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Report

European antimicrobial resistance surveillance Belgium (EARS-BE) 2017
– description of main findings (D/2018/14.470/16)

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Introduction

This report describes main findings of the “EARS-BE 2017” study, which covers data collection for Belgium and 2017 of the European antimicrobial resistance surveillance network (EARS-NET)[1]. Coordinated by the European center for disease prevention and control (ECDC, Stockholm), EARS-NET is het main surveillance system for monitoring occurrence and spread of antimicrobial resistance (AMR) in human pathogens across Europe. EARS-BE differs from EARS-NET only in the additional collection of data on Antimicrobial susceptibility tests (ASTs) on isolates from urine (next to blood and cerebrospinal fluid (CSF)). EARS-BE 2017 data on blood/CSF isolates were submitted in August 2018 to ECDC for inclusion in the Annual European report on antimicrobial resistance[1]; the ECDC report’s results for Belgium correspond directly with the results presented here.

The background and methodology of EARS-BE 2017 can be found elsewhere[2]. The results presented and discussed here are derived from the “EARS-BE 2017 statistical report”[3]. This report contains all EARS-BE 2017 reference data, including indicators on laboratory, patient and isolate characteristics, and AST results for studied sample types (bloodCSF, urine) and pathogens (*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter* spp.). For each AST, the number of laboratories contributing results, the overall testing percentage, and the percentage interpreted according to EUCAST (European committee on antimicrobial susceptibility testing) guidelines, are given as well. Furthermore, the statistical report presents results for isolates obtained from blood/CSF side-by-side with those from urine samples, and this for following sets of inclusion criteria and subgroups:

(1) general EARS-BE 2017 inclusion criteria, as defined in the surveillance protocol;

(2) (1), but for hospital laboratories only;

(3) (1), but for hospital laboratories and EUCAST-interpreted ASTs only;

(4) (1), but for non-hospital laboratories only;

(5) (1), but for non-hospital laboratories and EUCAST-interpreted ASTs only;

(6) (1), but for hospitalized patients only.

For blood/CSF isolates, results in this report will be based mostly on results of (1), note that these are (almost) entirely based on hospital laboratories (see further). For urine isolates of *E faecalis*, *E coli*, *P mirabilis*, *K pneumoniae* and *P aeruginosa*, we will present results of hospital laboratories (2 and 3) separately from those of non-hospital laboratories (4 and 5).

Participation

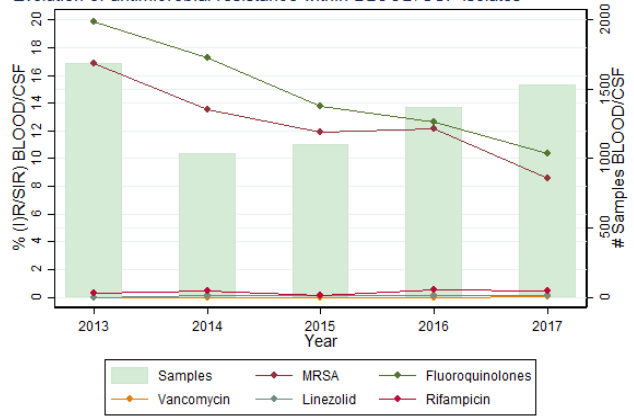
Blood/CSF isolates: thirty-two laboratories submitted AST results on isolates from blood/CSF samples taken in 2017 (statistical report Table OV.1). Of these 32 labs, one was not associated to an acute care hospital, submitting results on a single *E coli* blood isolate. Twenty-four labs (75%) continued their participation of 2016. Compared to 2016, the overall number of labs reporting results of blood/CSF samples remained stable (with 31 labs in 2016), but the total number of samples increased for all pathogens.

Urine isolates: Twenty-four labs submitted results for urine samples taken in 2017, 5 of these were not associated to an acute care hospital. Those 5 non-hospital laboratories were all situated in the north of the country, and contributed about 50% of the total number of *E coli* and *K pneumoniae* urine isolates. Comparing the group of hospital laboratories submitting blood/CSF isolates with those submitting urine isolates, we observed that the north of the country was slightly underrepresented for urine isolates (42% versus 58% comparing urine with blood/CSF isolates). Only 2 laboratories specified info on whether urine isolates resulted from screening practices, which was not the case for both labs. About 50% of hospital laboratories specified info on whether urine samples were derived from a catheter, these rates ranged from 12.2% for *E coli* isolates, 19.7% for *K pneumonia,* 20.8%% for *E faecalis*, 24% for *P mirabilis* and 33.8% for *P aeruginosa*. None of the non-hospital laboratories provided this information.

Use of EUCAST guidelines: In 2017, 24 (75%) labs reported the use of EUCAST guidelines for interpretation of ASTs on blood/CSF isolates, the represents an increase from the 57% reported in 2016. Of these 24, 23 were hospital laboratories, with the distribution over the three regions and hospital types being similar to the overall group. Out of 19 hospital labs submitting results on urine isolates, 12 (62%) reported the use of EUCAST guidelines. All 5 non-hospital labs submitting results on urine isolates reported the use of EUCAST guidelines, although these all switched from CLSI (Clinical & laboratory standards institute) to EUCAST during 2017.

Results for *Staphylococcus aureus*

Figure STA.1.1 *Staphylococcus aureus*.
Evolution of antimicrobial resistance within BLOOD/CSF isolates



Blood/CSF isolates: in 2017, 8.5% of *S aureus* isolates were non-susceptible to methicillin (MRSA), while 10.3% of isolates were resistant to fluoroquinolones. For both antibiotic groups, this represents a further decrease as

compared to previous years, with MRSA non-susceptibility and fluoroquinolones resistance in 2013 being 16.9% and 19.8%R (Figure STA.1.1). Resistance levels to vancomycin, linezolid and rifampicin were very low in 2017.

Results for *Streptococcus pneumoniae*

Results obtained from the national surveillance on invasive pneumococcal infections 2017

Results for AMR in *S pneumoniae* isolates are based on 2017 AST data of the national surveillance on invasive pneumococcal infections of the National reference center (UZ Leuven, KU Leuven), and shown in Statistical report Table STRN.1 (see the annual report[4] for complete results of this surveillance). The data included AST results on blood/CSF isolates submitted by 92 labs, with susceptibility results interpreted according to CLSI guidelines. Criteria for non-susceptibility to penicillins are based on those for parenteral penicillin (non-susceptibility for CSF: Minimal inhibitory concentration (MIC)>0.06mg/L; for blood: MIC>2mg/L). In 2017, non-susceptibility to penicillins, 3rd-generation cephalosporins (3GC) and fluoroquinolones were very low (0.2%, 0.1% and 0.2% respectively), while non-susceptibility to macrolides was 15.6%. Decreasing 4-year trends were observed for penicillins (1.4% in 2014) and macrolides (18.3% in 2014).

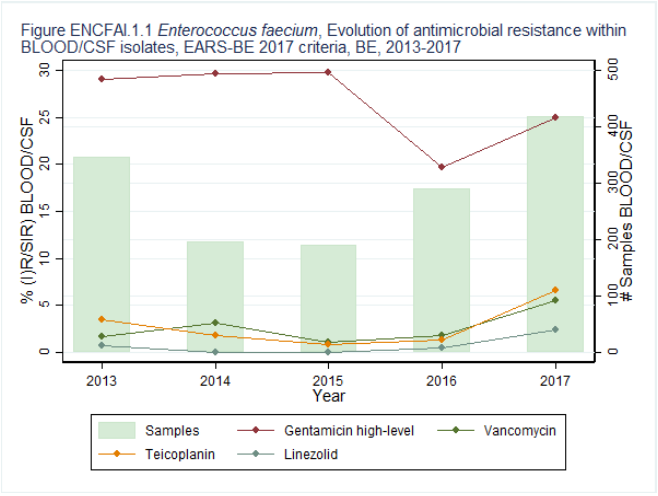
Results obtained from the EARS-BE 2017 data collection

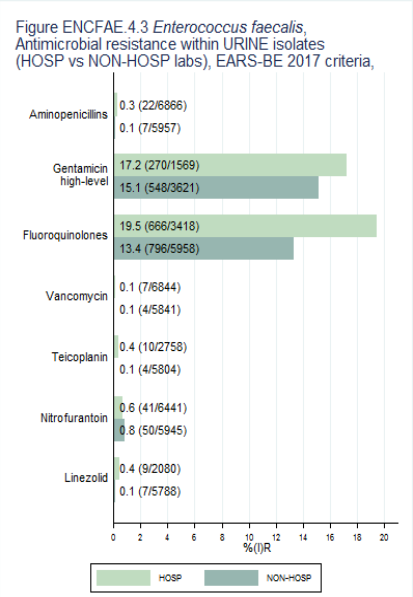
For the sake of completeness, the results of the EARS-BE 2017 data collection of *S pneumoniae* blood/CSF isolates (27 labs submitting results) are shown in Statistical report Table STR.1. Non-susceptibility to penicillins was 6.8% (34/496). When restricting the analysis to EUCAST-interpreted ASTs (65% of isolates, 18 labs submitting results), non-susceptibility to penicillins was 9.0%. Overall, macrolide resistance was 12.1%, while resistance to 3GC and fluoroquinolones were very low.

Results for Enterococci

Blood/CSF isolates: *E faecalis* isolates showed low resistance to aminopenicillins (0.4%), vancomycin (0.7%) and linezolid (1.1%), and no resistance to teicoplanin. This marked an increase of resistance to linezolid, with 4 (out of 25) laboratories reporting resistant isolates in 2017, and with the three previous years showing absence of any resistance. In *E faecium* isolates, we observed 88.5%R to aminipenicillins, 5.5%R to vancomycin, 6.5%R to teicoplanin, and 2.3%R to linezolid; these last three marking a substantial increase as compared to 2016, with levels of resistance in *E faecium* to vancomycin and to teicoplanin as measured by EARS-BE exceeding 5% since many years, see also figure ENCFAI.1.1. As can be seen from the percentiles of the distribution of lab means (statistical report table ENCFAI.1), multiple labs reported elevated levels of resistance for these antimicrobials in 2017, while this was only the case for single labs (if any) in 2016. For these three antimicrobials, a positive 5-year trend was also detected, with 2013 resistance rates being 3.1R% to vancomycin, 1.8%R to teicoplanin, and no resistance to linezolid.

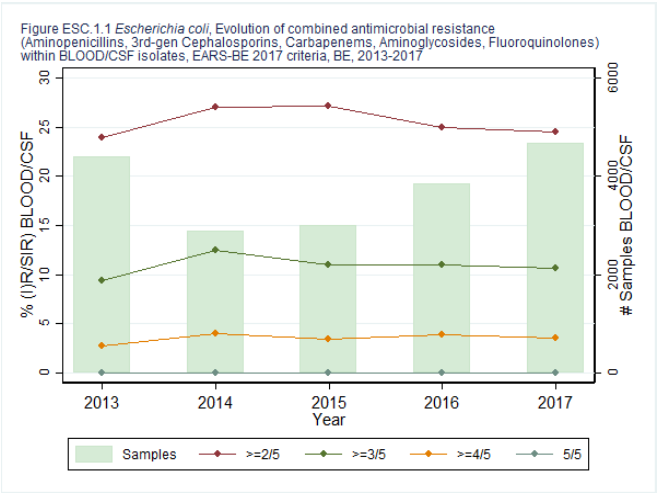
Urine isolates: in 2017, resistance of *E faecalis* urine isolates to aminopenicillins, nitrofurantoin, vancomycin, teicoplanin, and linezolid were all very low (<1%), and this both for isolates reported by hospital and non-hospital laboratories, see also figure ENCFAE.4.3 below. Fluoroquinolones (ciprofloxacin or levofloxacin) resistance was 19.5% and 13.4% in hospital and non-hospital laboratories respectively.





Results for *Escherichia coli*

Blood/CSF isolates: we observed 57.4%R to aminopenicillins, 25.5% R to amoxicillin-clavulanic acid, 23.8%R to fluoroquinolones, 8.1%R to piperacillin-tazobactam, 8.1%R to aminoglycosides, 9.8%R to 3GC, and almost no resistance to carbapenems. Seventy-eight per cent of 191 isolates resistant to 3GC were reported positive for Extended-spectrum beta-lactamase (ESBL, results submitted by 14 labs). For fluoroquinolones resistance, a decreasing 4-year trend was detected (26.9%R in 2014). Slowly decreasing 4-year trends were also observed for some indicators on combined resistance (based on resistance to aminopenicillins, 3GC, carbapenems, aminoglycosides and fluoroquinolones), for example from 27.1%R in 2013 to 24.5%R in 2017 for resistance to two (out of 5) antibiotic groups and from 12.5%R in 2013 to 10.6%R in 2017 for resistance to three (out of 5) antibiotic groups, see figure ESC.1.1.



Urine isolates from hospital laboratories: Levels of resistance within urine isolates of this group were only slightly lower as compared to blood/CSF isolates, with 51.1%R to aminopenicillins, 21.4%R to amoxicillin-clavulanic

acid, 19.1%R to fluoroquinolones, 5.3%R to piperacillin-tazobactam, 5.8%R to aminoglycosides, 6.7%R to 3GC (figure ESC.3.2). Within 1339 isolates resistant to 3GC, 89.5% were ESBL-positive (10 labs submitting results). Resistance to temocillin was 4.3%, 10.5%R to cefuroxime, 26.6%R to trimethoprim-sulfamethoxazole, 1.4%R to nitrofurantoin and 1.7%R to fosfomycin.

Figure ESC.3.2 *Escherichia coli*, Antimicrobial resistance within BLOOD/CSF and URINE isolates, EARS-BE 2017 criteria, Hospital labs only, BE, 2017

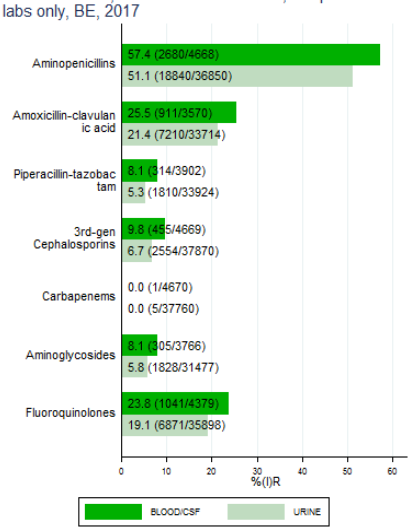
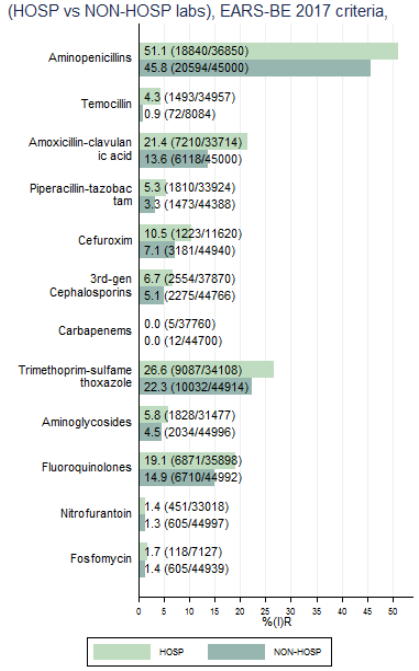


Figure ESC.4.3 *Escherichia coli*, Antimicrobial resistance within URINE isolates (HOSP vs NON-HOSP labs), EARS-BE 2017 criteria,



Urine isolates from non-hospital laboratories: Resistance levels in this group were slightly lower than isolates from hospital laboratories, see figure ESC.4.3 above. These differences became even smaller when restricting to EUCAST-interpreted ASTs; in the group of non-hospital labs, resistance to amoxicillin-clavulanic acid increased to 29.6%R, to 5.7%R for piperacillin-tazobactam and to 11.4%R for cefuroxime. EUCAST defines a less strict breakpoint for resistance to amoxicillin-clavulanic acid in uncomplicated urinary tract infection ('less strict' meaning having a higher MIC than the systemic breakpoint), but it is unknown how many interpretations resulted from using this breakpoint.

Results for *Proteus mirabilis*

Data on this pathogen were collected for the first time by EARS-BE in 2017 to cover the most frequent pathogens isolated from urine samples. Seventeen hospital labs and 5 non-hospital labs submitted results for 2017.

Urine isolates from hospital labs: Elevated levels of antimicrobial resistance were observed for aminopenicillins (44.7%), trimethoprim-sulfamethoxazole (35.6%), fluoroquinolones (27.5%) and fosfomycin (27.1%), see figure PRT.4.3. Resistance to temocillin was 0.5%, 3% to cefuroxime, 12.6% to amoxicillin-clavulanic acid, 1.1% to piperacillin-tazobactam, 1.4% to 3GC and 13.6% to aminoglycosides.

Urine isolates from non-hospital labs: Overall, resistance levels were very similar between isolates from hospital and non-hospital laboratories, see figures PRT.4.3 and PRT.4.4 below. Also here, resistance to amoxicillin-clavulanic acid increased substantially in the group of hospital labs when restricting to EUCAST-interpreted tests (from 4.1%R to 10.5%R). Only for resistance to aminoglycosides, results between hospital and non-hospital laboratories seemed to deviate substantially (14.1%R versus 6.7%).

Figure PRT.4.3 *Proteus mirabilis*, Antimicrobial resistance within URINE isolates (HOSP vs NON-HOSP labs), EARS-BE 2017 criteria,

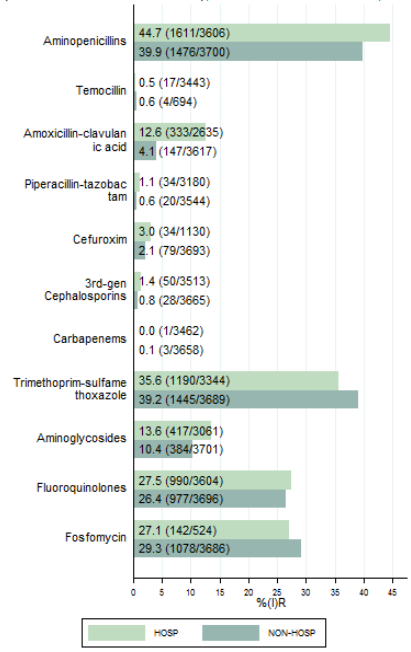
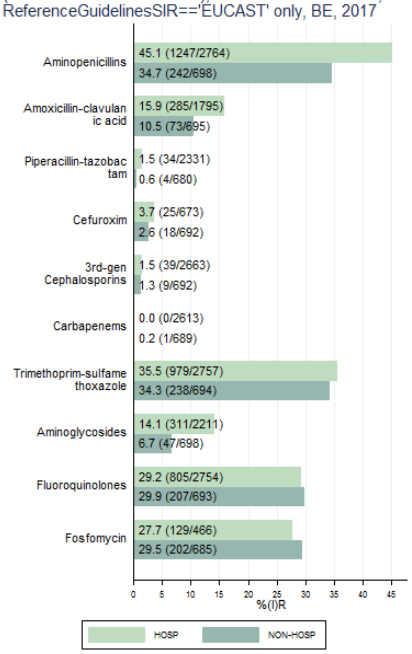


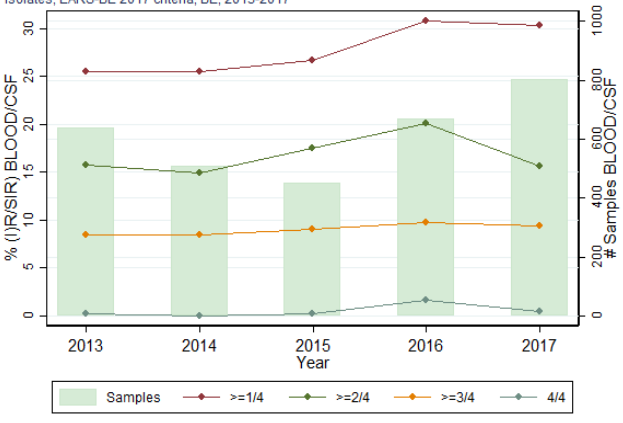
Figure PRT.4.4 *Proteus mirabilis*, Antimicrobial resistance within URINE isolates (HOSP vs NON-HOSP labs), EARS-BE 2017 criteria, ReferenceGuidelinesSIR=='EUCAST' only, BE, 2017



Results for *Klebsiella pneumoniae*

Blood/CSF isolates: In 2017, resistance to 3GC and to carbapenems was 19.3% and 1.1% respectively; this represented no further increase as compared to 2016. Ninety-two per cent of 72 isolates resistant to 3GC were ESBL-positive (results submitted by 14 labs). We observed 25.5%R to amoxicillin-clavulanic acid, 17.4%R to piperacillin-tazobactam, 12.5%R to aminoglycosides and 23.7%R to fluoroquinolones. An increasing 4-year trend was observed for resistance to fluoroquinolones, being 18.6%R in 2014. For indicators of combined antimicrobial resistance, nu further increase in 4-year trends was detected, see figure KLE.1.1 below.

Figure KLE.1.1 *Klebsiella pneumoniae*, Evolution of combined antimicrobial resistance (3rd-gen Cephalosporins, Carbapenems, Aminoglycosides, Fluoroquinolones) within BLOOD/CSF isolates, EARS-BE 2017 criteria, BE, 2013-2017



Urine isolates from hospital laboratories: Very similar levels of resistance were observed when comparing urine with blood/CSF isolates in this group, with only resistance to amoxicillin-clavulanic acid and piperacillin-tazobactam being slightly lower in urine isolates (figure KLE.3.2). Resistance to 3GC was 19.5%, with 96% of 496 isolates being ESBL-positive (results submitted by 10 labs). Resistance to temocillin was 4.3%, 25.3% to cefuroxime, 24% to trimethoprim-sulfamethoxazole, and 26.6% to fosfomycin.

Figure KLE.3.2 *Klebsiella pneumoniae*, Antimicrobial resistance within BLOOD/CSF and URINE isolates, EARS-BE 2017 criteria, Hospital labs only, BE, 2017

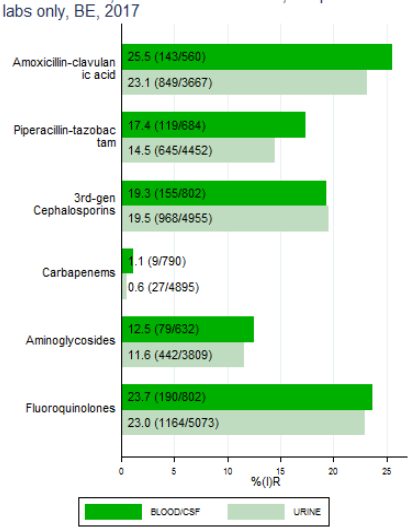
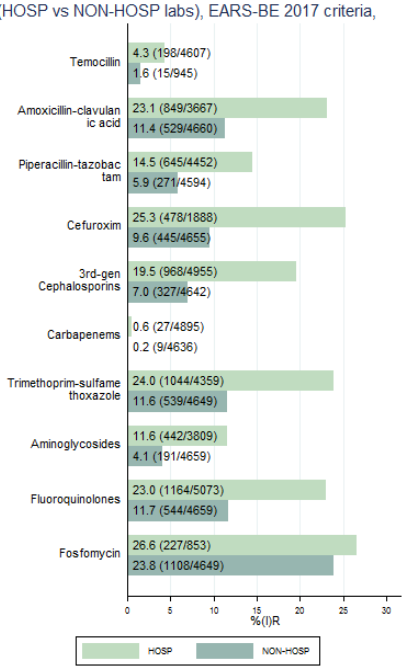


Figure KLE.4.3 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates (HOSP vs NON-HOSP labs), EARS-BE 2017 criteria,



Urine isolates from non-hospital laboratories: Except for resistance to fosfomycin, much lower levels of resistance were observed in this group, generally less than half the levels of resistance observed in the group of urine isolates from hospital laboratories, see figure KLE.4.3. However, when restricting to EUCAST-interpreted ASTs, resistance levels increased substantially for amoxicillin-clavulanic acid (from 11.4% to 17.9%) and piperacillin-tazobactam (from 5.9% to 11.3%).

Results for *Pseudomonas aeruginosa*

Blood/CSF isolates: we observed 10.5%R to piperacillin-tazobactam, 7.2%R to ceftazidime, 8.2%R to carbapenems, 7.7%R to aminoglycosides, and 10.5%R to fluoroquinolones. When restricting the analysis to ASTs interpreted according to EUCAST (results for blood/CSF isolates submitted by 23 laboratories), resistance levels increased substantially, for example 13.3%R to piperacillin-tazobactam, 9.4%R to ceftazidime, and 9.4%R to carbapenems (figures PSE.3.2 and PSE.3.3). Such upwards shift in resistance levels for EUCAST-interpreted ASTs might help explaining the difficulties in detecting meaningful longterm trends for resistance in *P aeruginosa* (Figure PSE.1.1), with the observed variability between years possibly due to a switch by laboratories from CLSI towards EUCAST over said period.

Figure PSE.3.2 *Pseudomonas aeruginosa*, Antimicrobial resistance within BLOOD/CSF and URINE isolates, EARS-BE 2017 criteria, Hospital labs only, BE, 2017

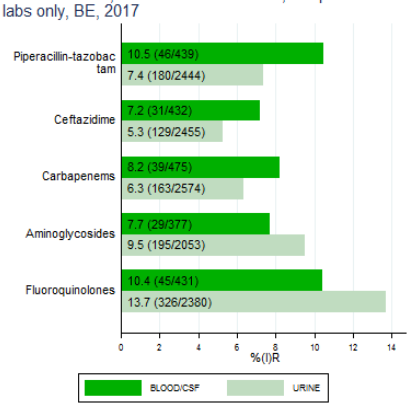


Figure PSE.3.3 *Pseudomonas aeruginosa*, Antimicrobial resistance within BLOOD/CSF and URINE isolates, EARS-BE 2017 criteria, Hospital labs, ReferenceGuidelinesSIR=='EUCAST' only, BE,

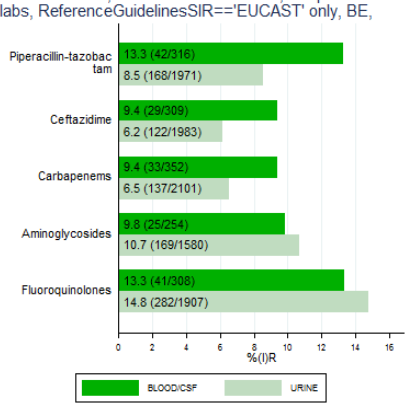
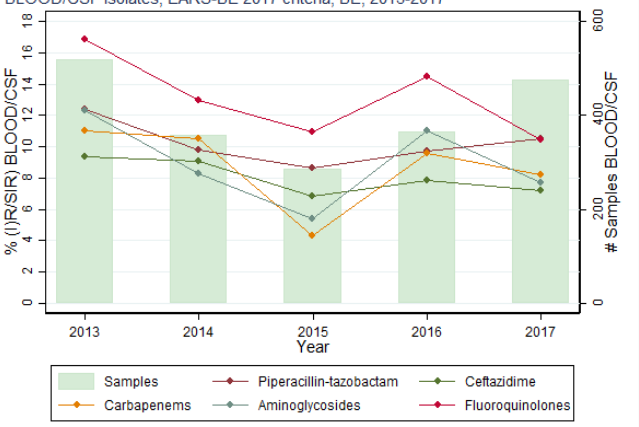


Figure PSE.1.1 *Pseudomonas aeruginosa*, Evolution of antimicrobial resistance within BLOOD/CSF isolates, EARS-BE 2017 criteria, BE, 2013-2017



Urine isolates from hospital laboratories: When comparing antimicrobial resistance levels between urine and blood/CSF isolates in this group, lower levels of resistance were observed in urine isolates for piperacillin-tazobactam (7.4%), ceftazidime (5.3%), carbapenems (6.3%), and (slightly) higher for aminoglycosides (9.5%R), and fluoroquinolones (13.7%R), see figure PSE.3.2. Also here, levels of resistance are corrected upwards when restricting to EUCAST-interpreted guidelines (figure PSE.3.3).

Urine isolates from non-hospital laboratories: Levels of antimicrobial resistance in urine isolates were substantially lower in this group, except for resistance to fluoroquinolones (14.6%R), see figures PSE.4.3 and PSE.4.4 below.

Figure PSE.4.3 *Pseudomonas aeruginosa*, Antimicrobial resistance within URINE isolates (HOSP vs NON-HOSP labs), EARS-BE 2017 criteria,

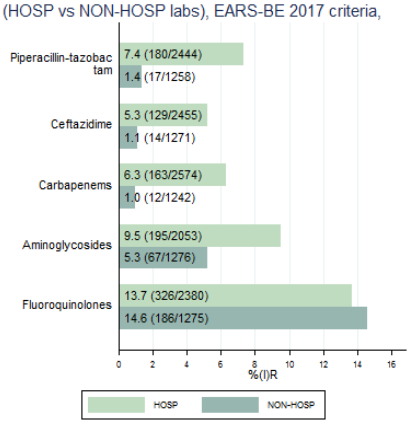
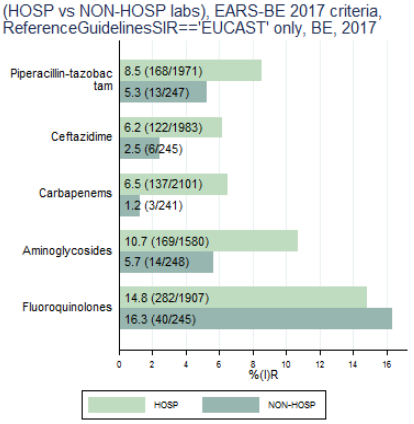


Figure PSE.4.4 *Pseudomonas aeruginosa*, Antimicrobial resistance within URINE isolates (HOSP vs NON-HOSP labs), EARS-BE 2017 criteria, ReferenceGuidelinesSIR=='EUCAST' only, BE, 2017



Results for *Acinetobacter* species

Blood/CSF isolates: data were collected on 131 isolates, with 21 labs submitting AST results, and 9 other labs reporting zero blood/CSF isolates for this pathogen in 2017. Such low number of isolates makes it difficult to obtain precise estimates of resistance prevalence on a national level. Also, 2017 is only the first year for which results for *Acinetobacter* spp were obtained from all participating laboratories, and only the first year where the total number of isolates exceeds 100, meaning that accurate comparisons with previous years are equally difficult. We observed 6.9%R to carbapenems, 13.1%R to aminoglycosides, and 10.8%R to fluoroquinolones. These levels of resistance were substantially higher as compared to 2016, with resistance levels to carbapenems and aminoglycosides surpassing the 5% level.

Colistin resistance in *E coli, K pneumoniae, P aeruginosa*

Estimation of national colistin resistance from data on routinely performed ASTs as collected by EARS-BE is difficult. This is due to only a subset of laboratories submitting test results and also because testing for this antibiotic varies according to sample type and/or pathogen. Focusing on hospital laboratories only, colistin test rates on blood/CSF isolates varied from 70.3% in *E coli* (15 labs reporting), 78.2% in *K pneumoniae* (13 labs reporting), to 84.4% in *P aeruginosa* (19 labs reporting). In urine isolates, these rates were 64.8% in *E coli* (8 labs reporting), 66.9% in *K pneumoniae* (10 labs reporting), and 80.4% in *P aeruginosa* (11 labs reporting). In *E coli*, resistance to colistin in 2017 was very low in both blood/CSF isolates and urine isolates (both 0.3%R). In *K pneumoniae* isolates, resistance was 1% in blood/CSF isolates and 1.3% in urine isolates. In *P aeruginosa*, resistance was 0.4% in both blood/CSF and urine isolates.

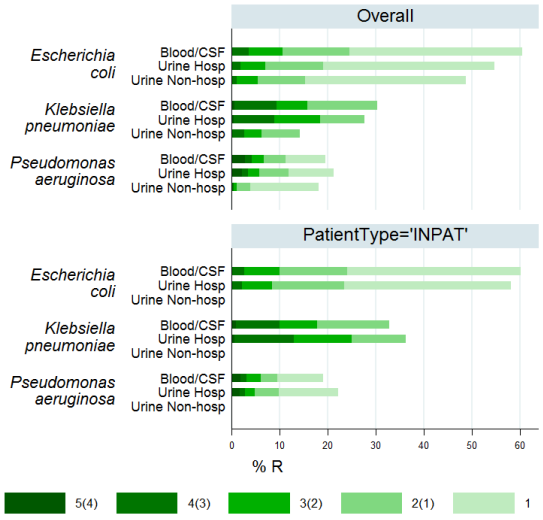
Conclusions

In blood and cerebrospinal fluid samples, *Staphylococcus aureus* non-susceptibility to methicillin (MRSA) and resistance to fluoroquinolones continued their decrease in 2017, resulting in a 50% decrease of resistance to these antimicrobials in the period 2013-2017. *Enterococcus faecium* resistance to vancomycin and teicoplanin saw an increase towards levels above 5%. For *Escherichia coli*, decreasing 4-year trends of combined antimicrobial resistance (resistance to 1 to 5 antibiotic groups out of aminopenicillins, 3rd generation cephalopsorins, carbapenems, aminoglycosides and fluoroquinolones) were observed. For *Klebsiella pneumoniae*, no further increase was observed for resistance to third-generation cephalosporins and carbapenems, but a 4-year increasing trend could be observed for fluoroquinolones. *Pseudomonas aeruginosa* showed resistance to almost all studied antibiotic groups, with levels of resistance increasing substantially when restricting to test results interpreted according to EUCAST. For *Acinetobacter* spp, the number of labs submitting results of blood/cerebrospinal fluid isolates should further increase to improve the detection of meaningful trends;

future data collection should also obtain results on AMR for the specific group of *Acinetobacter baumannii* isolates.

The EARS-BE 2017 study also collected results on antimicrobial resistance in urine isolates. For urine isolates analyzed in hospital laboratories, overall resistance levels followed more or less those of blood/CSF isolates. As shown in figure GNEG.1.5 below, combined antimicrobial resistance levels of urine isolates were only slightly lower than blood/CSF for *E coli*, while those of *K pneumoniae* and *P aeruginosa* were very similar between the two sample types. Within the group of hospitalized patients (figure GNEG.1.5 lower panel), differences for *E coli* isolates largely disappeared, while for *K pneumoniae* and *P aeruginosa* these became larger in favor of urine isolates. *K pneumonia* and *P aeruginosa* (but not *E coli*) isolates from non-hospital laboratories showed substantially lower levels of combined resistance as compared to those of hospital laboratories.

Figure GNEG.1.5 Gram-negative pathogens, combined antimicrobial resistance within blood/CSF and urine isolates, EARS-BE 2017 criteria, BE, 2017



Combined antimicrobial resistance: isolates resistant to 1, 2, 3, 4 or 5 (1,2,3,4 for *Kpneumoniae*) antibiotic groups among those tested for: *Ecoli*: aminopenicillins, 3rd-gen cephalosporins, carbapenems, aminoglycosides, fluoroquinolones; *Kpneumoniae*: 3rd-gen cephalosporins, carbapenems, aminoglycosides, fluoroquinolones; *Paeruginosa*: piperacillin-Tazobactam, ceftazidim, carbapenems, aminoglycosides,

The results of the data collection of urine isolates are certainly interesting, given the size of collected data and 2017 only being the first year in which detailed results on antimicrobial resistance were collected in both the hospital and non-hospital setting. In future studies, increase of participation is particularly needed for non-hospital laboratories from the central and south regions of the country. The unknown rate of urine isolates resulting from screening (ie. samples taken in absence of clinical signs or symptoms suggestive of urinary tract infection) is a limitation as well, because it could make observed resistance rates dependent on local practices. Furthermore, a substantial part of hospital laboratories not being able to provide a patient's hospitalization status prevents generalization of results for the group of hospitalized patients, as well as harmonization with other national surveillances on antimicrobial resistance such as NSIH-AMR and –SEP.

Finally, it should be noted that EARS-BE data collection proceeds without any official regulation nor funding, not on the level of participating laboratories nor of Sciensano. This is in contradiction with the widespread use of its results[1] combined with the substantial efforts needed to obtain these (both by laboratories and Sciensano). Correcting this imbalance should be an essential step in establishing national surveillance on antimicrobial resistance in Belgium that is as much detailed as it is accurate and robust.

References

1. European Centre for Disease Prevention and Control. Surveillance of antimicrobial resistance in Europe 2017. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2018. http://ecdc.europa.eu/sites/portal/files/documents/AMR-surveillance-EARS-Net-2017.pdf

2. Struyf T, Mertens K. The European Antimicrobial Resistance Surveillance Network Belgium (EARS-Net BE) protocol 2017: Including data call, instructions for participating laboratories, data definition, reporting procedure (Version 3, 26/02/2018). Sciensano. 2018. http://www.nsih.be/download/EARSNet_protocol_2017_v3.pdf

3. Mertens K, Struyf T. EARS-Net BE National statistical report 2017. Sciensano. 2018. http://www.nsih.be/download/EARSBE_20181205a.xlsx

4. Nationaal referentiecentrum voor invasieve *S. pneumoniae*. *Surveillance van de Pneumokokkeninfecties in België. Verslag voor 2017;* 2018. https://nrchm.wiv-isp.be/nl/ref_centra_labo/streptococcus_pneumoniae_invasive/Rapporten/Streptococcus%20pneumoniae%202017.pdf