Antibiotic Consumption and Resistance in Swiss Intensive Care Units

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BACKGROUND

- Intensive care units (ICUs) constitute a high-risk setting for antimicrobial resistance (AMR) due to increased patient susceptibility, exposure to broad-spectrum antibiotics (AB) and high patient turnover. We therefore aimed to assess temporal trends regarding AMR and AB use in Swiss ICUs.

METHODS

- We analysed data on AMR (2009-2018) and AB use (2009-2017) sent to ANRESIS. Only data of ICUs participating for ≥8 years were included.
- AMR (one sample per species/patient/year) was expressed as % of all isolates. The following pathogens were analysed: extended-spectrum cephalosporin-resistant *Escherichia coli* (ESCR-EC) and *Klebsiella spp.* (ESCR-K), carbapenem-resistant *Enterobacteriales* (CRE) and *Pseudomonas aeruginosa* (CRPA), methicillin-resistant *Staphylococcus aureus* (MRSA), and glycopeptide-resistant *Enterococci* (GRE). Temporal trends were analyzed with linear regression.
- Non-multidrug resistant MRSA - susceptible to at least three of the following agents: ciprofloxacin, clindamycin, tetracycline and trimethoprim-sulfamethoxazole (see PMID: 27631162) - was used as an approximation for community-acquired MRSA (caMRSA).
- Different phenotypes of CR-*Klebsiella spp.* (based on resistance pattern) within the different ANRESIS regions were analyzed over time.
- The use of systemic AB (ATC code J01) was calculated as defined daily doses (DDD) per 100 beddays (BD).

RESULTS

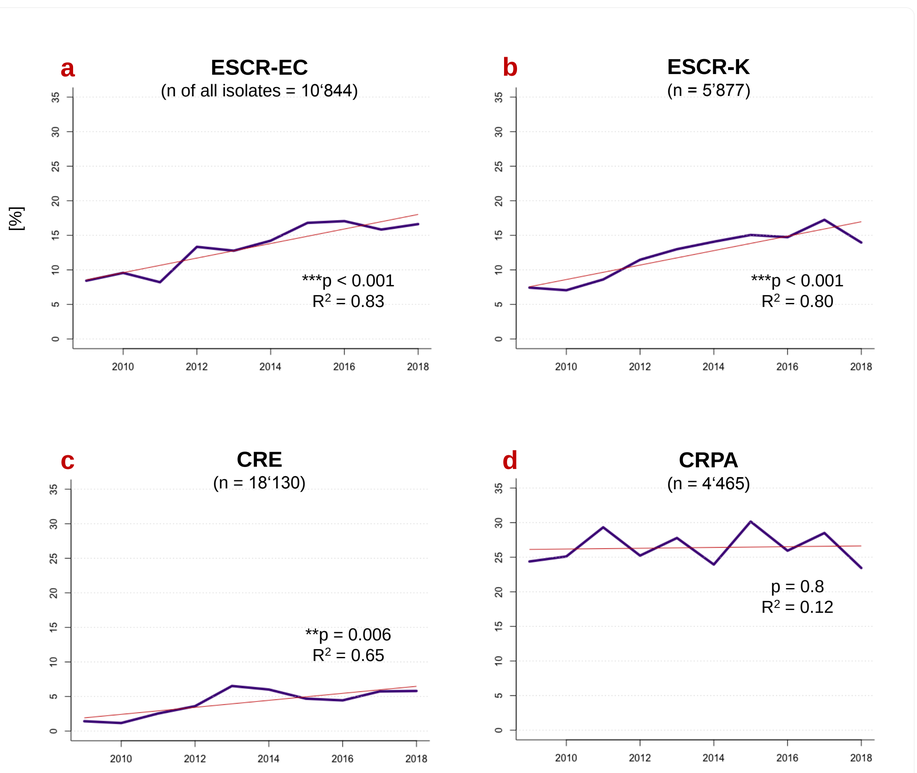
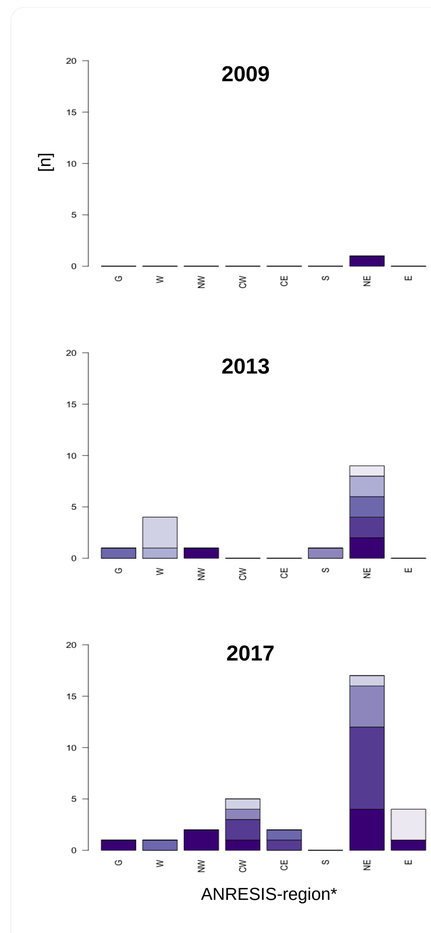


Figure 1. Resistant Gram-negative pathogens in Swiss ICUs (2009 to 2018)

- Within 15 ICUs from the French/Italian- and 13 from German-speaking parts we observed an increase for ESCR-EC (8% to 17%; P <.001) (**Fig 1a**), ESCR-K (7% to 14%; P <.001) (**1b**) and also CRE (1% to 6%; P=.006) (**1c**); CR-*Klebsiella spp.* increased in all ANRESIS regions between 2009 and 2017, with clustering of certain phenotypes in the ANRESIS-region Northeast (Fig 2). The proportion of CRPA (mean 26%) did not change over time (P=.8) (1d).
- The proportion of MRSA among *S. aureus* decreased from 16% to 7% (P=.002) (**Fig 3a**), with a relative increase of presumptive caMRSA from 20 to 54% among all MRSA (**3b**). No temporal trend was observed for GRE (mean 2% of 5’222).
- The overall AB use (13 ICUs from French/Italian-, 10 from German-speaking parts) did not change from 2009 (105 DDD/100 BD) to 2017 (101 DDD/100 BD) (**Fig 4a**). Also the overall use of reserve antibiotics (according to WHO´s AWaRe classification) did not change (+54%; P=.8).
- Imipenem use decreased (-48%; P <.001) whilst meropenem (+2%; P=.63) and ertapenem use (-14%; P=.81) remained stable (**4b**); piperacillin/tazobactam (+30%; P=.002) and ceftriaxone use (+19%; P=.03) increased, whereas the cefepime (+23%; P=.7) and ceftazidime use (+20%; P=.9) did not significantly alter.



Resistance pattern	p1	p2	p3	p4	p5	p6	p7	p8
Ertapenem	-	R	-	-	R	R	-	R
Imi-/Meropenem	R	S	R	R	S	S	R	S
Fluoroquinolones	R	R	S	R	S	R	S	S
Aminoglycosides	R	R	S	S	S	S	R	R

R: resistant, S: sensible

Figure 2. Spatiotemporal evolution of CR-*Klebsiella spp.* by resistance pattern

*ANRESIS-regions: G: Geneva, W: West, NW: North-west, CW: Central-West, CE: Central-East, S: South, NE: Northeast, E: East

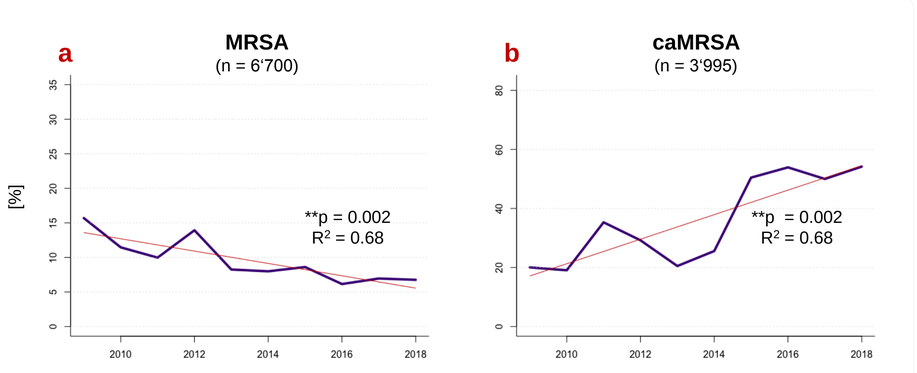


Figure 3. MRSA and proportion of caMRSA isolates in Swiss ICUs

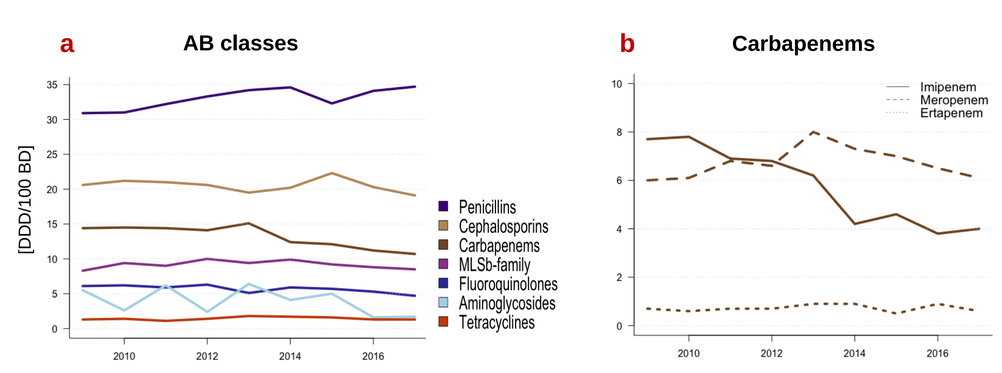


Figure 4. AB consumption of swiss ICUs.

CONCLUSIONS

- In Swiss ICUs, resistant Gram-negative pathogens have been steadily increasing over the last decade. Particularly worrisome is the rise of CRE and local clusters of phenotypically similar CR-*Klebsiella* spp. The proportion of CRPA among P. aeruginosa is considerable.
- Overall carbapenem use is decreasing, which suggests other factors than antibiotic selection pressure as drivers of carbapenem resistance.
- MRSA is clearly decreasing, mostly due to a reduction in presumable healthcare-associated MRSA and a consecutive relative increase of caMRSA.
- The overall and reserve AB use in Swiss ICUs has been stable during the last decade.

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