

Impact of national guidelines for the treatment of community-acquired urinary tract infections on antibiotic resistance in *Enterobacterales*

Introduction

Urinary tract infections (UTI) are among the first indications for antibiotic use in primary care. In France, national guidelines were released in 2017 for the treatment of community acquired urinary tract infection in adults. We assessed the impact of these guidelines on resistance to first line antibiotics in *Enterobacterales* isolated from urine samples in France.

Methods

- Period: 01/01/18 to 12/31/22
- Data: antibiotic susceptibility tests (AST) on urinary isolates of *E. coli*, *Klebsiella spp.* and *Enterobacter spp.*
- Data source: a national network of clinical laboratories dedicated to primary care
- Only the first AST results from urine sample per year, person and species was included
- Analysis: Proportions of resistance to fosfomycin (FOS), nitrofurantoin (NF), pivmecillinam (PIV), trimethoprim-sulfamethoxazole (SXT), amoxicillin (AMX), amoxicillin-clavulanic acid (AMC), 3rd-generation cephalosporins (3GC) and ciprofloxacin (CIP) - ESBL- and non-ESBL-producing strains were compared
- Statistic: logistic regression to adjust the impact of trends on contextual factors ($\alpha = 0,05$)

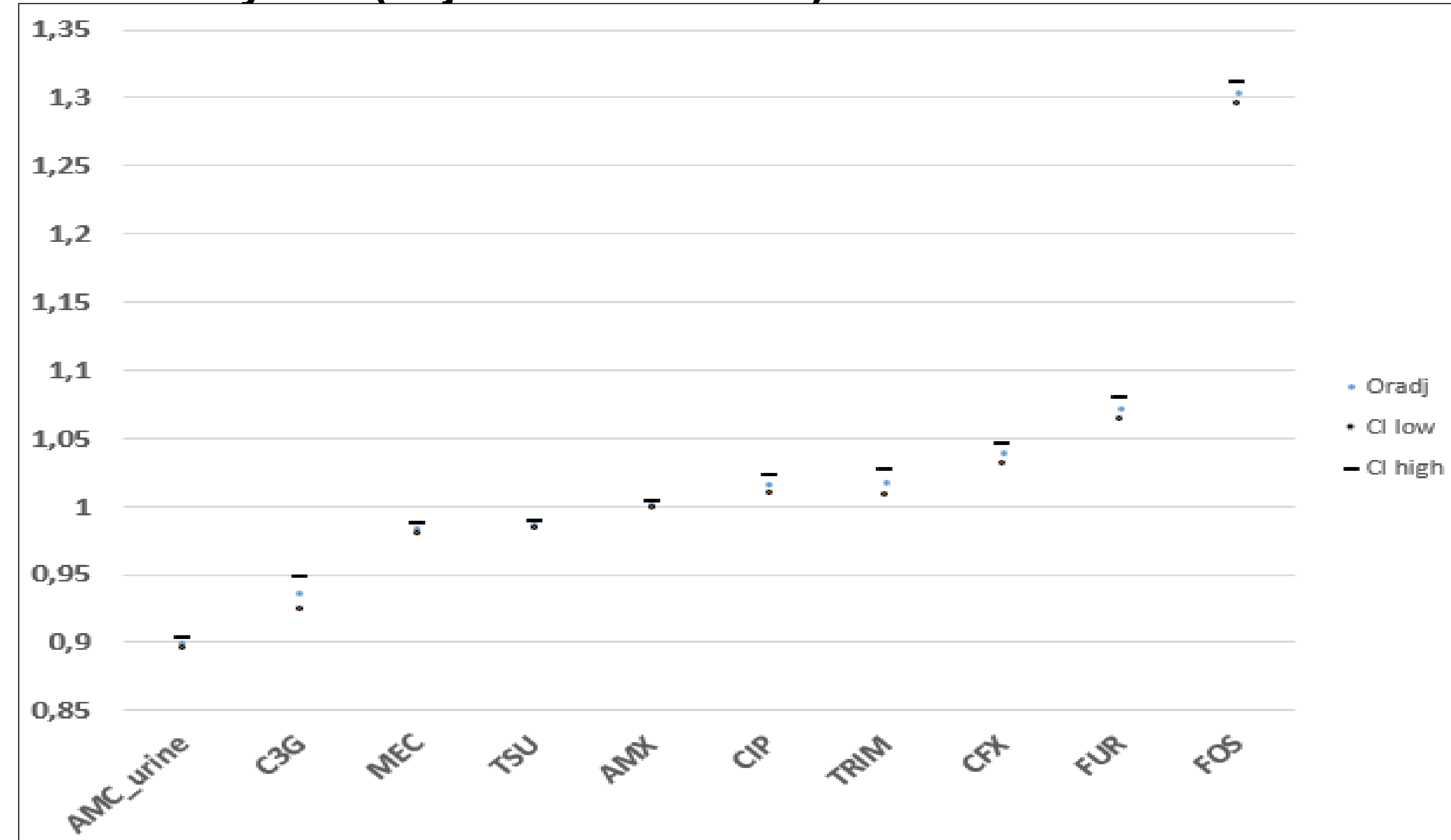
Results

- The study included 2,546,018 antibiograms of *Enterobacterales* strains isolated from urine samples
- *E. coli* accounted for 89.4% of strains, *Klebsiella spp.* for 9.0% and *Enterobacter spp.* for 1.6%
- Sex and age repartition: women between 15 and 50 yo (25.4%), women older than 50 (57.6%) and men (17.0%)

Between 2018 and 2022, urinary strains *Enterobacterales* resistance to fosfomycin and nitrofurantoin evolved more significantly than other first-line antibiotics.

Resistance rates to all antibiotics increased in isolates from for each first-line antibiotic regardless sex or age, except for 3rd-generation cephalosporins in strains isolated from women over the age of 50.

Table 1 : Risk of development of antimicrobial resistance over the years (adjusted odds ratio). France 2018-2022



AMC_urine: co-amoxiclav, C3G: 3rd-generation cephalosporins, MEC: mecillinam, TSU: trimethoprim-sulfamethoxazole, AMX: amoxicilline, CIP: ciprofloxacin, TRIM: trimethoprim, CFX: cefixim, FUR: nitrofurantoin, FOS: fosfomycine

Being a male was associated with higher rates of resistance to antibiotics except for fosfomycin. Age, catheter urines and production of ESBL were also associated with resistance to antibiotics (Table 3).

Table 2: Trends in *Enterobacterales* resistance to first-line antibiotics according to age and sex

Resistance rates in strains isolated from urinary samples in women (15-50 yo)					
ATB	2018	2019	2020	2021	2022
Fosfomycine	1.03	2.12	3.26	3.62	5.05
Nitrofurantoin	1.47	2.1	2.6	2.88	2.63
Mecillinam	6.77	6.39	7.45	7.67	7.38
Trimethoprim	16.76	0.74	1.16	5.72	19.6
Amoxicilline	38.23	44.9	44.13	44.85	46.45
Cefixime	2.76	3.3	3.29	3.47	3.9
Third-generation cephalosporins	1.995	2.12	2.14	2.15	2.51
Resistance rates in strains isolated from urinary samples in women (>50 yo)					
ATB	2018	2019	2020	2021	2022
Fosfomycine	2.04	3.83	5.08	5.29	6.73
Nitrofurantoin	2.27	3.11	3.36	3.38	3.19
Mecillinam	7.91	7.86	8.72	8.54	8.08
Trimethoprim	21.36	1.71	2.18	9.34	22.23
Amoxicilline	42.8	50.19	49.03	49.15	50.09
Cefixime	4.91	5.71	5.61	5.42	5.41
Third-generation cephalosporins	3.62	3.92	3.89	3.59	3.59
Resistance rates in strains isolated from urinary samples in men (> 15 yo)					
ATB	2018	2019	2020	2021	2022
Trimethoprim-Sulfamethoxazol	23.33	24.48	25	23.8	23.77
Third-generation cephalosporins	7.5	8.3	8.6	8.65	8.69
Ciprofloxacin	16.58	23.17	21.93	19.5	19.77

Table 3 : logistic regression modeling the relationship between variables in first column and resistance to first-line antibiotics

NB: all relationship were significant (p<0,001) except for association between catheter midstream and 3GC resistance (p=0,239)

	FOS		MEC		CIP		3GC		AMC_urine		TSU		AMX		FUR	
	Oradj	IC 95%	Oradj	IC 95%	Oradj	IC 95%	Oradj	IC 95%	Oradj	IC 95%	Oradj	IC 95%	Oradj	IC 95%	Oradj	IC 95%
Male	0.706	[0.692;0.721]	1.152	[1.138;1.167]	1.856	[1.822;1.891]	1.469	[1.415;1.525]	1.301	[1.287;1.316]	1.246	[1.236;1.257]	1.242	[1.232;1.251]	1.148	[1.126;1.171]
Age	1.01	[1.009;1.010]	1.002	[1.002;1.002]	1.011	[1.011;1.012]	1.016	[1.016;1.017]	1.003	[1.003;1.004]	1.004	[1.004;1.005]	1.002	[1.002;1.002]	1.002	[1.002;1.003]
Sample types	reference		reference		reference		reference		reference		reference		reference		reference	
Midstream urine	reference		reference		reference		reference		reference		reference		reference		reference	
Catheter urine	2.274	[1.957;2.644]	0.735	[0.619;0.873]	1.647	[1.419;1.911]	1.533 ^A	[1.192;1.973]	1.467	[1.295;1.661]	1.66	[1.520;1.814]	1.459	[1.326;1.605]	0.74	[0.622;0.880]
Pathogens	reference		reference		reference		reference		reference		reference		reference		reference	
<i>E.coli</i> (ESBL -)	reference		reference		reference		reference		reference		reference		reference		reference	
<i>E.coli</i> (ESBL +)	3.386	[3.262;3.515]	1.568	[1.529;1.609]	24.995	[24.183;25.835]			2.793	[2.733;2.854]	3.94	[3.880;4.002]			4.661	[4.420;4.915]
<i>K.pneumoniae</i> (ESBL -)	70.423	[69.219;71.645]	2.184	[2.138;2.232]	0.573	[0.558;0.588]	1.283	[1.204;1.366]	0.408	[0.399;0.417]	0.24	[0.235;0.244]			79.856	[78.186;81.561]
<i>K.pneumoniae</i> (ESBL +)	89.623	[85.737;93.684]	4.863	[4.612;5.127]	25.133	[23.984;26.338]			4.932	[4.745;5.126]	12.498	[12.070;12.941]			156.402	[150.735;162.282]
<i>Enterobacter spp.</i> (ESBL +)	52.603	[50.844;54.417]	0.441	[0.400;0.487]	0.696	[0.659;0.734]	39.692	[38.188;41.255]			0.314	[0.302;0.326]			42.23	[40.780;43.732]
<i>Enterobacter spp.</i> (ESBL -)	41.206	[37.705;45.033]	2.326	[2.027;2.668]	19.154	[17.549;20.906]					6.712	[6.310;7.141]			70.726	[65.680;76.159]

Conclusion

The released in 2017 of national guidelines for community acquired UTI was followed by a critical increased in resistance for FOS and NF, both recommended in first line treatment for female non complicated UTI. This shift may be partly attributed to changes in the EUCAST breakpoint for FOS.

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