# Proposal of a national definition of multidrug-resistant invasive gram-negative organisms by ANRESIS

P003

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## Background

- Surveillance of multidrug-resistant (MDR) microorganisms is key to national antimicrobial resistance programs
- Gram-negative MDR microorgansims (GN-MDRO) in particular MDR Enterobacterales (MDR-E) are increasing worldwide.
- In Switzerland, there is no generally accepted definition of GN-MDRO, neither for epidemiological surveillance nor for the purpose of infection prevention control (IPC).

## Objectives

- Development of two MDR-E definitions for Switzerland, one for epidemiological use and one for infection control purposes.
- International definitions are taken as a basis and adapted to the local test algorithms as well as to the resistance situation prevailing in Switzerland.

## Method

Using qualitative susceptibility data (S,I,R) from invasive isolates from 2019-2020 from the ANRESIS database, we analyzed test algorithms used by Swiss laboratories and cross-resistance within antibiotic groups to determine two different MDR-E definitions depending on the intended use, a broader one for epidemiological surveillance ("ANRESIS-EPI") and a more restrictive one for infection control ("ANRESIS-IPC"). Using these algorithms, the rates of invasive MDR-E identified in our national dataset were compared with international and national definitions.

**Table 1** Different MDR definition criteria and the corresponding antibiotic panels per antibiotic group for Enterobacterales are listed. The ECDC[1] definition contains 17 antibiotic categories, of which only the five categories corresponding to the other definitions are listed in the table.

| Antibiotic category | **ANRESIS-EPI** | **ANRESIS-IPC** | **ECDC** | **KRINKO** | **UHZ** |
|---|---|---|---|---|---|
| Aminoglycosides | At least 1 of: amikacin, gentamicin, tobramycin | Amikacin and gentamicin | Gentamicin or tobramycin or amikacin or netilmicin | | At least 2 of: amikacin, gentamicin, tobramycin |
| Antipseudomonal penicillins + BLI | Piperacillin-tazobactam | Piperacillin-tazobactam | Ticarcillin-clavulanic acid or piperacillin-tazobactam | Piperacillin-tazobactam | Piperacillin-tazobactam |
| Carbapenems | At least 1 of: ertapenem, imipenem, meropenem | Imipenem and/or meropenem | Ertapenem or imipenem or meropenem or doripenem | Imipenem and/or meropenem | At least 2 of: ertapenem, imipenem, meropenem |
| Fluoroquinolones | Ciprofloxacin and/or levofloxacin | Ciprofloxacin | Ciprofloxacin | Ciprofloxacin | Ciprofloxacin and levofloxacin |
| 3rd and 4th generation cephalosporins | At least 1 of: Ceftriaxone, ceftazidime, cefepime | Cefepime and ceftazidime | Cefotaxime or ceftriaxone or ceftazidime or cefepime | Cefotaxime and/or ceftadzidime | Ceftriaxone and ceftazidime and cefepime |
| MDR definiton criteria | MDR-E: resistant to at least 3 categories out of 5 categories | MDR-E resistant to at least 3 categories out of 5 categories | MDR-E resistant to at least 3 categories out of 17 categories | MDR-E: resistant to at least 3 categories out of 4 categories | MDR-E resistant to at least 3 categories out of 5 categories |

## Results

The highest MDR-E rates were found using the "ECDC-MDR" definition (N=3664). The number of MDR-E identified by using the ANRESIS-IPC (N=277) definition was comparable to those detected with the KRINKO[2] (N=267) respectively UHZ[3] definition (N=193) (Figure 1).

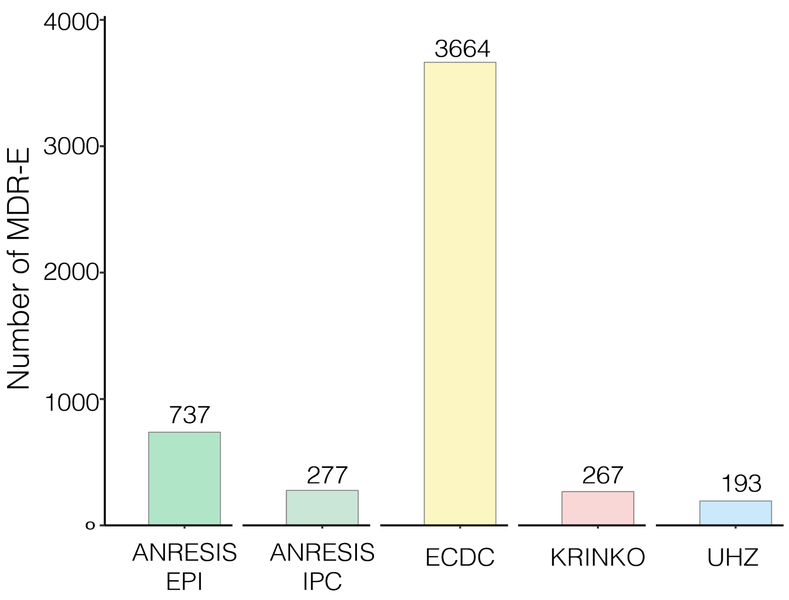


**Figure 1** Number of Enterobacterales isolates (N=16'879) meeting the respective MDR criteria are displayed.

The isolates classified as MDR-E by UHZ, KRINKO and ANRESIS-IPC (N=387) differed markedly. Only 101 of the isolates (26.1%) were commonly classified as MDR-E according to the KRINKO, UHZ and ANRESIS-IPC definitions (Figure 2). However, using the ANRESIS EPI definition, all of these 387 isolates are recognized as MDR-E.

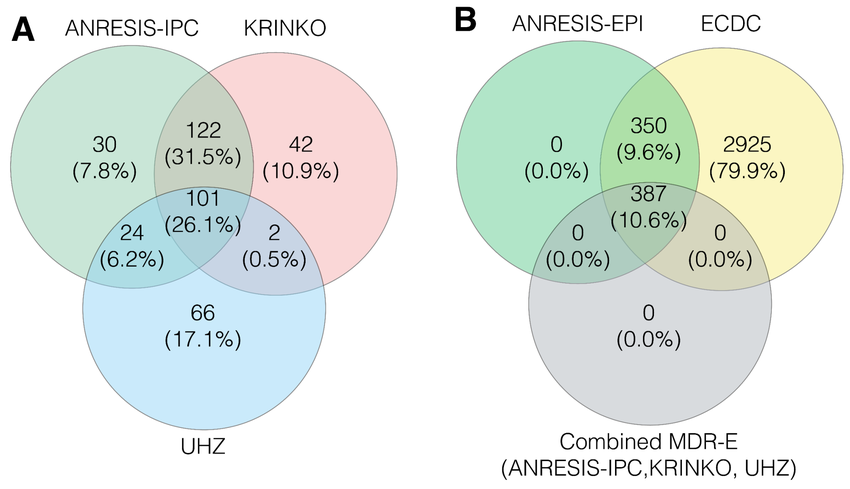


**Figure 2** **A)** Overlap in the number of Enterobacterales isolates classified as MDR after applying KRINKO, UHZ, and ANRESIS-IPC definitions.
**B)** Overlap in Enterobacterales isolates classified as MDR-E after application of the ECDC, ANRESIS-EPI, and isolates collectively classified as MDR-E with KRINKO, USZ, and ANRESIS-IPC definitions.

## Conclusion

The application of different MDR definitions leads not only to considerable variations in the rates of MDR-E, but also in the isolates that are finally classified as MDR-E. Different testing algorithms in Swiss laboratories make a uniform MDR-E definition difficult. The need for different definitions for different purposes and the importance of a commonly defined screening antibiotic panel are highlighted in this study.

## References

1. Magiorakos, et al. 2012; *Clin Microbiol Infect* 18 (3): 268–81.
2. KRINKO (2012). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 55(10): 1244-1310.
3. Wolfensberger, A., et al. (2019); Antimicrob Resist Infect Control 8: 193