired midstream and catheter urines in women with acute cystitis** (Hooton et al, NEJM 2013; 369: 1883-91)

Isolation of uropathogens from 202 paired specimens of voided midstream and catheter urine

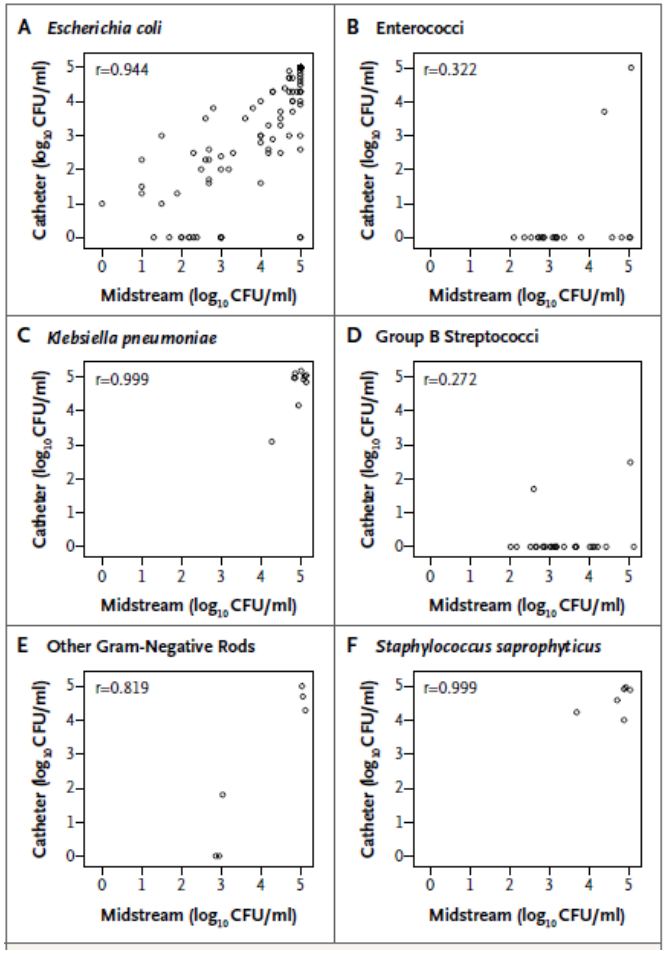
Table 2. Isolation of Uropathogens from 202 Paired Specimens of Voided Midstream Urine and Catheter Urine.*

Organism	Catheter Urine Only	Midstream Urine Only	Both Catheter and Midstream Urine	Neither Catheter nor Midstream Urine
	number of cultures (percent)			
Any uropathogen	1 (<1)	16 (8)	141 (70)	44 (22)
Gram-negative uropathogen	1 (<1)	11 (5)	133 (66)	57 (28)
Escherichia coli	1 (<1)	11 (5)	120 (59)	70 (35)
Non–*Escherichia coli*	0	2 (1)	14 (7)	186 (92)
Klebsiella pneumoniae	0	0	10 (5)	192 (95)
Enterobacter aerogenes	0	1 (<1)	2 (1)	199 (99)
Proteus mirabilis	0	0	1 (<1)	201 (>99)
Citrobacter diversus	0	0	1 (<1)	201 (>99)
Pseudomonas species	0	1 (<1)	0	201 (>99)
Gram-positive uropathogen	0	37 (18)	10 (5)	155 (77)
Enterococci	0	18 (9)	2 (1)	182 (90)
Group B streptococci	0	23 (11)	2 (1)	177 (88)
Staphylococcus saprophyticus	0	0	6 (3)	196 (97)

* A positive culture was defined as a culture with more than 0 colony-forming units per milliliter.

Hooton et al NEJM 2013

Correlation between CFU in catheter vs midstream urine cultures



Hooton et al NEJM 2013

- **Lowering of cut-off to 10-10^2 cfu/ml in order to reduce false negatives in E coli and K pneumoniae infection (high correlation)**

- **No criteria for Gram positive infection (poor correlation) → cut off of 10^5 cfu/ml in order to discriminate between true bacteriuria and perineal contamination**

CYSTITIS

See also ref 1L.13, ref 1L.14, ref 1L.15, ref 1L.16, ref 1L.17, ref 1L.18, ref 1L.19, ref 1L.20, ref 1L.21.

Cystitis: acute, uncomplicated in woman (pyuria dysuria syndrome).

- **Characteristics.**
  - * Diagnosis based on history of urinary irritative symptomatology (dysuria, frequency and urgency) and the absence of vaginal discharge or irritation, in women who have no other risk factors for complicated urinary tract infections.
  - * A colony count of > 10^3 CFU/ml of uropathogens is microbiologically diagnostic.
  - * Not hospital acquired, not occurring after a urologic procedure.
  - * Temperature < 38.5 °C, absence of costovertebral angle tenderness and absence of sepsis.
- **Culture** only indicated (no routine culture) if suspected acute pyelonephritis; if symptoms do not resolve or recur within 14 to 28 days after the completion of treatment, in women who present with atypical symptoms and in pregnant women. If results of culture are negative, infection due to *Chlamydia trachomatis*, *Mycobacterium tuberculosis*, *Herpes simplex virus*, *Neisseria gonorrhoeae* or other pathogens causing vaginitis has to be considered.
- **Antibacterials for empirical therapy.**
  - * Nitrofurantoin (ref 1L.22) and nifurtoinol are not always effective versus *Staphylococcus saprophyticus*, neither is fosfomycin.
  - * Fosfomycin is only moderately active (higher early recurrency rates) and there are no comparative data versus standard regimens.
  - * Nevertheless, nitrofurantoin, nifurtoinol and fosfomycin are recommended as agents of primary choice in order to limit the increase of resistance of Enterobacteriaceae to FQ[3] (see also ref 1L.23).
  - * Risk factors for infection due to FQ[3] resistant pathogens include recent FQ[3] exposure (in preceding 30 days), healthcare or hospital acquired urinary tract infection, ...

- Non pregnant women.		
° *Escherichia coli* ° *Staphylococcus saprophyticus* ° enterococci	- Primary choices: nitrofurantoin or nifurtoinol or fosfomycin. - Alternatives. * Absence of risk factors for infection due	**Duration[12] of empirical (+ documented) antibacterial therapy** (ref 1L.24, ref 1L.25, ref 1L.26). - Nitrofurantoin and nifurtoinol (should not be used in patients with G6PD deficiency): 5 days. - Fosfomycin: single dose (ref 1L.27). - Amoxicillin-clavulanate and cefuroxime axetil: 7 days.
° other Enterobacteriaceae (*Proteus mirabilis*, *Klebsiella* spp., ...)	to FQ[3] resistant pathogen: ciprofloxacin or levofloxacin. * Presence of risk factors for infection due to FQ[3] resistant pathogen: amoxicillin-clavulanate or cefuroxime axetil.	- Ciprofloxacin and levofloxacin: 3 days. Patients who fail on initial regimen: 14 days of antibacterial therapy with alternative antibacterial.
- Pregnant women.		
° *Escherichia coli* ° *Staphylococcus saprophyticus* ° enterococci ° other Enterobacteriaceae (*Proteus mirabilis*, *Klebsiella* spp., ...) ° group B[15] streptococci	Nitrofurantoin or nifurtoinol or fosfomycin or amoxicillin-clavulanate or cefuroxime axetil.	For data on use of antibacterials during pregnancy, consult table 35. **Duration[12] of empirical (+ documented) antibacterial therapy:** 3 to 5 days, regardless of chosen antibacterial, except fosfomycin (3 gm, single dose). Patients who fail on initial regimen: 14 days of antibacterial therapy with other antibacterial mentioned alongside.

Table 1: Etiology of UTI in ambulatory setting, The Netherlands 2013 (2014 Nethmap)

	≤ 12 year old		> 12 year old	
	Number	**%**	**Number**	**%**
E coli	7726	67,9	62043	57,5
K pneumoniae	188	1,7	6528	6,1
P mirabilis	562	4,9	6351	5,9
P aeruginosa	196	1,7	2427	2,3
other enterobacteriaceae *	525	4,6	8131	7,5
other non-fermenters **	199	1,7	1996	1,9
Enterococccus spp	1324	11,6	10269	9,5
other gram positives	663	5,8	10114	9,4
Total	11383		107859	

**Morganella* spp, *Citrobacter* spp, *Serratia* spp, *Providencia* spp, *Enterobacter* spp, *Proteus non-mirabilis* spp, and *Klebsiella non-pneumoniae* spp

***Acinetobacter* spp, *Pseudomonas non-aeruginosa* spp, and *Stenotrophomonas* spp

Microbiology survey of true first line cystitis (G Claeys, S Heytens, Ugent, endorsed by BVIKM)

Preliminary results

Positive urine samples

Threshold	N=120	%
$\geq 10^5$	72	60,0
$\geq 10^4$	87	72,5
$\geq 10^3$	89	74,2
$\geq 10^2$	91	75.8

Distribution of uropathogens (%)

	1995 % (n=176)	2005 % (n=111)	2015 % (n = 49)
E. coli	78.4	77.5	77.6
S. saprophyticus	9,1	13.5	12.2
Proteus spp.	4	2.7	
Klebsiella pneumoniae	0	0.9	2.0
Other gram –	2.8	3.6	
Other Gram +	4.5	1.8	8,1

- Cut off: 10^5 CFU/ml
- Age18 – 54 jaar
- Gr+ = Staf aureus + other CNS + Enterococcen

Distribution of uropathogens (%)

	1995 % (n=176)	2005 % (n=111)	2015 % (n = 49)*1	2015 % (n= 92)*2
E. coli	78.4	77.5	77.6	83.7%
S. saprophyticus	9,1	13.5	12.2	8.7%
Proteus spp.	4	2.7		
Klebsiella pneumoniae	0	0.9	2.0	2.2
Other gram –	2.8	3.6		
Other Gram +	4.5	1.8	8,1	5.6

- Cut off: 10^5 CFU/ml
- *1Age 18-54 jaar; *2All ages
- Gr+ = Staf aureus + other CNS + Enterococcen

Distribution of uropathogens 2015

	18-54 y N (%) (n = 49)*1	All ages N (%) (n= 92)*2	Age ≥ 55 y N (n = 23)
E. coli	38 (77.6%)	60 (83.7%)	22
S. saprophyticus	6 (12.2%)	6 (8.7%)	0
Klebsiella pneumoniae	1 (2.0%)	2 (2.2%)	1
Other Gram +	4 (8,1%)	4 (5.6%)	0

- Cut off: 10^5 CFU/ml
- Gr+ = Staf aureus + other CNS + Enterococcen

AUGMENTED RESISTANCE TO AMPI EN COTRIMOX

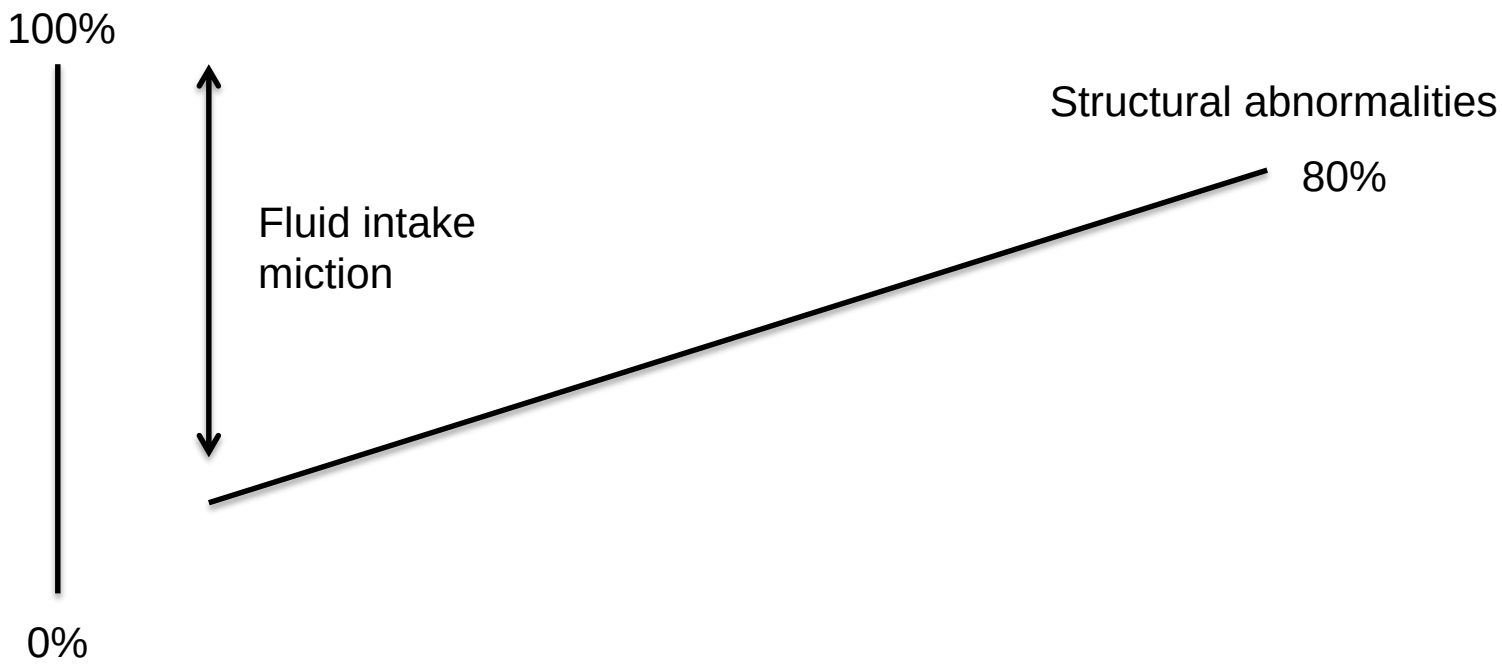
Antibiotic	2015		2005	1995
antibiotic	18-54 year (n=38) %	All ages (n=60) %	18-54 year (n=86) %	18-54 year (n=138) %
Ampicillin	52.6	58.3	62.8	73.2
Cotrimoxazole	71.1	78.3	86.0	83.3
Trimethoprim	71.1	78.3		
Nitrofurantoin	100	100	100	99.3
Ofloxacin/levofloxacin	94.7	95	100	99.3

Resistance pattern

Antibiotic	Age 18-54	All ages
	10^5 (n=38)	10^5 (n=60)
Ampicillin	52.6	58.3
Cotrimoxazole	71.1	78.3
Trimethoprim	71.1	78.3
Nitrofurantoin	100	100
Cefuroxim	97.4	98.3
Fosfomycin	100	100
Ofloxacin/levofloxacin	94.7	95
Amoxi-clav	94.7	95

Relative contribution of empiric/directed antimicrobial therapy to cure

UNCOMPLICATED —— COMPLICATED —— SEPTIC SHOCK



Empirical Use of Ciprofloxacin for Acute Uncomplicated Pyelonephritis Caused by *Escherichia coli* in Communities Where the Prevalence of Fluoroquinolone Resistance Is High

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Seoul National University Bundang Hospital, Seongnam, Republic of Korea,[a] and Seoul National University College of Medicine, Seoul, Republic of Korea[b]

There is little information about the effectiveness of ciprofloxacin in regions where ciprofloxacin-resistant *Escherichia coli* is prevalent. This study was conducted to evaluate whether ciprofloxacin is effective as the initial empirical antibiotic for treatment of uncomplicated acute pyelonephritis (APN) due to ciprofloxacin-resistant *E. coli*. A total of 255 women with clinical diagnoses of uncomplicated APN due to *E. coli* were enrolled in the emergency department between March 2005 and December 2008. All enrolled patients were initially treated with ciprofloxacin. Patients were followed up 4 to 7 days after the start of therapy and 14 to 21 days after its completion. At the first follow-up visit, ciprofloxacin was changed to the appropriate antibiotic when necessary, depending on the antibiotic susceptibility results. Not only improvement of symptoms and signs but also microbiologic eradication was assessed at each visit. Fifteen percent (39/255) of the *E. coli* isolates were resistant to ciprofloxacin. There was no statistically significant difference between the clinical cure rates of the ciprofloxacin-susceptible group and the ciprofloxacin-resistant group at the first follow-up (87.0% versus 76.9%, $P = 0.135$) or the second follow-up (98.6% versus 94.9%, $P = 0.177$). However, there was a lower microbiologic cure rate in the ciprofloxacin-resistant group than in the ciprofloxacin-susceptible group (92.4% versus 41.7%, $P = 0.000$) at the first follow-up visit. No complications occurred in the ciprofloxacin-resistant group during the follow-up period. Our findings indicate that ciprofloxacin is an appropriate choice for empirical therapy of uncomplicated APN and has no serious adverse outcomes, if it is tailored appropriately, even for women infected with ciprofloxacin-resistant *E. coli*.

CYSTITIS

See also ref 1L.13, ref 1L.14, ref 1L.15, ref 1L.16, ref 1L.17, ref 1L.18, ref 1L.19, ref 1L.20, ref 1L.21.

Cystitis: acute, uncomplicated in woman (pyuria dysuria syndrome).

- **Characteristics.**
  - * Diagnosis based on history of urinary irritative symptomatology (dysuria, frequency and urgency) and the absence of vaginal discharge or irritation, in women who have no other risk factors for complicated urinary tract infections.
  - * A colony count of > 10^3 CFU/ml of uropathogens is microbiologically diagnostic.
  - * Not hospital acquired, not occurring after a urologic procedure.
  - * Temperature < 38.5 °C, absence of costovertebral angle tenderness and absence of sepsis.
- **Culture** only indicated (no routine culture) if suspected acute pyelonephritis; if symptoms do not resolve or recur within 14 to 28 days after the completion of treatment, in women who present with atypical symptoms and in pregnant women. If results of culture are negative, infection due to *Chlamydia trachomatis*, *Mycobacterium tuberculosis*, *Herpes simplex virus*, *Neisseria gonorrhoeae* or other pathogens causing vaginitis has to be considered.
- **Antibacterials for empirical therapy.**
  - * Nitrofurantoin (ref 1L.22) and nifurtoinol are not always effective versus *Staphylococcus saprophyticus*, neither is fosfomycin.
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  - * Risk factors for infection due to FQ[3] resistant pathogens include recent FQ[3] exposure (in preceding 30 days), healthcare or hospital acquired urinary tract infection, ...

- Non pregnant women.		
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Cystitis: acute, recurrent uncomplicated in woman (recurrent pyuria dysuria syndrome).

- Recurrent: ≥ 3 episodes in 1 year or ≥ 2 episodes in 6 months.
- Risk factors for infection due to FQ[3] resistant pathogens include recent FQ[3] exposure (in preceding 30 days), healthcare or hospital acquired urinary tract infection, ….

- Premenopausal women.
  See also ref 1L.28.

° Enterobacteriaceae	- Absence of risk factors for infection due to FQ[3] resistant pathogen and pregnancy excluded: ciprofloxacin or levofloxacin. - Presence of risk factors for infection due to FQ[3] resistant pathogen or pregnancy: amoxicillin-clavulanate or cefuroxime axetil.	Eradication of infection (see above), followed by prophylaxis (see page 182) or self diagnosis and self initiated treatment of each episode with a 3-day course of ciprofloxacin or levofloxacin. In sexually active young women, recent intercourse, use of diaphragm and/or spermicide and history of recurrent urinary tract infections are associated with increased risk of symptomatic infection. Nitrofurantoin and nifurtoinol are not recommended for prolonged use (ref 1L.29) because of risk of serious hepatic impairment (cytolysis, chronic, active hepatitis, cirrhosis) and serious pulmonary side effects (interstitial pneumopathies, fibrosis). Intravaginal administration of probiotics (lactobacilli) may reduce risk of recurrent lower urinary tract infection (ref 1L.30).

- Postmenopausal woman.
  See also ref 1L.31.

° Enterobacteriaceae ° enterococci	- Absence of risk factors for infection due to FQ[3] resistant pathogen: ciprofloxacin or levofloxacin. - Presence of risk factors for infection due to FQ[3] resistant pathogen: amoxicillin-clavulanate or cefuroxime axetil.	Often related to urological factors: post-voiding residual urine volume of > 50 ml, cystocoele or incontinence. Eradication of infection (see above). If possible, urological anomalies must be corrected; if not, prophylaxis (see page 182) or self diagnosis and self initiated treatment of each episode with a 3-day course of ciprofloxacin or levofloxacin.

Cystitis: acute, uncomplicated in man.

See also ref 1L.32 (self management).

- Risk factors for infection due to FQ[3] resistant pathogens include recent FQ[3] exposure (in preceding 30 days), healthcare or hospital acquired urinary tract infection, …

° Enterobacteriaceae	- Absence of risk factors for infection due	Always culture and susceptibility testing
	- Presence of risk factors for infection due to FQ[3] resistant pathogen: amoxicillin-clavulanate or cefuroxime axetil.	due to FQ[3] resistant organisms (see above): aztreonam. **Duration[12] of empirical (+ documented) antibacterial therapy:** 7 days.

Cystitis: acute, complicated.

- With systemic symptoms.
  Treatment as for pyelonephritis [see below (pyelonephritis in adults)].

- In patients with underlying disease.
  Refers to urinary tract infection occurring in an individual with functional or structural abnormalities of the genito-urinary tract such as obstruction (urolithiasis, tumours, prostatic hypertrophy, ureteric and urethral abnormalities, bladder diverticuli, renal cysts, pelvicalyceal junction obstruction), presence of foreign bodies (indwelling catheter, ureteric stent, nephrostomy tubes), metabolic and other illnesses (diabetes mellitus, renal failure, after renal transplantation, medullary sponge kidney), functional abnormalities [neurogenic bladder (ref 1L.33, ref 1L.34), vesico-ureteric reflux], urinary instrumentation, presence of ileal conduits and other urinary diversions.

° Gram-negative bacilli ° Gram-positive cocci		May or may not be associated with clinical symptoms such as dysuria, urgency, increased frequency, fever, …. Management of the underlying disease is mandatory. Empirical antibacterial therapy (see pyelonephritis below) is only warranted in patients with severe symptoms (urine sample must be obtained before starting empirical therapy); in other patients, choice of antibacterials should be based on results of culture and susceptibility testing. **Duration[12] of empirical (+ documented) antibacterial therapy:** 7 to 14 days (or longer in patients with delayed res-

Table 2: Etiology of UTI in urological clinics, The Netherlands 2013 (2014 Nethmap)

	Ambulatory patients		Hospitalized patients	
	Number	**%**	**Number**	**%**
E coli	10811	43,8	1384	34,0
K pneumoniae	1801	7,3	264	6,5
P mirabilis	1307	5,3	234	5,7
P aeruginosa	802	3,2	220	5,4
E. faecalis	2485	10,1	515	12,7
other enterobacteriaceae	2693	10,9	598	14,7
other non-fermenters	354	1,4	93	2,3
Enterococccus spp	955	3,9	220	5,4
other gram positives	3500	14,2	543	13,3
Total	24708		4071	

Table 3: Etiology of UTI in hospital setting, The Netherlands 2013 (2014 Nethmap)

	Ambulatory patients		Hospitalized patients	
	Number	**%**	**Number**	**%**
E coli	21821	46,4	16099	45,3
K pneumoniae	3317	7,0	2550	7,2
P mirabilis	2552	5,4	2625	7,4
P aeruginosa	1519	3,2	1752	4,9
E. faecalis	4235	9,0	3706	10,4
other enterobacteriaceae	4601	9,8	3706	10,4
other non-fermenters	586	1,2	301	0,8
Enterococccus spp	1995	4,2	1134	3,2
other gram positives	5003	10,6	2611	7,3
S. aureus	1442	3,1	1082	3,0
Total	47071		35566	

Table 4: Percentage of *E. coli* isolates resistant to commonly used antibiotics, Belgium 2013*

		Ambulatory	Hospitalized	Blood Culture**
Ciprofloxacin	*N°*	*7672*	*5180*	*311*
	%	**16.6**	**27.7**	**21.2**
Co-Amoxyclav	*N°*	*2575*	*3777*	*156*
	%	26.2	39.2	34.0
Co-trimethoprim	*N°*	*2573*	*3809*	*154*
	%	25.0	30.9	36.4
Fosfomycin	*N°*	*776*	*1630*	-
	%	6.1	2.5	
Nitrofurantoin	*N°*	*2573*	*2357*	-
	%	3.3	3.0	
Gentamycin	*N°*	*1800*	*741*	-
	%	5.1	8.6	
Amikacin	*N°*	*1800*	*741*	-
	%	1.9	4.5	
Ceftazidim	*N°*	*1800*	*740*	-
	%	6.2	8.6	
Temocillin	*N°*	*1785*	*737*	-
	%	0.1	0.1	

FQ restrictions as 1st line empirical treatment

- **Urologic clinics**
- **FQ prior treatment in last 6 months**
- **In- or outpatient hospital care**

(SWAB 2013)

FQ resistant E coli in intestinal flora of pts undergoing transrectal prostate biopsy

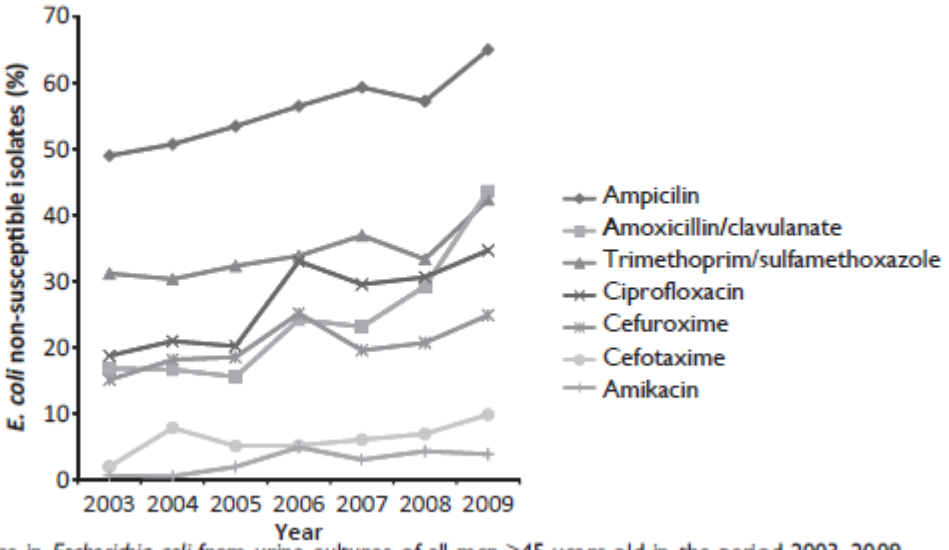


FIG. 2. Antibiotic resistance in *Escherichia coli* from urine cultures of all men ≥45 years old in the period 2003–2009.

Steensels et al Clin Microbiol and Infection 2012; 18: 575-81

TABLE I. Analysis of risk factors for carriage of fluoroquinolone-resistant microorganisms

		Ciprofloxacin-resistant (*N* = 58)	
	Ciprofloxacin-sensitive (*N* = 178)	*Escherichia coli* (*N* = 52)	Other[a] (*N* = 6)
Mean age (years)	65.8	67.2	68.3
Median PSA before biopsy (μg/L)	6.7	6.7	9.9
Previous biopsy, no. (%)	69 (38.8)	22 (42.3)	3 (50.0)
Use of fluoroquinolones <6 months before biopsy	15 (8.4)	20 (38.5)	1 (16.7)
Chronic prostatitis	5 (2.8)	11 (21.1)	1 (16.7)
Hospitalization after biopsy	0 (0)	7 (13.5)	0 (0)

PSA, prostate-specific antigen.
[a]*Pseudomonas aeruginosa* (*N* = 2), *Comamonas kerstersii* (*N* = 2), *Proteus mirabilis* (*N* = 1), and *Candida albicans* (*N* = 1).

Steensels et al Clin Microbiol and Infection 2012; 18: 575-81

TABLE 3. Proposal for protocol for antimicrobial prophylaxis at UZ Leuven

	Antimicrobial of choice	Duration of therapy
Patients without risk factors	FQ 500 mg 2 h before biopsy	Single dose
Patients with risk factors	Rectal swab: FQ	
FQ use in the previous 6 months	FQ:S → FQ 500 mg 2 h before biopsy	Single dose
Prior infectious complications of TRUSPB	FQ: R → ceftriaxone 1 g IM 1–3 h before biopsy (or IV 30 min before biopsy)	Single dose
Recurrent bacterial prostatitis or UTIs	ESBL → meropenem 1 g IV 30 min before biopsy	Single dose

ESBL, extended spectrum β-lactamase; FQ, fluoroquinolone; IM, intramuscular; IV, intravenous; TRUSPB, transrectal ultrasound-guided prostate biopsy; UTI, urinary tract infection.

Steensels et al Clin Microbiol and Infection 2012; 18: 575-81

PYELONEPHRITIS (ACUTE) IN ADULTS

See also ref 1L.35.

Pyelonephritis (acute) in adults: outpatient.

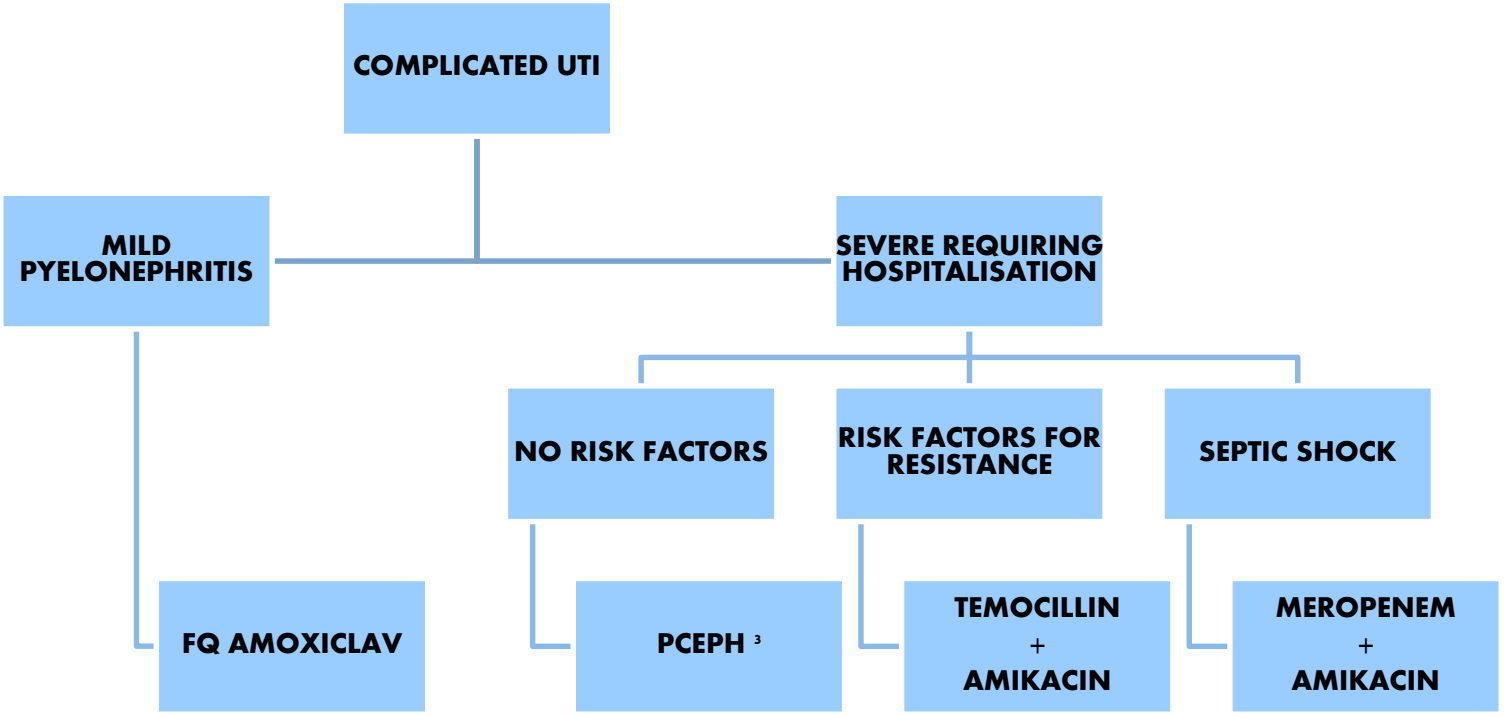
- Uncomplicated [occurring in otherwise healthy patient without criteria for hospitalization (see below)].
- Risk factors for infection due to FQ[3] resistant pathogens include recent FQ[3] exposure (in preceding 30 days), healthcare or hospital acquired urinary tract infection, ... (in view of increasing resistance, susceptibilities should be checked and empirical antibacterial therapy adapted if warranted).

° *Escherichia coli* ° *Staphylococcus saprophyticus* ° other Enterobacteriaceae (*Proteus mirabilis*, *Klebsiella* spp., ...)	- Absence of risk factors for infection due to FQ[3] resistant pathogen: ciprofloxacin or levofloxacin. - Presence of risk factors for infection due to FQ[3] resistant pathogen: amoxicillin-clavulanate or cefuroxime axetil.	Evaluation of the upper urinary tract (ultrasound or CT scan) not routinely recommended, but to be considered if no clinical improvement after 72 hours of appropriate therapy, after 2 recurrences of acute pyelonephritis or in case any complicating factor is identified. **Empirical antibacterial therapy in patients with IgE mediated allergy to pencillins[13]** and risk factor for infection due to FQ[3] resistant organisms (see above): aztreonam. **Duration of empirical (+ documented) antibacterial therapy.** - Ciprofloxacin and levofloxacin: at least 7 days. - Other regimens: 14 days.

Pyelonephritis (acute) in adults: hospitalized patient.

- Criteria for hospitalization: inability to maintain oral intake of drugs (nausea and vomiting), presence of underlying disease(s), severe pain, clinical evidence of severe sepsis, presence of risk factors for complicated urinary tract infection, uncertain diagnosis, impossibility to arrange correct follow-up, pregnancy (ref 1L.36), lack of response to outpatient therapy.
- Risk factors for infection due to FQ[3] resistant pathogens include recent FQ[3] exposure (in preceding 30 days), healthcare or hospital acquired urinary tract infection, ... (in view of increasing resistance, susceptibilities should be checked and empirical antibacterial therapy adapted if warranted).
- Uncomplicated (= occurring in otherwise healthy patient).

° *Escherichia coli* ° *Staphylococcus saprophyticus* ° other Enterobacteriaceae (*Proteus mirabilis*, *Klebsiella* spp., ...)	- Absence of risk factors for infection due to FQ[3] resistant pathogen and pregnancy excluded: ciprofloxacin or levofloxacin. - Presence of risk factors for infection due to FQ[3] resistant pathogen and pregnancy excluded: (temocillin or amoxicillin-clavulanate or cefuroxime axetil) + amikacin. - Presence of risk factors for infection due to FQ[3] resistant pathogen and pregnancy: temocillin or amoxicillin-clavulanate or cefuroxime axetil.	Prompt imaging required in hypotensive patients. Patients should become afebrile within 72 hours. If this is not the case, obstruction, intrarenal or perinephric abscess must be ruled out (ultrasound or CT scan). **Empirical antibacterial therapy in patients with IgE mediated allergy to pencillins[13]** and risk factors[18] for infection due to FQ[3] resistant pathogens or (potential) pregnancy: (aztreonam or, as an alternative, meropenem) with (non pregnant women) or without (pregnant women) amikacin. **Duration[12] of empirical (+ documented) antibacterial therapy.** - Ciprofloxacin and levofloxacin: at least 7 days (or longer in patients with delayed response). If possible, immediate start with therapy po. Otherwise iv start followed by po therapy to complete course of minimum 7 days (or longer in patients with delayed response). - Other antibacterials (except amikacin): iv therapy until patient is afebrile for 24 to 48 hours and then switch to therapy po for a total course of 7 to 14 days. - Amikacin: single dose (pending results of susceptibility testing).
- Complicated.		
° Enterobacteriaceae ° *Pseud. aeruginosa* ° enterococci ° *Staphylococcus aureus*	- Primary choice: piperacillin-tazobactam. - Alternative: meropenem.	Infection is complicated (ref 1L.37) in: - patients with anatomical, structural or functional alterations of the urinary tract (stents, urine transport disturbances, instrumentation of the urinary tract, stones, tumors, neurological disorders, ...). - patients with impaired renal function due to parenchymal diseases or pre-, intra- or postrenal nephropathies (acute or chronic renal insufficiencies, cardiac insufficiency, ..). - patients with underlying diseases that impair the immune status of the patient (diabetes mellitus, hepatic or renal impairment, immunosuppression, cancer, HIV infection/AIDS[19], hypothermia, ...). - presence of urinary catheter (ref 1L.38, ref 1L.39, ref 1L.40, ref 1L.41, ref 1L.42, ref 1L.43, ref 1L.44, ref 1L.45). A urine specimen for culture should be obtained prior to initiating antibacterial therapy because of the wide spectrum of potential pathogens and the increased likelihood of resistance. - If use of catheter is not indicated, a voided midstream urine specimen should be obtained prior to initiation of antibacterial therapy. - If use of catheter is indicated, a (new) catheter should be placed (to hasten resolution of symptoms and reduce risk of subsequent asymptomatic bacteriuria or infection) prior to collecting urine specimen and subsequent initiation of antibacterial therapy. Choice of antibacterial for empirical therapy: local epidemiology and recent antibacterial therapy must be taken into account. **Empirical antibacterial therapy in patients with IgE mediated allergy to pencillins[13]:** aztreonam or, as an alternative, meropenem. **Duration[12] of empirical (+ documented) antibacterial therapy:** 14 days.



Beyond antibiotic selection: concordance with IDSA guidelines for uncomplicated UTI

- **Historical review of medical records at university based internal medicine clinic**

- **Concordance on antibiotic type, frequency and duration**

(Kim et al, Infection, 2015: 43: 89-94)

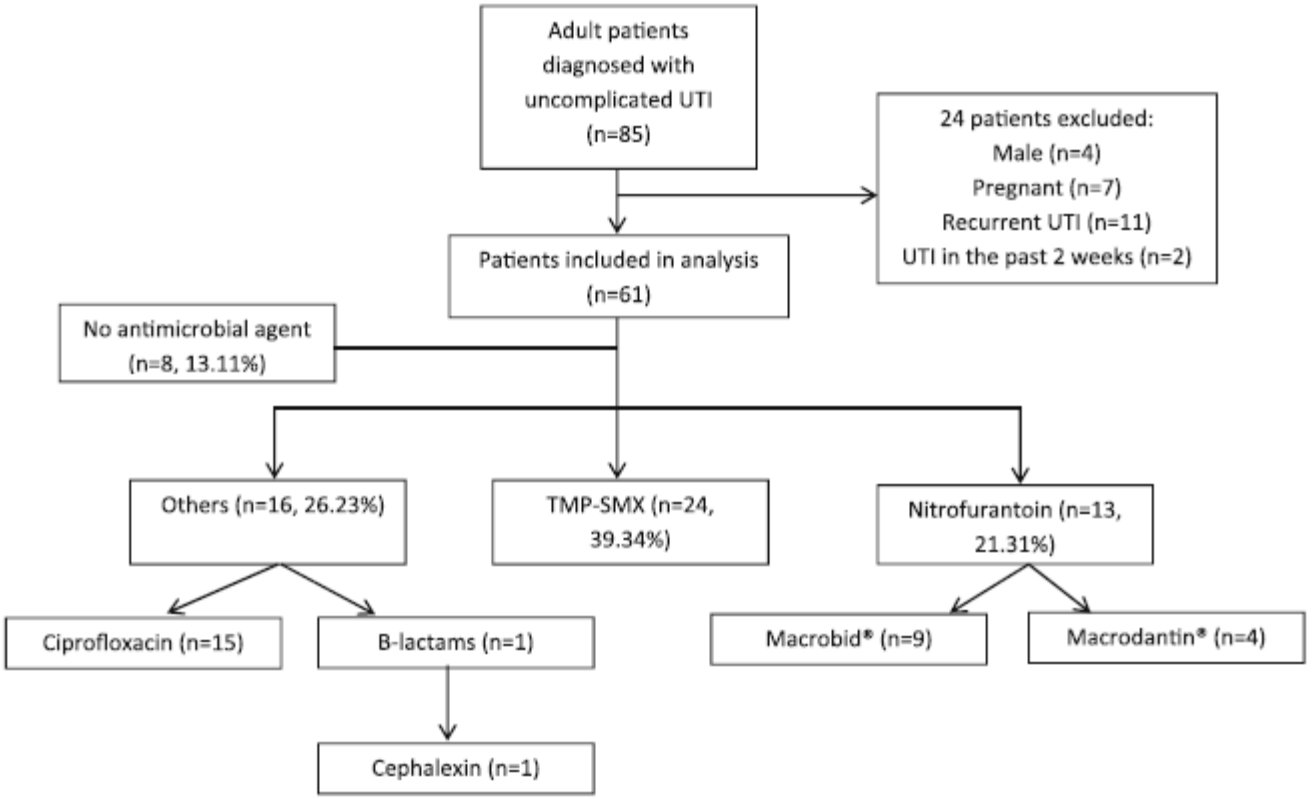


Fig. 1 Patient selection and antimicrobial agents prescribed

Table 1 Demographics

Variable	
Age, mean (SD) (year), $n = 61$	41.02 (17.94)
18–44 (%) (no. of patients)	39 (63.93)
45–64	15 (24.59)
65 and older	7 (11.48)
Primary diagnosis, $n = 61$	
ICD-9-CM 599.0 (%) (no. of patients)	56 (91.8 %)
ICD-9-CM 595.9	2 (3.28 %)
ICD-9-CM 595.0	3 (4.92 %)
Race, $n = 61$	
White, non-Hispanic (%) (no. of patients)	32 (52.46)
African-American	8 (13.11)
Hispanic	3 (4.92)
Other[a]	18 (29.51)
Antibiotic allergy (%) (no. of patients)	21 (34.43)
Types of antibiotic allergy	
Penicillin (%) (no. of patients)	8 (38.1)
Cephalosporins	3 (14.29)
Sulfa	6 (28.57)
Penicillin and Sulfa	1 (4.76)
Penicillin and fluoroquinolones	1 (4.76)
Other[b]	2 (9.52)
Renal dysfunction, $n = 3$	
Types of payment[c], $n = 61$	
Medicaid (%) (no. of patients)	27 (44.26)
Medicare	11 (18.03)
Private insurance	15 (24.59)
Self-pay	10 (16.39)

[a] Patients were considered as "other" if their records show "undetermined" as their races

[b] This includes clindamycin ($n = 1$) and tetracycline ($n = 1$) allergies

[c] Some patients had more than one type of insurance

Table 2 Concordance with the IDSA guidelines if prescribed an antibiotic [*n* (%)], total $n = 53$

Antibiotic selected	Agent	Dose	Frequency	Duration	Entire Regimen
Nitrofurantoin (Macrobid®) ($n = 9$)	9 (100)	9 (100)	9 (100)	3 (33.33)	3 (33.33)
Nitrofurantoin (Macrodantin®) ($n = 4$)	0 (0)	4 (100)	2 (50)	2 (50)	0 (0)
TMP/SMX ($n = 24$)	24 (100)	24 (100)	22 (91.67)	15 (62.50)	15 (62.50)
Ciprofloxacin ($n = 15$)	1 (6.67)	9 (60.0)	13 (86.67)	7 (46.67)	0 (0)
Cephalexin ($n = 1$)	0	0 (0)	1 (100)	1 (100)	0 (0)
Overall concordance	34 (64.15)	46 (86.79)	47 (88.68)	28 (52.83)	18 (33.96 %)

Beyond antibiotic selection: concordance with IDSA guidelines for uncomplicated UTI

- **Historical review of medical records at university based internal medicine clinic**
- **Concordance on antibiotic type, frequency and duration**
- **Aggregated concordance 33.9 %; judged suboptimal**
- **Possible quality indicator, if agreement on population delineation and antimicrobial choices**

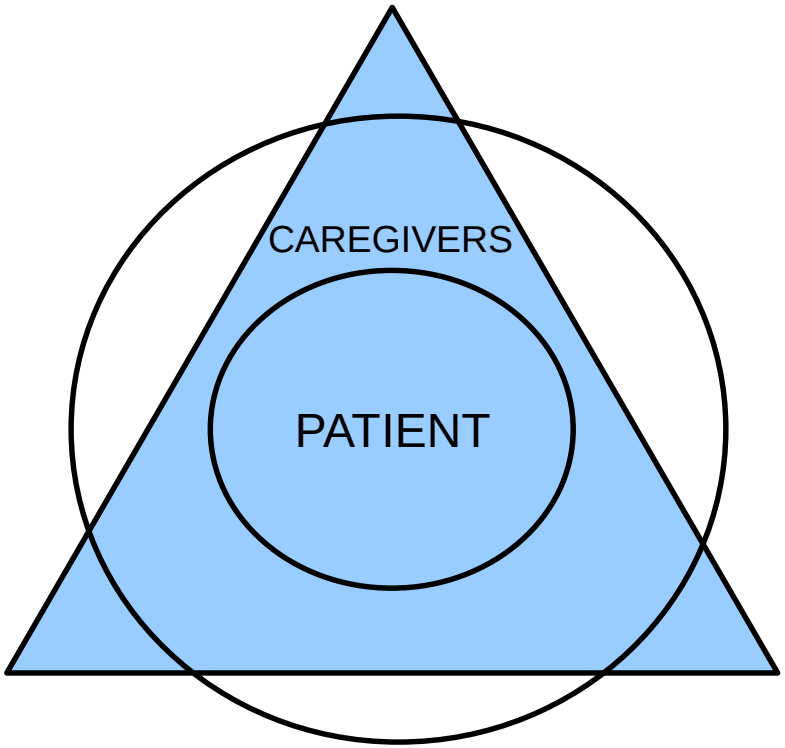
(Kim et al, Infection, 2015: 43: 89-94)

Verwachting van clinicus naar microbiologen?

- **Geconcenteerde inspanning om in wel omschreven categoriëen structureel epidemiologische gegevens op te volgen (resistentiecijfers)**
- **Basis voor correctere besluitvorming in empirische keuzes voor ongecompliceerde en gecompliceerde UWI**

Multidisciplinarity

CLINICAL INFECTIOLOGY
(GENERAL INTERNAL MEDICINE)



CLINICAL MICROBIOLOGY

HOSPITAL HYGIENE