7 Resistance in bacteria from human clinical isolates

7.1 *Escherichia coli*

Escherichia coli is the most frequent Gram-negative microorganism causing bacteremia and the most frequent pathogen in humans. It is a colonizer of the intestinal tract and as such the most frequent microorganism causing urinary tract infections. As urinary tract infections are (after respiratory tract infections) the second most frequent infectious disease in ambulatory care, increasing resistance trends directly affect the hospital as well as the ambulatory settings.

In 2019, resistance to fosfomycin and nitrofurantoin was still very low (Table 7. a), although it is known that plasmid-encoded fosfomycin resistance determinants are circulating in Switzerland. These antibiotics can only be used for non-invasive urinary tract infections and represent an important option in ambulatory care. Trimethoprim-sulfamethoxazole still remains a first-line option in lower urinary tract infections [https://ssi.guidelines.ch/]. Non-susceptibility rates decreased from 29.9% in 2015 to 27.3 % in 2019, and are even significantly lower in urinary samples (22.1% in 2019, Figure 7. a). Since resistance testing is usually not performed for uncomplicated lower urinary tract infections, ANRESIS data still overestimate the resistance rate. In a recent study by A. Plate *et al.*, susceptibility rates to trimethoprim-sulfamethoxazole in uncomplicated lower urinary tract infections were 85.7% [1].

Fluoroquinolones should not be used as first-line treatment for lower urinary tract infections, in particular to reserve its efficacy for invasive infections. Fluoroquinolone non-susceptibility has steadily increased from 10.3% in 2004 to 20.5% in 2015, but has since stabilized between 18.6 and 20.5% (18.7% in 2019). Whether this is already due to the promotion of ciprofloxacin-free antibiotic regimens for uncomplicated lower urinary tract infections has to be further analyzed. In EU/EAA states, a slight but significant increase in fluoroquinolone resistance from 24.8 to 25.3% was observed from 2015 to 2018 [2]. Because *E. coli* is also one of the most important pathogens in the outpatient setting, we

Table 7. a: Non-susceptibilitiy rates of invasive *Escherichia coli* isolates in humans for 2019.

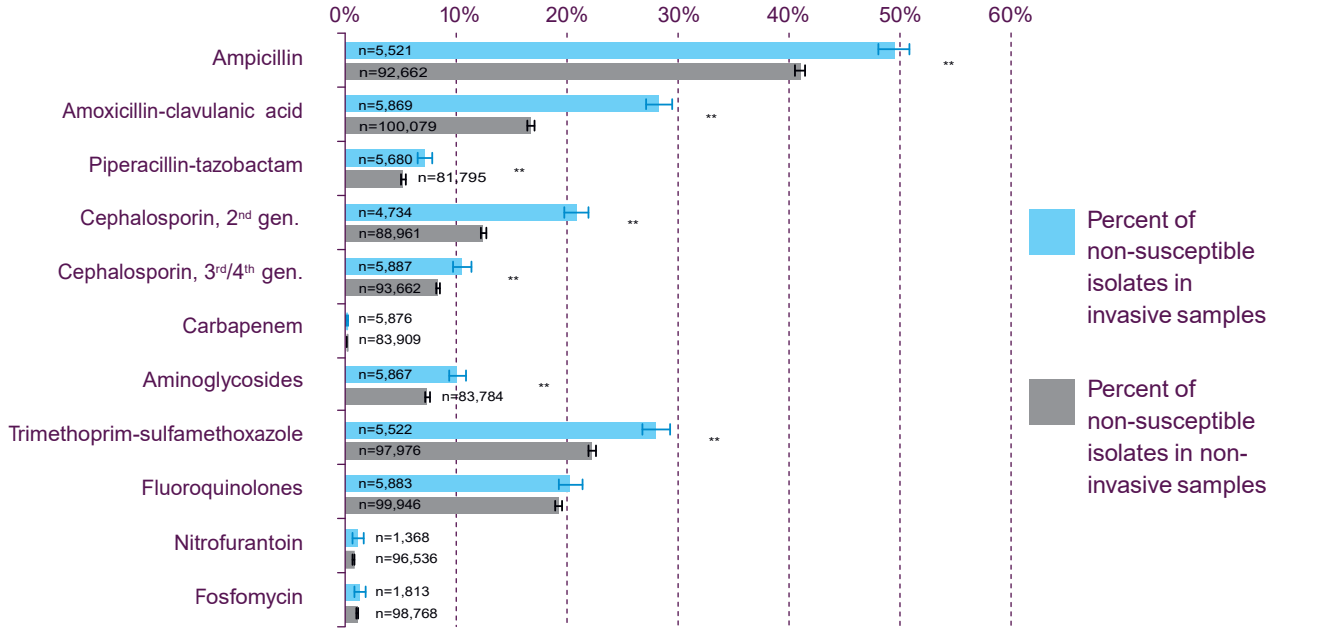
***Escherichia coli* (invasive)**											**2019**
	West		**North–East**		**South**		**Total**			**Trend**	
Antimicrobial	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**95% CI**	**4y**	**10y**
Aminopenicillins	1,358	54.6%	3,810	48%	366	45.9%	5,534	49.5%	48.8–50.2	–	↓
Amoxicillin-clavulanic acid	1,359	36.3%	4,157	27%	366	21.3%	5,882	28.8%	28.2–29.4	–	↑
Piperacillin-tazobactam	1,354	11.2%	3,972	7.7%	366	5.5%	5,692	8.4%	8.0–8.8	–	↑
Cephalosporin, 2nd generation	910	18.2%	3,468	21.9%	366	15.3%	4,744	20.7%	20.1–21.3	↑	–
Cephalosporin, 3rd/4th generation	1,359	14.8%	4,175	10.3%	366	11.2%	5,900	11.4%	11.0–11.8	↑	↑
Carbapenems[1]	1,359	0.1%	4,164	0.0%	366	0.0%	5,889	0.1%	0.1–0.1	–	↑
Aminoglycosides	1,354	11.9%	4,160	9%	366	11.2%	5,880	9.8%	9.4–10.2	–	↑
Trimethoprim-sulfamethoxazole	1,359	29.3%	3,806	26.6%	366	26.5%	5,531	27.3%	26.7–27.9	–	↓
Fluoroquinolones[2]	1,359	23.4%	4,169	17.3%	366	16.1%	5,894	18.7%	18.2–19.2	–	↑
Nitrofurantoin	416	1.2%	954	0.4%	0	0.0%	1,370	0.7%	0.5–0.9	–	↓
Fosfomycin	650	2.2%	1,165	1.2%	0	0.0%	1,815	1.5%	1.2–1.8	–	–

[1] Carbapenems: imipenem, meropenem
[2] Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin
West (GE, NE, VD, JU, FR), South (TI), North–East (other cantons) according to linguistic regions.
95% confidence intervals (CI) were calculated by the Wilson score method, calculations of trends were performed by logistic regression.
Trends were modelled with logistic regressions. Arrows represent a significant effect ($p < 0.05$) of the year on the correspondent outcome (increase, decrease).

have compared non-susceptibility rates of outpatient urinary samples with invasive samples (Figure 7. a), demonstrating a lower non-susceptibility rate in the outpatient setting for most of the antibiotics tested.

As for quinolones, the steadily increasing non-susceptibility rates to 3rd/4th generation cephalosporins from 0.9% in 2004 to 11.7% in 2018 did not further increase in 2019, but stabilized at 11.4%. However, this too could be due to the connection of additional laboratories to ANRESIS, more frequently sending resistance data from first-line hospitals. In EU/EAA states, a slight increase from 14.6% to 15.1% was observed between 2015 and 2018 [2]. Non-susceptibility rates for aminoglycosides and piperacillin-tazobactam have also stabilized since 2015, which, at least in part, could be attributable to cross-resistance. Multiresistance is frequent.

Figure 7. a: Comparison of non-susceptibility rates in invasive versus outpatient urinary samples in *Escherichia coli* isolates in humans for 2019.



n = number of isolates tested with error bars indicating 95% confidence intervals. Fisher Exact Tests were performed to assess for independence:
* = p-value <0.05; ** = p-value <0.01.

Figure 7. b: Non-susceptibility rates in invasive *Escherichia coli* isolates in humans between 2010 an 2019.

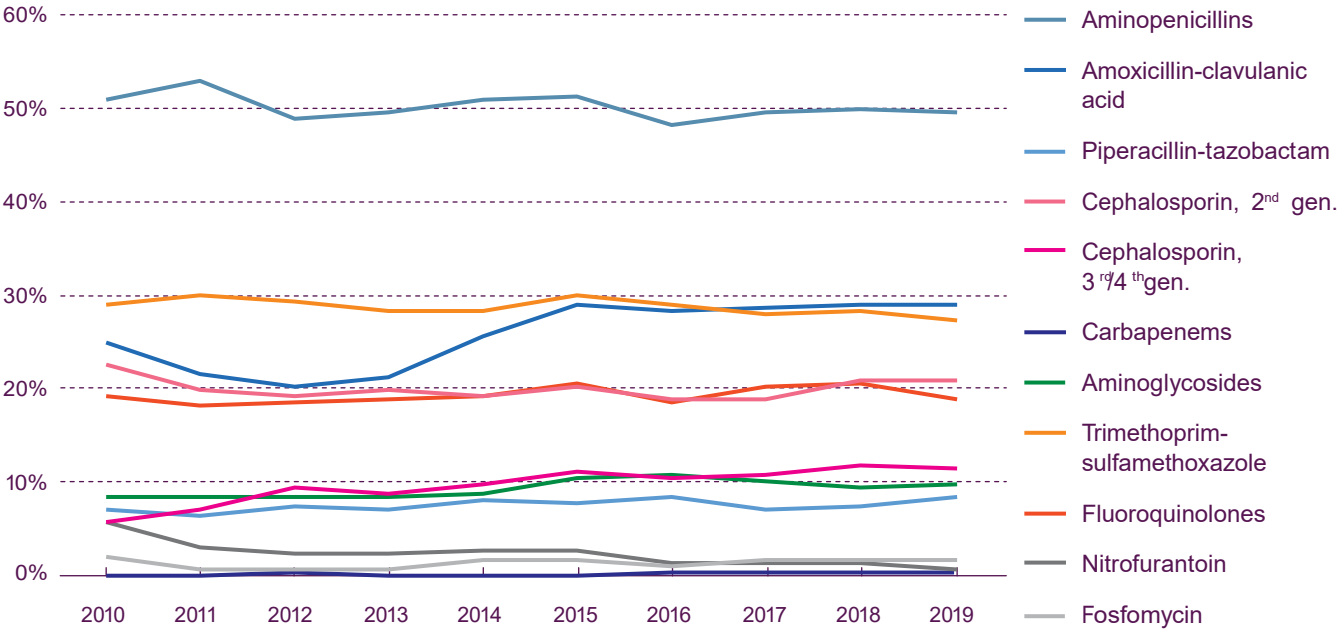


Table 7. b: Non-susceptibility combinations in invasive *E. coli* isolates in humans 2019. Only isolates tested against all five antibiotic groups (aminopenicillins, third-generation cephalosporins, carbapenems, aminoglycosides, fluoroquinolones) were considered (n = 5513/5901[93.4%]).

Resistance patterns	Number of isolates	% of total
Fully susceptible	**2,606**	**47.3%**
Single resistance (to indicated antimicrobial group)		
Total (all single resistance types)	**1,732**	**31.4%**
Aminopenicillins	1,560	28.3%
Aminoglycosides	17	0.3%
Fluroquinolones	155	2.8%
Resistance to two antimicrobial groups		
Total (all two-group combinations)	**557**	**10.1%**
Third-generation cephalosporins + fluoroquinolones	1	0.0%
Aminopenicillins + fluoroquinolones	311	5.6%
Aminopenicillins + third-generation cephalosporins	130	2.4%
Aminoglycosides + fluoroquinolones	4	0.1%
Aminopenicillins + aminoglycosides	111	2.0%
Resistance to three antimicrobial groups		
Total (all three-group combinations)	**379**	**6.9%**
Aminopenicillins + third-generation cephalosporins + fluoroquinolones	218	4.0%
Aminoglycosides + third-generation cephalosporins + fluoroquinolones	1	0.0%
Aminopenicillins + fluoroquinolones + aminoglycosides	114	2.1%
Aminopenicillins + third-generation cephalosporins + aminoclycosides	46	0.8%
Resistance to four antimicrobial groups		
Total (all four-group combinations)	**238**	**4.3%**
Aminopenicillins + carbapenems + third-generation cephalosporins + fluoroquinolones	1	0.0%
Aminopenicillins + third-generation cephalosporins + aminoglycosides + fluoroquinolones	237	4.3%
Resistance to five antimicrobial groups		
Total (all five-group combinations)	**1**	**0.0%**
Aminopenicillins + third-generation cephalosporins +aminoglycosides + fluoroquinolones + carbapenems	1	0.0%

However, no clear trend for *E. coli* isolates resistant to two to five antibiotic groups was observed during the last ten years (Table 7. b, Figure 7. c).

Carbapenem-resistance in *E. coli* is still very rare (0.1%) and comparable to the EU/EAA states (<0.1% on average in 2018). Nevertheless, increasing rates of carbapenemase-producing Enterobacteriaceae (CPE) around the world are alarming. In order to survey these trends more accurately, knowledge regarding the genetic mechanisms is indispensable. The Federal Office of Public Health has therefore introduced an obligation to report CPE starting 1.1.2016, and all strains are collected by the National Reference Center for Emerging Antibiotic Resistance in Fribourg (NARA, www.nara-antibiotic-resistance.ch) since 2019. A detailed analysis of Swiss data from 2013 to 2018 has been accepted for publication in Eurosurveillance [3] and is summarized in chapter 13 of this report.

Colistin, a rather toxic reserve antibiotic belonging to the polymyxin group, might in future become more important as a "last resort antibiotic" for the treatment of infections due to carbapenemase producers. Actually, colistin resistance is rare in Switzerland, but reports from China describing a mobile plasmid encoding a colistin resistance gene (mcr types), are worrisome [4]. So far, colistin resistance is not systematically tested in Switzerland, although testing algorithms and adequate testing methods have been published by the NARA.

Figure 7. c: Multiresistance in invasive *E. coli* isolates in humans between 2010 and 2019 (for details refer to Table 7. b).