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Surveillance of multidrug resistant Enterobacterales is affected by the new EUCAST guidelines

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BACKGROUND / AIM

Surveillance of multidrug resistant (MDR) microorganisms is key in national antibiotic resistance programs, and especially MDR Enterobacterales (MDR-E) are increasing worldwide. The new EUCAST guidelines from 1.1.2019 introduced two essential modifications with the potential to influence MDR-E classification. First, category "I" was redefined as "susceptible, increased exposure" and therefore excluded from the earlier category non-susceptible ("I"+"R"), which has been used to define MDR-E. Second, breakpoints for the category "I" were changed for several antibiotics, of which mainly aminoglycosides and carbapenems are used in MDR-E definitions[1,2,3] (Figure 1A).

METHODS

Using interpreted qualitative susceptibility data (SIR) of blood culture isolates reported to the ANRESIS national antibiotic resistance database from 2017-2021, we analyzed the impact on MDR-E classification under EUCAST guideline 11.0 (2021) compared with version 8.0 (2018). The provided quantitative resistance data were evaluated in three ways; I) according to the old guidelines where "I" and "R" are considered as non-susceptible, II) according to the new guidelines where only "R" is considered as non-susceptible and III) according to the new guidelines, additionally considering the breakpoint changes that lead to modifications in the SIR classification of quantitative resistance data. MDR-E was defined according to ECDC[4], KRINKO[5], and the ANRESIS-EPI[6] algorithm. The MDR-E algorithms differ not only in the selection and number of antibiotic groups, but also in the antibiotics considered in each group. The ECDC definition includes 17 antibiotic groups, the KRINKO definition includes 4, and the ANRESIS definition includes 5 antibiotic groups, 3 of which must be non-susceptible to classify an isolate as MDR-E in all algorithms. The ANRESIS-EPI algorithm considers aminoglycosides in addition to the antibiotic groups included in the KRINKO MDR-E definition.

RESULTS

- Overall requiring "R" instead of non-susceptible ("R"+"I") reduced the number of MDR-E by 15.8%, 45.5% and 23.1% using the ECDC, KRINKO and ANRESIS-EPI algorithm (Figure 1B).
- Breakpoint changes for aminoglycosides slightly increased the number of MDR-E as for this antibiotic group, category "I" was suspended in favor of category "R" (Figure 1B).
- Manual correction of the database showed a declining effect over time, which could be explained by successive introduction of the new EUCAST guidelines by the different laboratories (Figure 1C).

RESULTS

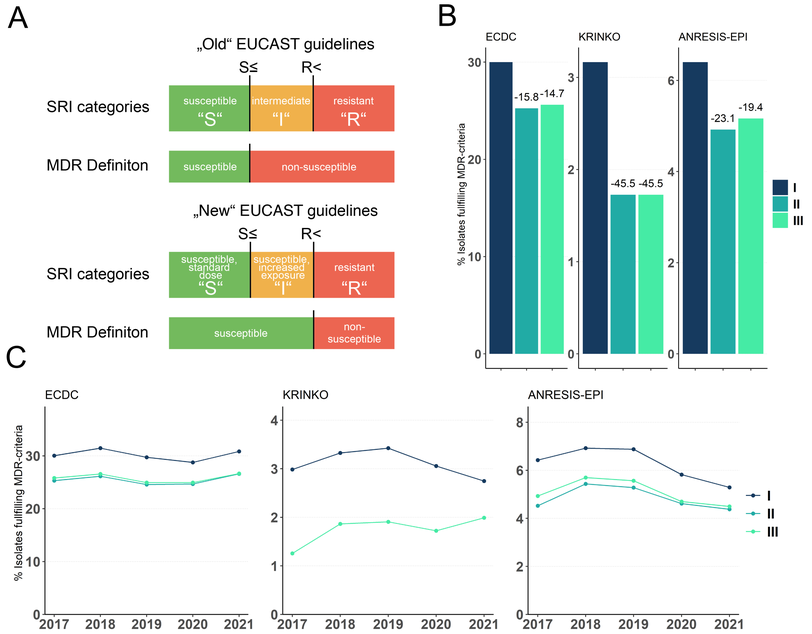

Figure 1: Proportion of MDR-E isolates identified by applying different MDR-E definitions to all isolates reported to ANRESIS. **A)** Re-definition of the susceptibility categories by EUCAST. **B)** Changes in the proportion of isolates classified as MDR-E from 2017-2021, using different algorithms and either applying the "new" or "old" EUCAST guidelines. **I:** MDR-E definition according to EUCAST 8.0, reporting "I"+"R" as resistant. **II:** MDR-E definition reporting "R" only as resistant, **III:** MDR-E definition B with retrospective manual correction of antibiotics, where breakpoint changes resulted in "I" being reclassified as "R". **C)** Time course of the proportion of the number of MDR-E cases in the adjustments mentioned in B).

- MDR-E definitions that do not consider aminoglycosides (e.g. KRINKO) are less affected by breakpoint changes (Figure 1 B&C).
- Manual correction for changing breakpoints of some antibiotics (e.g. meropenem) was impossible, due to shifts within the "I"-category and missing MIC- or inhibition zone data for most of the ANRESIS laboratories.

RESULTS

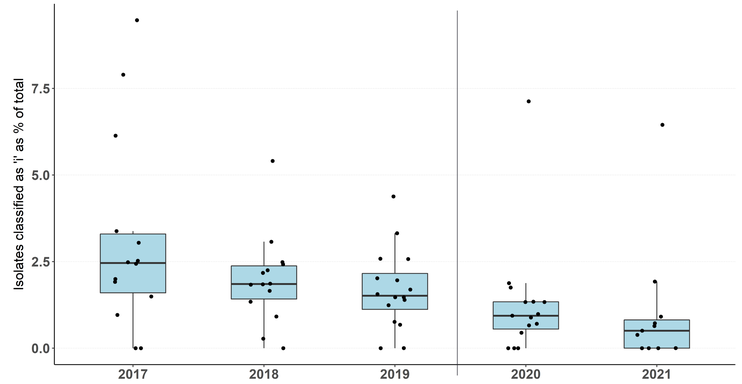

Figure 2: Proportion of amikacin AST results correctly classified by laboratories as "I" before, and misclassified as "I" after altered EUCAST breakpoints in 2020.

- Prompt implementation of changes to EUCAST guidelines are critical to reliably interpret and compare resistance data.
- The number of isolates misclassified is steadily decreasing, but a latency period is evident, as seen in the case of amikacin resistance results misclassified as "I". (Figure 2).

CONCLUSION

Changes in EUCAST guidelines can substantially affect MDR-E statistics. Although some manual corrections are feasible in retrospect using qualitative resistance data, a clear communication to clinicians and health care authorities is needed. Although altered breakpoints have less impact on MDR-E surveillance, interpretation is more complex and requires MIC/DD data.

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