7.4 *Acinetobacter* spp.

Acinetobacter spp. are Gram-negative, strictly aerobic coccobacilli. These opportunistic pathogens, which can be found in soil and water, are intrinsically resistant to many antibiotic agents. *Acinetobacter* spp. can roughly be divided into two groups: The *Acinetobacter calcoaceticus – Acinetobacter baumannii* (ACB) complex and the non-ACB group, including a large number of environmental species with low pathogenicity. Because the correct identification to the species level is difficult, we herein analyze, in accordance with the European resistance networks EARS-Net and CAESAR, resistance trends on the genus level.

Acinetobacter spp. infections are a big concern for hospital-acquired infections. They can cause respiratory, urinary, wound infections and septicemia. Meningitis has also been reported. Risk factors for multidrug-resistant *Acinetobacter* spp. are severe underlying diseases, prolonged hospital stays, especially in ICUs during antibiotic administration, mechanical ventilation and surgical procedures.

Around one quarter of *Acinetobacter* spp. isolates are not susceptible to at least one of the three most important antibiotics, i.e. carbapenems (14%), aminoglycosides (17%) and ciprofloxacin (15%, Table 7. g, 7. h). Except for ciprofloxacin, non-susceptibility rates are higher in western Switzerland than in north-eastern Switzerland. Although a north-south gradient in antibiotic resistance can be observed in Europe for nearly all antibiotics, differences are most prominent in *Acinetobacter* spp. In 2016, resistance rates ranged from < 5% in northern countries to > 80% in southern/eastern countries for all of the antibiotics tested. The EU/EEA population means in 2016 were 35% for carbapenems and aminoglycosides, and 39% for fluoroquinolones [1]. In Switzerland, no significant trend can be observed since 2008 (Table 7. g and Figure 7. h). Notably we could not find an increase in carbapenem-resistance as described for Europe (see Textbox: "Carbapenem-Resistant *Acinetobacter baumannii* from 2005 to 2016 in Switzerland"). Details on multiresistances are given in Table 7. h and Figure 7. I

Table 7. g: Non-susceptibility rates of invasive *Acinetobacter* spp. isolates in humans for 2017. Due to small numbers, non-susceptibility rates for southern Switzerland are not shown.

Acinetobacter spp.											2017
Antimicrobial	West		North-East		South		Total			Trend	
	n	%	n	%	n	%	n	%	95%CI	4y	10y
Carbapenem	27	25.9%	61	9.8%	5	0.0%	93	14.0%	8.4-22.5	-	-
Aminoglycosides	27	25.9%	58	13.8%	5	0.0%	90	16.7%	10.4-25.7	-	-
Trimethoprim-sulfamethoxazole	25	24.0%	53	13.2%	5	0.0%	83	15.7%	9.4-25	-	-
Ciprofloxacin	27	14.8%	61	16.4%	5	0.0%	93	15.1%	9.2-23.7	-	-

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.
[1] Carbapenems: imipenem, meropenem

Textbox

Carbapenem-Resistant *Acinetobacter baumannii* from 2005 to 2016 in Switzerland

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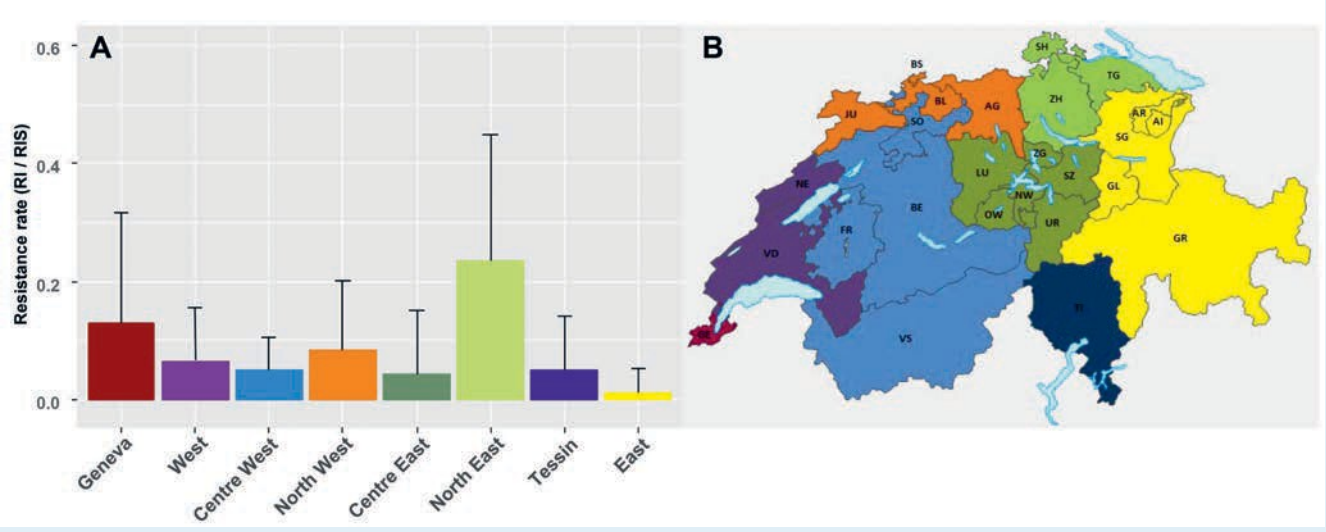
Over the last years, the endemic establishment of *A. baumannii* resistant to carbapenems, a last-line group of -lactam antibiotics used to treat patients infected with multidrug-resistant Gram-negative bacteria, has worsened in Europe and worldwide. In the *Acinetobacter* genus, several species present a risk for opportunistic infections and belong to the so-called *Acinetobacter calcoaceticus-Acinetobacter baumannii* (ACB) complex. In contrast, "non-ACB" *Acinetobacter* species generally present lower pathogenicity and are often found in the environment. We have analyzed the temporal and regional fluctuations of the number of carbapenem-susceptible and -resistant *Acinetobacter* spp. in Switzerland. We have restricted our analyses to invasive isolates from blood cultures or cerebrospinal fluid to ensure that they are comparable with international reports. We have used the qualitative data (SIR) and accompanying epidemiological information, such as sample location, provider of the sample, patient sex and age group, as provided by the participating laboratories.

From 2005 to 2016, a total of 800 invasive *Acinetobacter* isolates were identified in the anresis.ch database, consisting of 707 carbapenem-susceptible and 93 carbapenem-resistant isolates, respectively. After removal of duplicates, 58 resistant or intermediate isolates were identified out of 632 cases (resistance rate 9.2%) over the study period. Four out of 58 carbapenem-resistant isolates were isolated from cerebrospinal fluid, the rest from blood cultures. Co-resistance to other antibiotics, such as aminoglycosides (47/55, 86%), trimethoprim-sulfamethoxazole (42/54, 78%) and fluoroquinolones (47/55, 86%), was high, whereas no colistin resistance was reported for 23 isolates tested. There was a significant increase in the total number of *Acinetobacter* isolations over time, with about 30 isolates per year on average, increasing at a yearly rate of about three new isolates. When only ACB complex species were considered, there were 18 isolates per year on average, increasing at an average rate of one new isolate per year. The largest number of resistant isolates belonged to the ACB complex (55/299, 18.4%), while resistance rates were much lower in non-ACB species (1/184, 0.5%).

Yet, from 2005 to 2016, the overall yearly number of carbapenem-resistant ACB and non-ACB isolates did not increase, with an average of about five *Acinetobacter* isolates per year (mostly ACB isolates). The north-eastern region, with a total of 24 resistant *Acinetobacter* (22 of which were ACB) isolations from 2005 to 2016, was significantly above all other regions in terms of number of resistant strains. This was mainly attributable to an outbreak in a single hospital (data not shown). These geographic differences were confirmed when examining yearly average resistance rates per region (Fig. 1A, 1B): there was no significant temporal trend

Figure 1: *Acinetobacter* resistance rates (number of resistant isolates compared to total number of isolates) per region from 2005 to 2016 in Switzerland. Standard deviation bars represent annual fluctuations per region. B) Map of the Swiss regions defined in this study.



in resistance rates for all *Acinetobacter* or ACB isolates. Only the north-eastern region presented higher rates on average than other regions.

In summary, this first nationwide surveillance study indicates that resistance rates of invasive carbapenem-resistant *Acinetobacter* in Switzerland are stable at a low level on a yearly basis, but that they display large temporal and regional disparities. Our results also indicate the existence of a diverse pool of *A. baumannii* and related species in Swiss hospital settings. We have confirmed the implication of carbapenem-resistant ACB complex isolates in the vast majority of clinical infections and nosocomial outbreaks that involved *Acinetobacter* isolates. Our analyses, which conjointly cover both multiple years and multiple regions, highlight the usefulness of surveillance approaches that integrate different temporal and spatial resolution levels. Further surveillance efforts are needed to detect and control *Acinetobacter* outbreaks, and to limit the endemic establishment of resistant isolates in new health facilities and across regions.

See related publication:

Ramette A, Kronenberg A, and the Swiss Centre for Antibiotic Resistance (ANRESIS) 2018 Prevalence of carbapenem-resistant *Acinetobacter baumannii* from 2005 to 2016 in Switzerland. BMC Infect Dis. 2018 Apr 3;18(1):159. doi: 10.1186/s12879-018-3061-5. www.ncbi.nlm.nih.gov/pubmed/29614963

Figure 7. h: Non-susceptibility rates of invasive *Acinetobacter* spp. isolates in humans between 2008 and 2017.

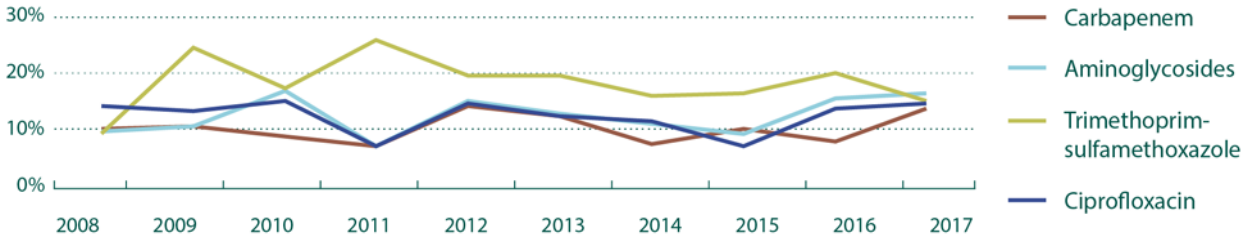


Table 7. h: Non-susceptibility combinations in invasive *Acinetobacter* spp. isolates in humans in 2017. Only isolates tested against all three antibiotic groups (aminoglycosides, ciprofloxacin and carbapenems) were considered (n=90/93 [96.8%]).

Resistance patterns	Number of Isolates	% of total
Fully susceptible	68	75.6%
Single resistance (to indicated antimicrobial group)		
Total (all single resistance types)	11	12.2%
Ciprofloxacin	4	4.4%
Aminoglycosides	4	4.4%
Carbapenems	3	3.3%
Resistance to two antimicrobial groups		
Total (all two-group combinations)	2	2.2%
Ciprofloxacin + aminoglycosides	1	1.1%
Aminoglycosides + carbapenems	1	1.1%
Resistance to three antimicrobial groups		
Third-generations cephalosporins + aminoglycosides + fluoroquinolones	9	10.0%

Figure 7. i: Multiresistance in invasive *Acinetobacter* spp. isolates in humans between 2008 and 2017 (for details refer to Table 7. h).