Short report

European antimicrobial resistance surveillance for Belgium (EARS-BE) 2021 – description of main findings.

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Acknowledgements

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Contents

INTRODUCTION

This report describes main findings of the "EARS-BE 2021" survey, which covers annual national data collection for Belgium and 2021 of the European antimicrobial resistance surveillance network (EARS-NET)[1,2]. Coordinated by the European center for disease prevention and control (ECDC, Stockholm), EARS-NET is the main surveillance system for monitoring occurrence and spread of antimicrobial resistance (AMR) in human pathogens across Europe. EARS-BE differs from EARS-NET in the additional collection of data on Antimicrobial susceptibility tests (ASTs) on isolates from urine (next to blood and cerebrospinal fluid (CSF)). EARS-BE 2021 data on blood/CSF isolates were submitted in August 2022 to ECDC for inclusion in the Annual European report on antimicrobial resistance[3] and the online Surveillance atlas of infectious diseases (https://atlas.ecdc.europa.eu/public/index.aspx); the ECDC report's results for Belgium will correspond (save for minor differences due to calculation of indicators) with results of ASTs interpreted according to EUCAST (European committee on antimicrobial susceptibility testing) guidelines presented here. In turn, ECDC shares EARS-NET annual data (including those of BE collected by EARS-BE) with the Global Antimicrobial surveillance system (GLASS, under coordination by the World Health Organization[4]), for inclusion in the annual WHO report on antimicrobial resistance in Europe[5],

The background and methodology of EARS-BE 2021 can be found elsewhere[2]. The results presented and discussed here are derived from the "EARS-BE 2021 statistical report"[6], which contains exhaustive EARS-BE 2021 reference data, including indicators on laboratory, patient and isolate characteristics, and AST results for studied sample types (blood, CSF, 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 resistance percentage interpreted according to EUCAST 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 2021 inclusion criteria, as defined in the surveillance protocol;

(2) (1), restricted to hospital laboratories;

(3) (1), restricted to hospital laboratories and EUCAST-interpreted ASTs;

(4) (1), restricted to non-hospital laboratories;

(5) (2), restricted to hospitalized patients.

For blood/CSF isolates, results in this report will be based mostly on results of (1), which are almost entirely based on isolates from hospital laboratories. For urine isolates of Enterococci, *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). Due to the majority of laboratories using EUCAST guidelines (see further), the results of analyses (2) and (3) are very similar.

PARTICIPATION

Blood/CSF isolates: Thirty-five laboratories submitted AST results on isolates from blood/CSF samples taken in 2021 (statistical report Table MAIN.1); thirty-three of these were associated to an acute care hospital. Compared to 2020, the overall number of labs reporting results of blood/CSF samples increased slightly (with 31 hospitals labs having submitted 2020 data). Annual participation of hospital laboratories to EARS-BE for blood/CSF isolates (being the default option) is now increasing since 2019, see Figure PART.EVO.1 below. Note that reporting of results from blood/CSF isolates by non-hospital labs is only sporadic.

In terms of regional distribution of hospital laboratories submitting 2021 data, Flanders (21/33 labs = 64%) and Brussels (5/31 labs = 15%) continue to be overrepresented (as in 2020), with Wallonia (7/31 labs=21%) being underrepresented by about 10% when compared to the national distribution of hospital laboratories. In terms of type of hospitals, participating laboratories from primary hospitals were underrepresented by about 5% as compared to the national distribution.

Figure PART.EVO.1,
Laboratory participation for BLOOD/CSF isolates, EARS-BE, 2012-2021

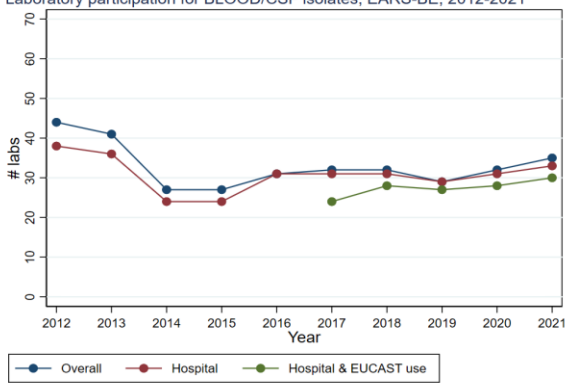
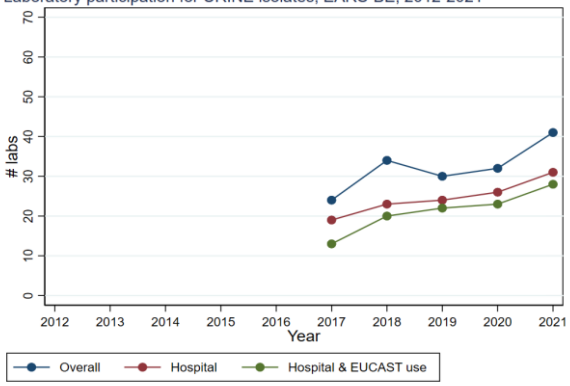


Figure PART.EVO.2,
Laboratory participation for URINE isolates, EARS-BE, 2012-2021



Urine isolates: Forty-one laboratories submitted results for urine samples taken in 2021, 10 of these were not associated to an acute care hospital. Distribution of the 31 participating hospital laboratories over the three regions and hospital types was similar to the distribution for blood/CSF samples. The non-hospital laboratories submitting results on urine samples were equally divided between Flanders and Wallonia. Reporting of results of urine isolates by hospital laboratories is steadily increasing since its introduction in 2017, and also for non-hospital laboratories due to participation in 2021 of laboratories situated in Wallonia, see figure PART.EVO.2 above.

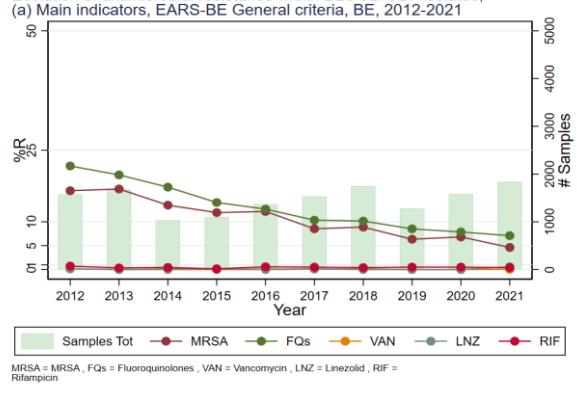
Use of EUCAST guidelines: Of all laboratories submitting results, two reported the use of guidelines for interpretation of ASTs other than EUCAST, these two laboratories both being associated to an acute care hospital. For laboratories reporting blood/CSF results, 6 laboratories reported the use of EUCAST V10 (or later) guidelines in 2021, implementing the new definition of *intermediate resistance* categorization as 'susceptible, increased exposure'[7].

The statistical report includes a section with results for EUCAST-interpreted ASTs only, but because these results only deviate minimally from those based on all ASTs, these will not be discussed in further detail.

RESULTS FOR *S. AUREUS*

Blood/CSF isolates: in 2021, 4.6% (85/1835) of *S. aureus* isolates were resistant to methicillin (MRSA), while 7.1% (130/1832) of isolates were resistant to fluoroquinolones. This represents a further continuation of the long-term decreasing trend for both indicators, and marking the lowest result since EARS-NET follow-up started in 2000, see also figure STA.EVO.0.1.1. Almost none to very low resistance was observed for vancomycin, linezolid and rifampicin.

Figure STA.EVO.0.1.1 *Staphylococcus aureus*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2012-2021

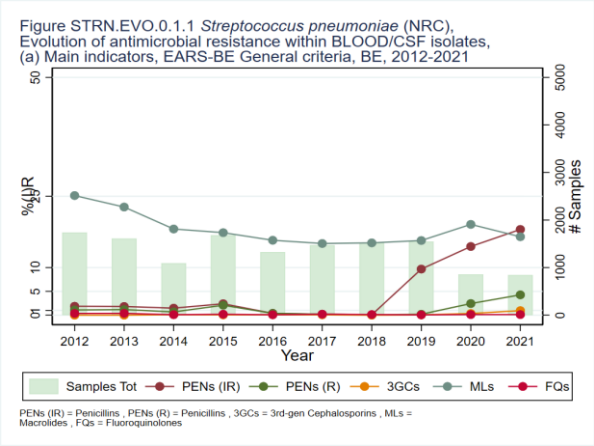


RESULTS FOR *S. PNEUMONIAE*

Results obtained from the national surveillance on invasive pneumococcal infections 2021

Results for AMR in *S. pneumoniae* isolates are based on 2021 AST data obtained by the national surveillance on invasive pneumococcal infections of the National reference center (NRC UZ Leuven), and shown in statistical report table STRN.1, but also see the dedicated annual report[8] for complete results of this national surveillance. The data included AST results on blood/CSF isolates submitted by 82 labs, with susceptibility results interpreted according to EUCAST guidelines. EUCAST V11 criteria for non-susceptibility (%IR) to penicillins are as follows[7]: (1) for CSF isolates: Minimal Inhibitory Concentration (MIC)>0.06mg/L: R; (2) for blood isolates: MIC<=0.06: S; 0.06<MIC=<2 mg/L: I; >2mg/L: R. For blood isolates these interpretation criteria were changed in 2019 (up to 2018: blood isolates: MIC>2mg/L: IR), causing an increase in penicillin non-susceptibility in 2019 as compared to 2018. In 2020, the NRC changed its method for susceptibility testing from E-test to broth microdilution in response to EUCAST recommendations. Finally, ECDC requested that results from invasive isolates from 2021 reported to EARS-NET would be interpreted according to EUCAST V11 breakpoints for non-meningitis (corresponding to above criteria for blood) and irrespective of specimen type (blood or CSF), which implied re-interpreting some CSF penicillin-R AST results to "I". Also, in line with new definitions for resistance introduced by EUCAST in 2019, ECDC reports penicillin resistance in *S. pneumoniae* as 'Penicillin non-wild-type resistance'[1], denoting the percentage of isolates interpreted as 'susceptible, increased exposure (I)' and 'resistant (R)', assuming MICs to benzylpenicillin above those of the wild-type isolates (i.e. >0.06 mg/L).

In 2021, non-wild type resistance to penicillins was 18% (152/843), marking a further increase as compared to 2020, see also figure STRN.EVO.0.1.1 below. Resistance to penicillins (%R) was observed to be 4.3% (36/843), also a further increase as compared to 2020, and which would have been even larger if meningitis breakpoints were used for CSF isolates. Resistance levels to 3rd-generation cephalosporins (3GC) and fluoroquinolones were both very low (<1%), while resistance to macrolides was 16.5% (139/843), resistance among all three classes remaining stable as compared to pre-COVID19 years.



Results obtained from the EARS-BE 2021 data collection

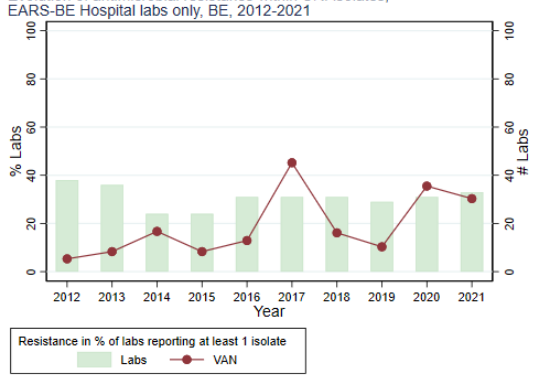
The results of the EARS-BE 2021 data collection of *S. pneumoniae* blood/CSF isolates (33 labs submitting results) are shown in Statistical report Table MAIN.1. Non-wild-type resistance to penicillins was 12.9% (49/380), macrolide resistance was 17% (68/399), and resistance to fluoroquinolones and 3GC was very low (around 1%).

RESULTS FOR *E. FAECALIS* AND *E. FAECIUM*

Blood/CSF isolates: In 2021, *E. faecalis* isolates showed no resistance to vancomycin (out of 794 isolates) and very low resistance (<1%) to aminopenicillins, teicoplanin and linezolid. In *E. faecium* isolates, we observed 89.3%R (503/563) to aminopenicillins, 2.6%R (15/571) to vancomycin, 3.7%R (12/322) to teicoplanin, and very low resistance to linezolid. Because teicoplanin and linezolid susceptibility results were not submitted for all *E. faecium* and *E. faecalis* isolates, their reported %R might be biased upwards under the hypothesis of selective testing.

For followed antimicrobials within both species, no clear trends can be detected in %R expressed on the total of invasive isolates. However when expressed as the % of labs reporting at least one vancomycin-resistant invasive isolate, we observe more recent years with higher occurrence of labs reporting vancomycin-resistant *E faecium* (11 out of 30 in 2020, 10 out 33 laboratories in 2021), see figure ENCFAE.EVO.1.1.b below.

Figure ENCFAI.EVO.1.2.b *Enterococcus faecium*,
Evolution of antimicrobial resistance within URI isolates,
EARS-BE Hospital labs only, BE, 2012-2021



Urine isolates: in 2021, 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 figure ENCFAE.4.3.1 below. No difference was observed with resistance in blood/CSF isolates.

In *E. faecium* urine isolates from hospital laboratories taken in 2021, resistance to vancomycin, teicoplanin and linezolid was very low (<1%). Resistance against these antimicrobials reported by non-hospital laboratories was similar, see figure ENCFAI.4.3.1 below.

Figure ENCFAE.4.3.1 *Enterococcus faecalis*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs,
EARS-BE, BE, 2021

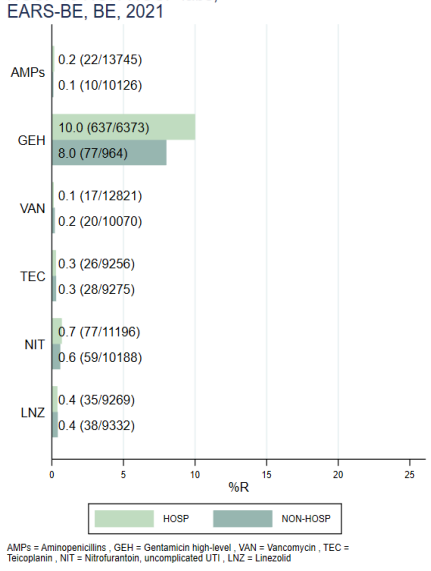
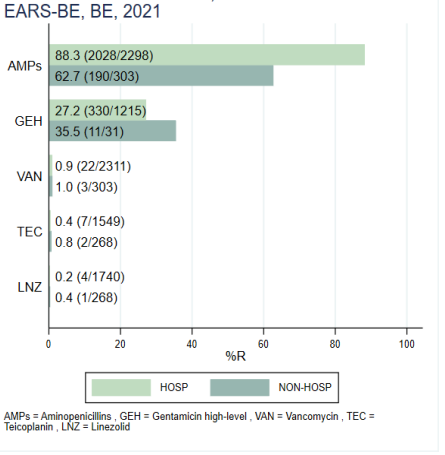


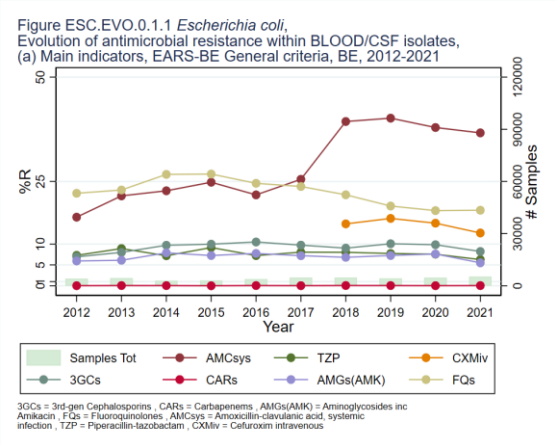
Figure ENCFAI.4.3.1 *Enterococcus faecium*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs,
EARS-BE, BE, 2021

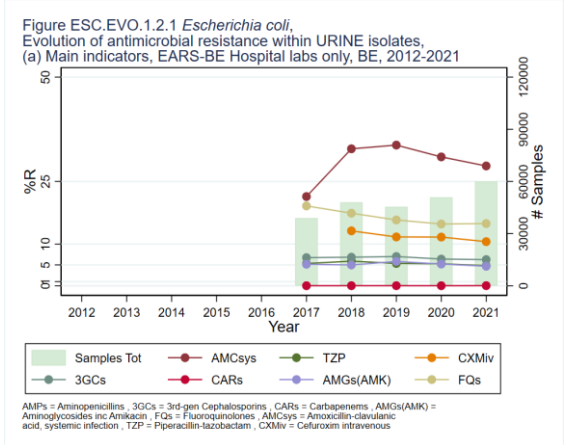


RESULTS FOR *E. COLI*

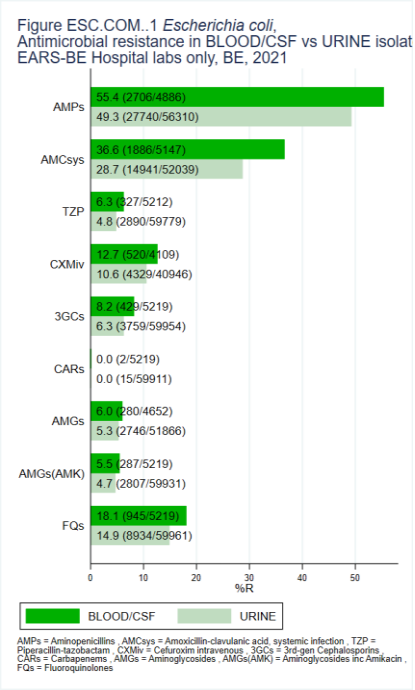
Blood/CSF isolates: For isolates obtained in 2021, we observed 36.6%R (1886/5148) to amoxicillin-clavulanic-acid, 18.1%R (945/5220) to fluoroquinolones, 12.6%R (520/4110) to cefuroxime, 8.2%R (429/5220) to 3GC, 6.3%R (327/5213) to piperacillin-tazobactam, 5.5%R (287/5220) to aminoglycosides, and almost no resistance to carbapenems. Decreasing trends over the past 4 years were observed for many of these antimicrobials, see

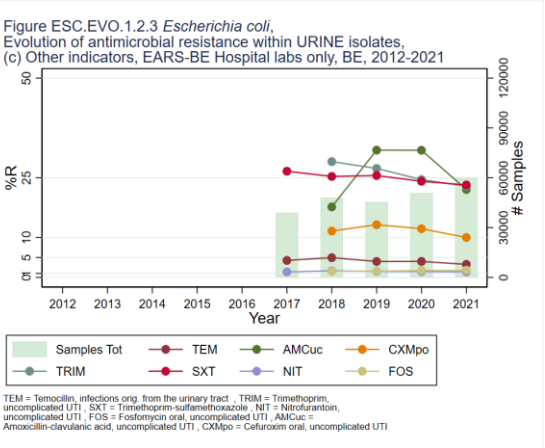
also figure ESC.EVO.1.1.1 below. As such, multidrug resistance rates were observed to decline as well, for example resistance against at least 3 antimicrobials followed above (7.9% in 2021 being the lowest in the past 10years, highest being 12%R in 2014).





Urine isolates from hospital laboratories: Within urine isolates obtained in 2021, levels of **main indicators for resistance** were generally lower as compared to blood/CSF isolates, see figure ESC.COM.1 below. Also here, decreasing trends (over 4 years) of resistance to main antimicrobials was observed (see figure ESC.EVO.1.2.1 above), and as such also against multidrug resistance.



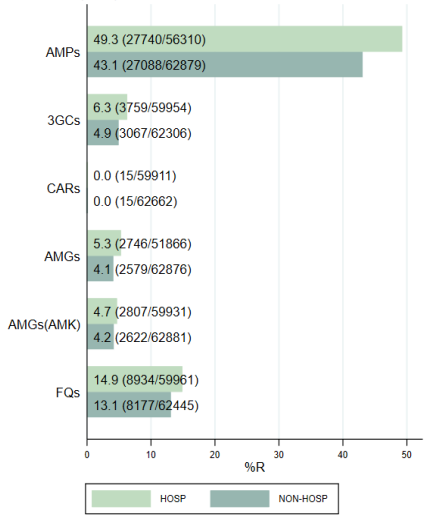


For other antimicrobials typically used for treatment of **urinary tract infection (UTI)**, we observed 23.2% (11950/51523) to trimethoprim-sulfamethoxazole, 3.3% (1828/55958) to temocillin, 1.4%R (639/45882) to nitrofurantoin and 1.8%R (800/44217) to oral fosfomycin. For these, some decreasing trends were observed over the last couple of years, including resistance against trimethoprim-sulfamethoxazole and temocillin (see ESC.EVO.1.2.3 above).

Urine isolates from non-hospital laboratories: Resistance levels in this group were mostly similar or only slightly lower to those of hospital laboratories, see figures ESC.4.3.1 (a) and (b) below. Exception to this was the higher observed resistance to amoxicillin-clavulanic acid (systemic breakpoints, 32.8%R versus 28.7%R in hospital laboratories). Decreasing resistance trends were observed for many of these, see figure ESC.EVO.3.2.1 below,

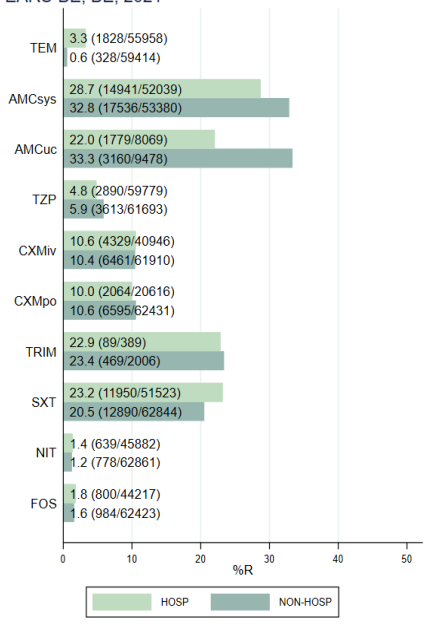
most notable resistance against amoxicillin-clavulanic acid (39.8%R in 2018 vs 32.8% in 2021), cefuroxime (16% in 2018 vs 10.4% in 2021), and fluoroquinolones (16.7% in 2018 vs 13.1% in 2021).

Figure ESC.4.3.1 *Escherichia coli*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2021



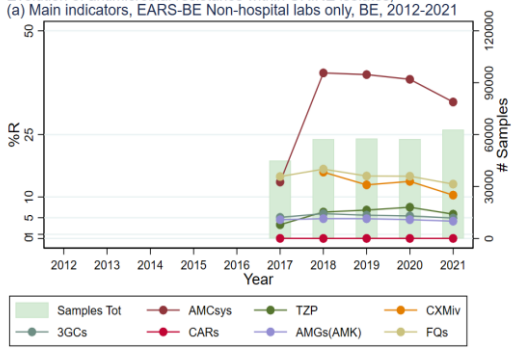
AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure ESC.4.3.2 *Escherichia coli*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs (b), EARS-BE, BE, 2021



TEM = Temocillin, infections orig. from the urinary tract , AMCsys = Amoxicillin-clavulanic acid, systemic infection , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous , CXMpo = Cefuroxim oral, uncomplicated UTI , TRIM = Trimethoprim, uncomplicated UTI , SXT = Trimethoprim-sulfamethoxazole , NIT = Nitrofurantoin, uncomplicated UTI , FOS = Fosfomycin

Figure ESC.EVO.3.2.1 *Escherichia coli*, Evolution of antimicrobial resistance within URINE isolates, (a) Main indicators, EARS-BE Non-hospital labs only, BE, 2012-2021



AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , AMCsys = Amoxicillin-clavulanic acid, systemic infection , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous

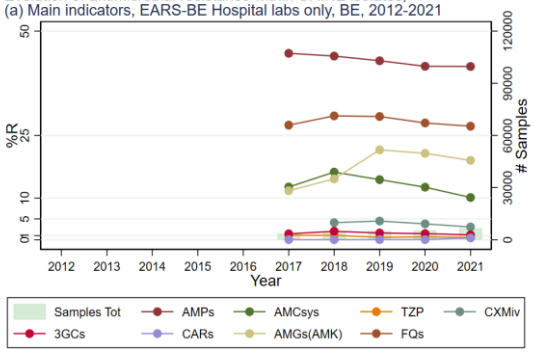
RESULTS FOR *P. MIRABILIS*

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**.

Urine isolates from hospital labs: In 2021, we observed 41.5%R (2500/6020) to aminopenicillins, 27.2%R (1644/6043) to fluoroquinolones, 22.6%R (1233/5465) to aminoglycosides, 10.1%R (564/5566) to amoxicillin-clavulanic acid, 3.1%R (109/3555) to cefuroxime, 1.2%R (77/6555) to 3GC, very low resistance (0.6%R) to piperacillin-tazobactam (0.6%R) and to carbapenems (0.4%R). Over the 4 observed years of follow-up, an increase was observed in resistance to aminoglycosides (16.7% in 2017), see also figure PRT.EVO.1.2.1 below.

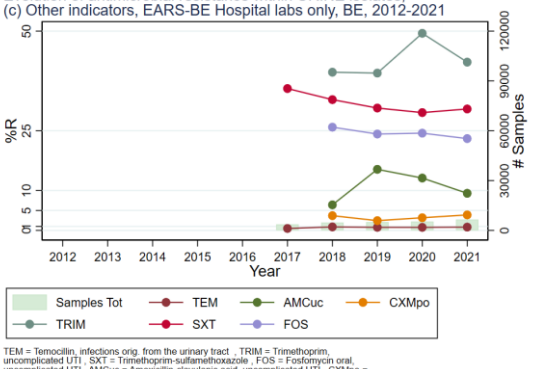
For other antimicrobials for treatment of UTI, resistance was 30.5%R (1681/5517) to trimethoprim-sulfamethoxazole, 23%R (833/3616) to oral fosfomycin, and very low resistance (0.8%R) to temocillin. Of these, a steady decrease was observed for resistance to trimethoprim-sulfamethoxazole and to fosfomycin, see also figure PRT.EVO.1.2.3 below

Figure PRT.EVO.1.2.1 *Proteus mirabilis*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Hospital labs only, BE, 2012-2021



AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , AMCsys = Amoxicillin-clavulanic acid, systemic infection , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous

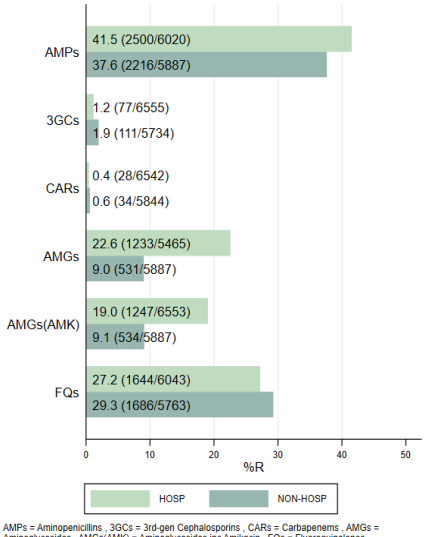
Figure PRT.EVO.1.2.3 *Proteus mirabilis*,
Evolution of antimicrobial resistance within URINE isolates,
(c) Other indicators, EARS-BE Hospital labs only, BE, 2012-2021



TEM = Temocillin, infections orig. from the urinary tract , TRIM = Trimethoprim, uncomplicated UTI , SXT = Trimethoprim-sulfamethoxazole , FOS = Fosfomycin oral, uncomplicated UTI , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , CXMpo = Cefuroxim oral, uncomplicated UTI

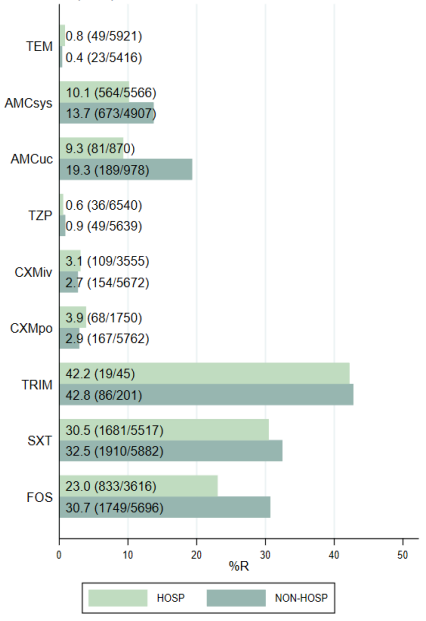
Urine isolates from non-hospital labs: Overall, resistance levels were similar (within 10% relative difference) between isolates from hospital and non-hospital laboratories, exceptions were the much lower resistance observed against aminoglycosides (9%R) and the higher resistance against amoxicillin-clavulanic acid (13.7%R), and fosfomycin (30.7%R) in isolates of non-hospital laboratories, see figures PRT.4.3.1 and PRT.4.3.2 below. Decreasing trends were observed for fluoroquinolones (34.4%R in 2018 vs 29.2%R in 2021) and amoxicillin-clavulanic acid (39.8%R vs 32.8%R in 2021), see figure PRT.EVO.3.2.1 below. Of note is the emerging resistance against carbapenems observed in the last 4 years, from no resistance in 2018 to 0.6%R in 2021, a trend which is also observed in *P. mirabilis* urine isolates from hospital labs but to a lesser extent (0.4%R in 2021).

Figure PRT.4.3.1 *Proteus mirabilis*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs,
EARS-BE, BE, 2021

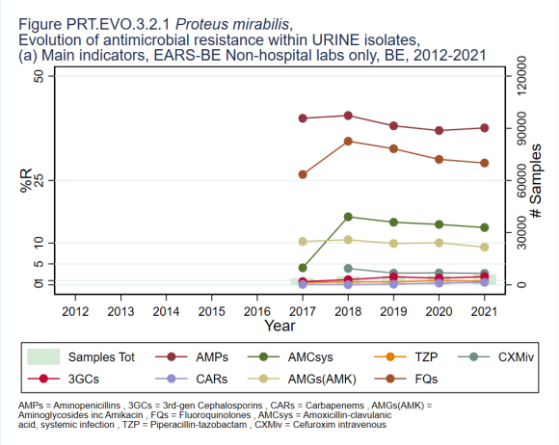


AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure PRT.4.3.2 *Proteus mirabilis*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs (b),
EARS-BE, BE, 2021



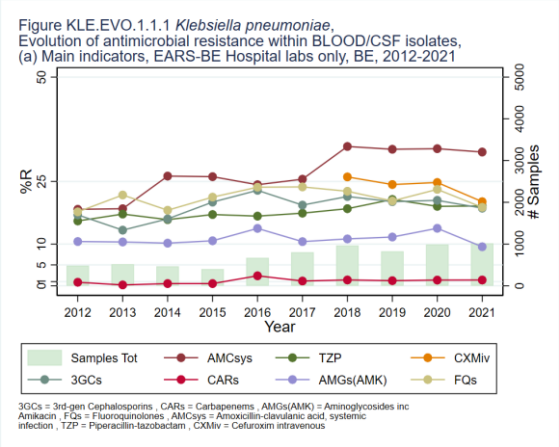
TEM = Temocillin, infections orig. from the urinary tract , AMCsys = Amoxicillin-clavulanic acid, systemic infection , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous , CXMpo = Cefuroxim oral, uncomplicated UTI , TRIM = Trimethoprim, uncomplicated UTI , SXT = Trimethoprim-sulfamethoxazole , FOS = Fosfomycin oral, uncomplicated UTI

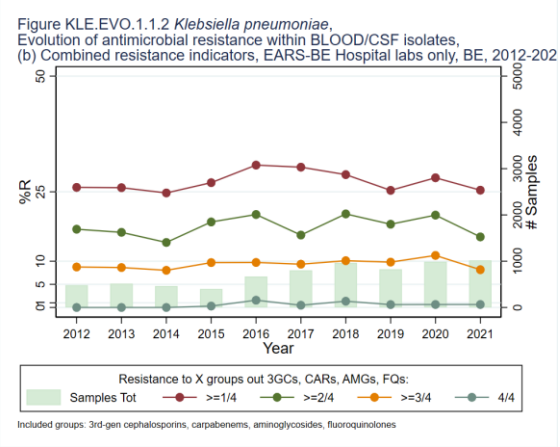


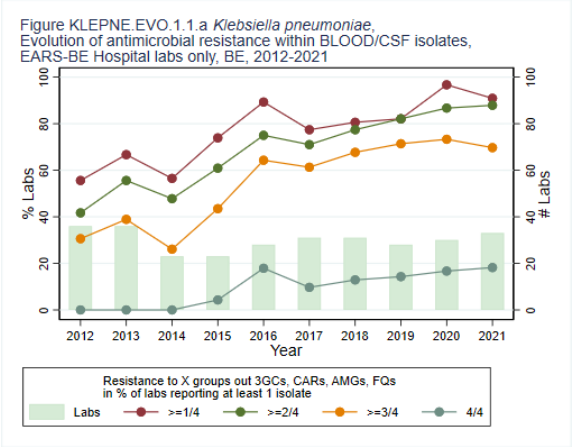
RESULTS FOR *K. PNEUMONIAE*

Blood/CSF isolates: In 2021, we observed 32%R (324/1011) resistance to amoxicillin-clavulanic acid, 20.1%R (160/794) to cefuroxime, 19.1%R (194/1014) to piperacillin-tazobactam, 18.8%R (191/1016) to fluoroquinolones, 18.6%R (189/1016) to 3GC, 9.4%R (95/1016) to aminoglycosides and 1.4%R (14/1016) to carbapenems. Except for a decreasing trend of resistance to cefuroxime (26.1%R in 2018), no clear trends could be observed for these antimicrobials, although many (including 3GC, aminoglycosides and fluoroquinolones) showed the lowest resistance of the last 4 years, see also figure KLE.EVO.1.1.1 below. Furthermore, resistance to carbapenems remained stable at just over 1%R.

Indicators of multi-resistance in *K. pneumoniae* blood/CSF isolates (to one or more of main antimicrobials 3GC, carbapenems, aminoglycosides, fluoroquinolones) within *K. pneumoniae* blood/CSF isolates did not see much change during last years (see figure KLE.EVO.1.1.2 below), but increasing trends were observed when multi-resistance is expressed as the % of laboratories reporting at least one multi-resistant isolate, see figure KLE.EVO.1.1.a below. For example, up to 2014, no labs reported Blood/CSF isolates resistant to all four followed antimicrobials, but this has since then increased to almost 20% of participating laboratories (5 out of 30 in 2020 and 6 out of 33 in 2021).

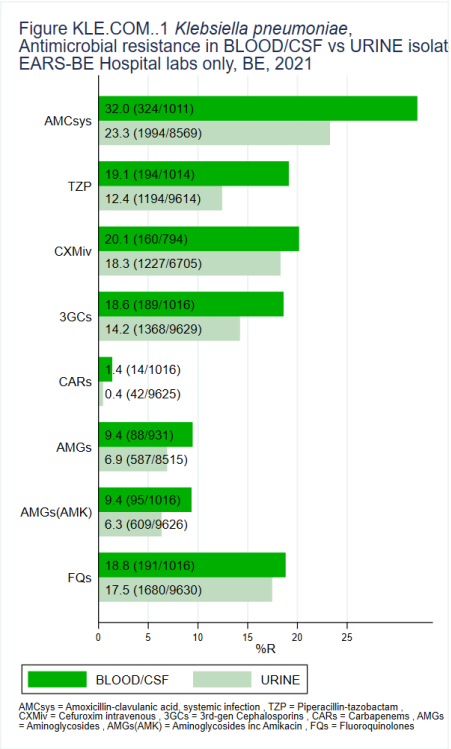


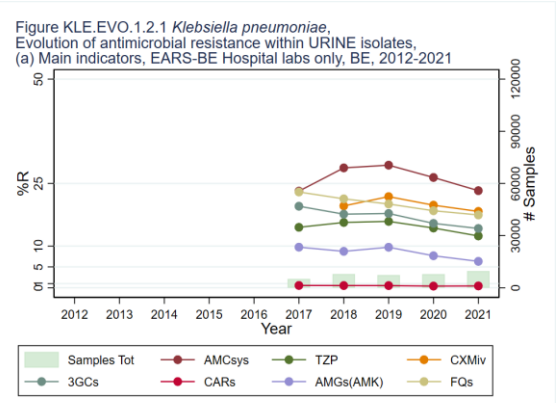


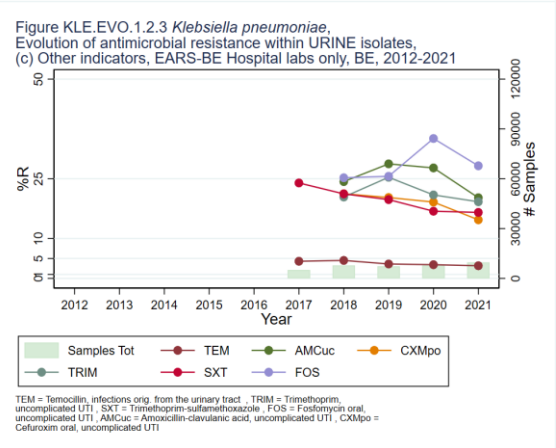


Urine isolates from hospital laboratories: Levels of resistance of these isolates to **main resistance indicators** were generally lower than those observed in blood/CSF isolates, see figure KLE.COM.1 below. Decreasing 4-year trends were observed for many followed antimicrobials (see figure KLE.EVO.1.2.1 below), most notable for resistance against amoxicillin-clavulanic acid (28.7%R in 2018 vs 23.3%R in 2021), 3GC (17.6%R in 2018 vs 14.2%R in 2021) and fluoroquinolones (21.3%R in 2018 vs 17.5%R in 2021), as well as for the indicators of combined resistance in the statistical report[3].

Decreasing trends were also observed for resistance against **other antimicrobials** used for treatment of UTI, including trimethoprim-sulfamethoxazole, see figure KLE.EVO.1.2.3 below.

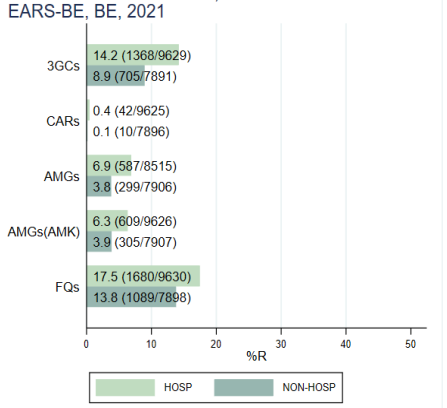






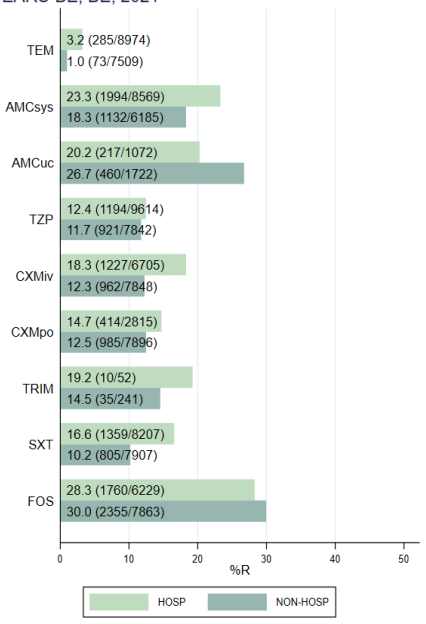
Urine isolates from non-hospital laboratories: Substantially lower levels of resistance were observed in this group, ie about 50-30% less of levels of resistance observed as compared to urine isolates from hospital laboratories, see figures KLE.4.3.1 and KLE.4.3.2 below. For main antimicrobials, similar decreasing trends could be observed as for *K. pneumoniae* urine isolates from hospital laboratories, see figure KLE.EVO.3.2.1 below.

Figure KLE.4.3.1 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2021



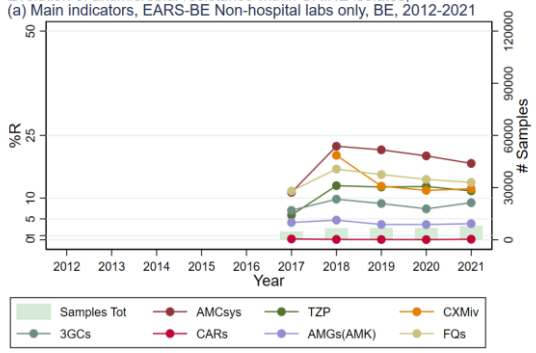
3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure KLE.4.3.2 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs (b), EARS-BE, BE, 2021



TEM = Temocillin, infections orig. from the urinary tract , AMCsys = Amoxicillin-clavulanic acid, systemic infection , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous , CXMpo = Cefuroxim oral, uncomplicated UTI , TRIM = Trimethoprim, uncomplicated UTI , SXT = Trimethoprim-sulfamethoxazole , FOS = Fosfomycin oral, uncomplicated UTI

Figure KLE.EVO.3.2.1 *Klebsiella pneumoniae*, Evolution of antimicrobial resistance within URINE isolates, (a) Main indicators, EARS-BE Non-hospital labs only, BE, 2012-2021



3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , AMCsys = Amoxicillin-clavulanic acid, systemic infection , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous

RESULTS FOR *P. AERUGINOSA*

Blood/CSF isolates: We observed 11.1%R (59/534) to piperacillin-tazobactam, 8.6%R (45/520) to ceftazidime, 10.8%R (58/535) to carbapenems, 7.5%R (40/534) to aminoglycosides, and 14.9%R (80/535) to fluoroquinolones. Trends for the last 4-5 years were more or less stable for these antimicrobials, although it remains difficult to detect meaningful trends due to high year-to-year volatility in resistance rates, see figure PSE.EVO.1.1.1 below. Moreover, trends in multidrug-resistant *P. aeruginosa* from blood/CSF isolates seem to be slowly increasing, for example resistance to at least 3 out of the 5 antimicrobials above increased from 5.5%R

in 2018 to 7.4%R in 2021, see also figure PSE.EVO.0.1.2 below. These increasing trends become more visible when the analysis is restricted to *P. aeruginosa* blood/CSF isolates from hospitalized patients (reported by 32 out of 33 hospital laboratories submitting results), and this both for followed main antimicrobials (figure PSE.EVO.5.1.1 below) and multidrug resistance indicators (figure PSE.EVO.5.1.2 below), such that 2021 resistance rates are the highest observed since 2017 for this pathogen in this subgroup. For example, %R to carbapenems increased from 6.9% in 2018 to 11.8% in 2021, and resistance to 3 out of 5 followed antimicrobials increased from 4.8% in 2018 to 8.9% in 2021.

Figure PSE.EVO.0.1.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2012-2021

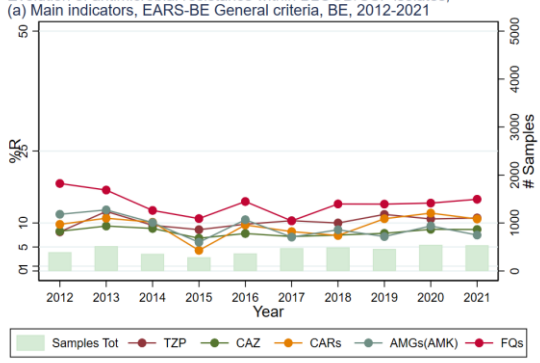


Figure PSE.EVO.0.1.2 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(b) Combined resistance indicators, EARS-BE General criteria, BE, 2012-2021

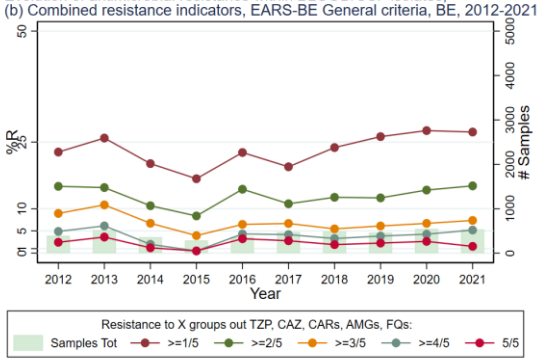


Figure PSE.EVO.5.1.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE PatientType='INPAT' only, BE, 2012-2021

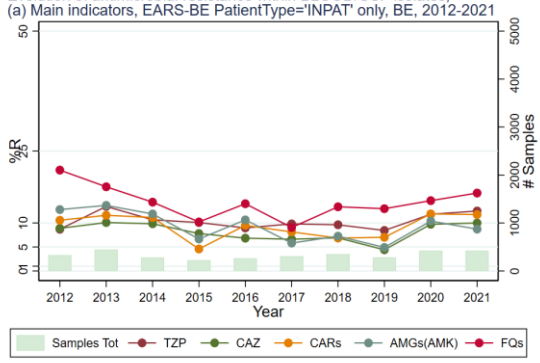
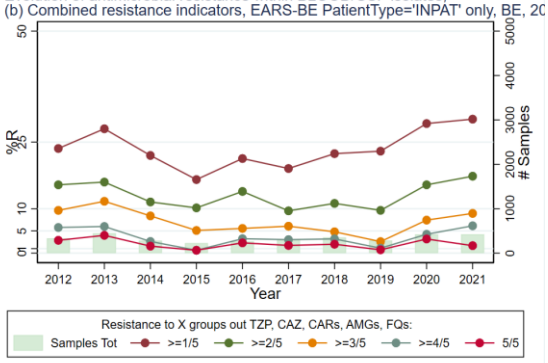
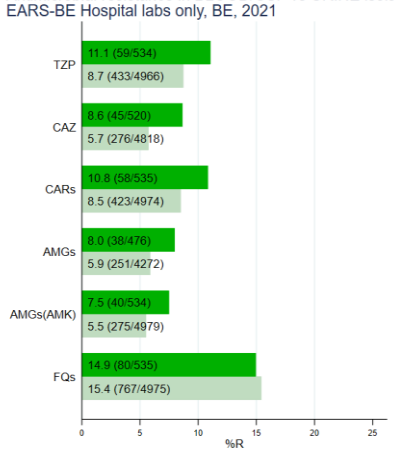


Figure PSE.EVO.5.1.2 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(b) Combined resistance indicators, EARS-BE PatientType='INPAT' only, BE, 20



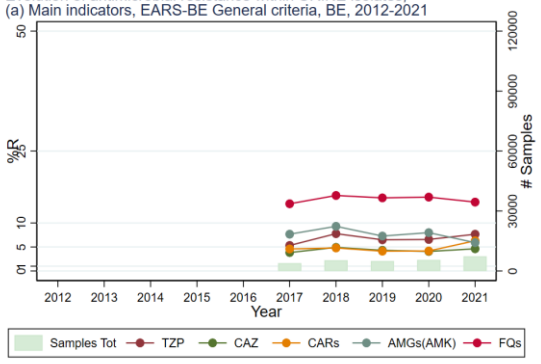
Urine isolates from hospital laboratories: When comparing antimicrobial resistance levels between urine and blood/CSF isolates in this group, lower levels of resistance were observed in urine isolates for piperacillin-tazobactam (8.7%R), ceftazidime (5.7%R), carbapenems (8.5%R), and aminoglycosides (5.9%R), while similar levels were observed for fluoroquinolones (15.4%R), see figure PSE.COM.1. As compared to blood/CSF isolates, trends in resistance were more clearly distinguishable within *P. aeruginosa* urine isolates, but remaining generally stable, including trends in multidrug resistance (see figures PSE.EVO.0.2.1/2 below). However, when restricting the analysis to hospitalized patients, we observed similar increases in resistance to carbapenems and multidrug resistance as observed for blood/CSF *P. aeruginosa* isolates, see the statistical report (Main indicators worksheet) for details.

Figure PSE.COM..1 *Pseudomonas aeruginosa*,
Antimicrobial resistance in BLOOD/CSF vs URINE isolat
EARS-BE Hospital labs only, BE, 2021



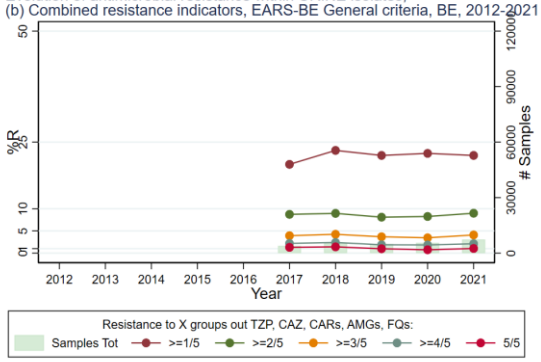
TZP = Piperacillin-tazobactam , CAZ = Ceftazidime , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure PSE.EVO.0.2.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2012-2021



CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , TZP = Piperacillin-tazobactam , CAZ = Ceftazidime

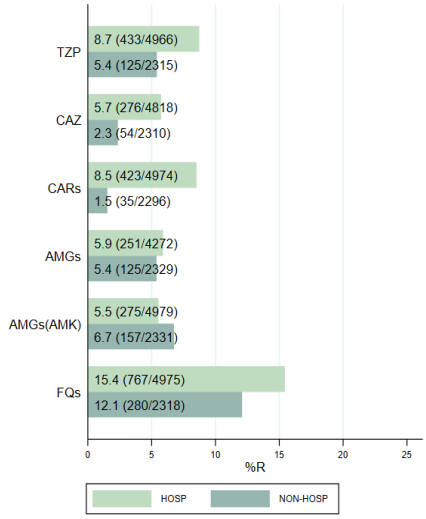
Figure PSE.EVO.0.2.2 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within URINE isolates,
(b) Combined resistance indicators, EARS-BE General criteria, BE, 2012-2021



Included groups: piperacillin-tazobactam, ceftazidim, carpabenems, aminoglycosides, fluoroquinolones

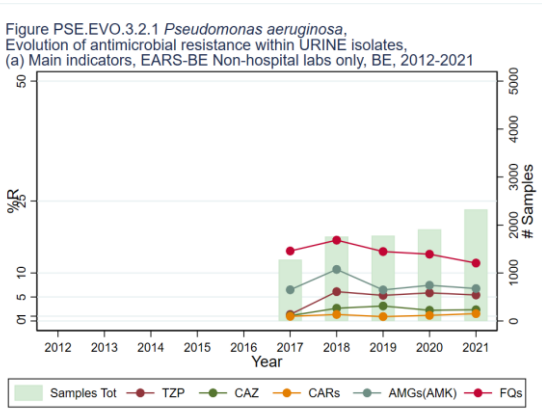
Urine isolates from non-hospital laboratories: Levels of antimicrobial resistance in urine isolates were generally lower in this group as compared to those of hospital laboratories, see figure PSE.4.3.1 below. Trends in resistance are relatively stable except for a decrease in resistance against fluoroquinolones, from 16.9% in 2018 to 12.1% in 2021, see figure PSE.EVO.3.2.1 below.

Figure PSE.4.3.1 *Pseudomonas aeruginosa*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs,
EARS-BE, BE, 2021



TZP = Piperacillin-tazobactam , CAZ = Ceftazidime , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure PSE.EVO.3.2.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Non-hospital labs only, BE, 2012-2021



CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , TZP = Piperacillin-tazobactam , CAZ = Ceftazidime

RESULTS FOR *ACINETOBACTER* SPECIES

Blood/CSF isolates: For 2021, results were obtained from 30 labs on 198 isolates. For those, we observed 1%R (2/196) to carbapenems, 4.1%R (8/197) to aminoglycosides, and 10.9%R (20/183) to fluoroquinolones. As compared to previous years, these levels remained at a similar level, see figure ACISPP.EVO.0.1.1 below.

For *A. baumannii* isolates (results from 17 labs on 32 isolates available), we observed 6.3%R (2/32) to carbapenems, 9.4%R (3/32) to aminoglycosides, and 15.6%R (5/32) to fluoroquinolones. Of these, resistance is increasing since 2019, however detection of meaningful trends is difficult given such small number of isolates, see figure ACIBAU.EVO.0.1.1.

Figure ACISPP.EVO.0.1.1 *Acinetobacter* spp,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2012-2021

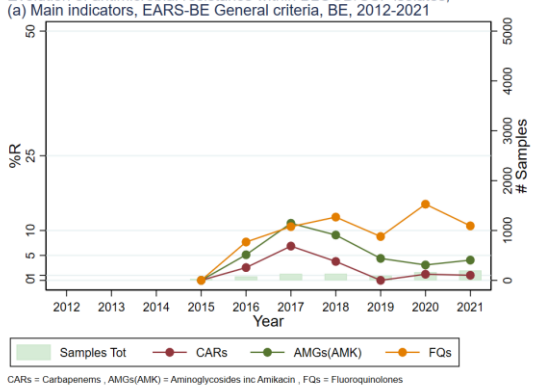
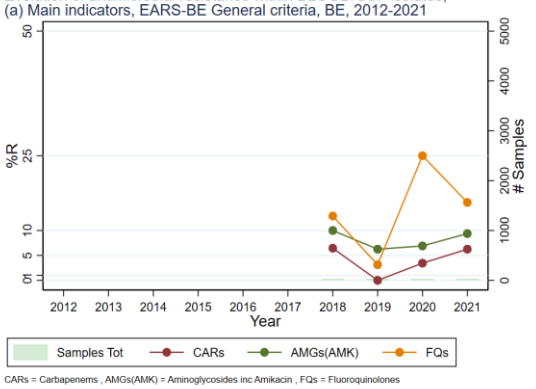


Figure ACIBAU.EVO.0.1.1 *Acinetobacter baumannii*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2012-2021



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 (1) only a subset of laboratories submitting test results, (2) selective testing for this antibiotic (according to sample type, pathogen and other factors such as multidrug resistance vs susceptible AST phenotype), and (3) likely not all laboratories relying on broth microdilution for testing colistin resistance, ie the method recommended by EUCAST/CLSI[8]. The resistance rates reported here therefore come with the above limitations, and need confirmation from national microbiological surveillance[9].

Restricting the analysis to hospital laboratories, colistin testing rates on blood/CSF isolates varied from 58.3% in *E. coli* (of 19 labs reporting), 63.6% in *K. pneumoniae* (of 18 labs reporting), to 70.1% in *P. aeruginosa* (of 16 labs reporting). In urine isolates, these rates were 58.1% in *E. coli* (19 labs reporting), 57.6% in *K. pneumoniae* (19 labs reporting), and 52.8% in *P. aeruginosa* (20 labs reporting). In *E. coli*, resistance to colistin in 2021 was 1.3% (20/1594) in blood/CSF isolates and 1% (173/18003) in urine isolates. In *K. pneumoniae* isolates, resistance was 2% (6/304) in blood/CSF isolates and 1.9% (53/2781) in urine isolates. In *P. aeruginosa*, resistance was 0.6% (1/169) in blood/CSF and 4.1% (68/1656) in urine isolates. But again, due to selective testing, these rates are most likely biased upwards.

CONCLUSIONS AND RECOMMENDATIONS

As part of EARS-BE 2021 data collection, 33 hospital laboratories submitted results to Sciensano on isolates from blood or cerebrospinal fluid (CSF) samples taken in 2021, while 31 hospital labs submitted results on urine isolates taken in 2021. Furthermore, 10 non-hospital laboratories submitted results on urine isolates. Participation to EARSBE surveillance clearly increased as compared to previous years, now being at the highest level since 2014.

In *S. aureus* isolates from blood or cerebrospinal fluid (CSF) samples taken in 2021, resistance to methicillin (MRSA, 4.6%R) and to fluoroquinolones (7.1%R) continued their long-term decreasing trend, both attaining the lowest level of resistance since the start of EARSBE surveillance in 2000. In Enterococci blood/CSF isolates, no vancomycin resistance was observed in *E. faecalis* isolates, while this reached 2.8% in *E. faecium* isolates. Resistance to vancomycin in *E. faecium* urine isolates remains low (1%R).

In *S. pneumoniae* blood/CSF isolates, non-susceptibility to penicillins further increased to 18%, while resistance to penicillins increased to 4.3%. While these are the highest levels of the past years, these are considered to be due to recent changes in use of breakpoints and of method for susceptibility testing rather than an underlying change in the epidemiology of penicillins-non-susceptible *S. pneumoniae*.

For *E. coli* blood/CSF and urine isolates, steadily decreasing trends in resistance were observed for many followed antimicrobials, including of indicators for multidrug resistance. In *K. pneumoniae* blood/CSF isolates, clear trends of resistance were difficult to observe due to variable rates during the last couple of years, however in urine *K. pneumoniae* isolates from hospital labs, decreasing trends in resistance were observed for many antimicrobials. Resistance to carbapenems was (almost) not observed in *E. coli* and very low (around 1%) in *K. pneumoniae*. In *P. mirabilis* urine isolates, carbapenems resistance was very low (<1% in hospital and non-hospital laboratories), but seems to have emerged over the last couple of years. Interestingly, indicators of multi-resistance in *K. pneumoniae* blood/CSF isolates show a clearly increasing trend since 2014-15 when expressed as the % of laboratories reporting at least one (multi-resistant) isolate.

P. aeruginosa blood/CSF isolates showed resistance to almost all studied antibiotic groups (piperacillin-tazobactam, ceftazidime, carbapenems, aminoglycosides, fluoroquinolones). While it remains difficult to detect meaningful trends of resistance in blood/CSF and urine isolates in the *overall* group of patients, increasing trends of resistance against ceftazidime, carbapenems, aminoglycosides and of multidrug resistance were observed in isolates obtained from hospitalized patients. In *Acinetobacter* spp blood/CSF isolates (including those of *A. baumannii*), with 2022 results available on 197 isolates reported by 30 laboratories, resistance levels remained stable, with resistance to carbapenems remaining low.

In frequently reported urinary pathogens such as *E. coli, P. mirabilis,* and *K. pneumonia*e reported by non-hospital laboratories, decreasing trends of resistance against several antimicrobials were observed, including amoxicillin-clavulanic acid and fluoroquinolones.

The above findings demonstrate the complex and multi-dimensional nature of national antimicrobial resistance surveillance, with findings being different between patient types, pathogens and antimicrobial markers. While decreasing trends are observed for principal markers of antimicrobial resistance of *S. aureus*, *E. coli* and *K. pneumoniae*, we also observe increasing resistance in *P. aeruginosa*, as well emerging resistance in *P. mirabilis* and *K. pneumoniae*. Analysis of these trends, including their association with antimicrobial use, affected patient types, and clinical practice should be the focus of further analysis.

Participation to EARSBE increased over the last couple of years, however is still lacking within certain regions and laboratory types. Also, the burden of registration remains high, in turn leading to delays in data collection and validation efforts, and to delays in reporting and interpretation of national results. Current initiatives for development of national EARSBE surveillance focus on harmonizing data collection with other surveillances of AMR and Healthcare-associated infections, and this to avoid parallel data flows, to decrease registration burden, and to increase participation to EARSBE surveillance. Future plans revolve around automating data collection on AMR with the objective to decrease burden of (manual) registration, avoid manual errors and differences in standardization of electronic AST results between laboratories, and consequently to increase the frequency of data collection and reporting of national results on AMR.

Since 2017, EARSBE includes collection of AST results on uropathogens, including those of laboratories not associated to an acute care hospital. Under the hypothesis of selective testing for UTI within the group of non-acute care patients, EARSBE results on uropathogens might only have limited clinical relevance. A new NAP-AMR[12]-funded project will start in 2023 focusing on *clinical surveillance* of AMR within primary care, which will give the opportunity to validate EARSBE results on urine isolates.

In 2022, another NAP-AMR-funded project started on the expansion of national genomic surveillance of Multidrug-resistant organisms (MDRO). Over 3 years, this project will focus on establishing surveillance of genotypes of MDRO circulating in BE using techniques for whole-genome and next-generation sequencing (NGS), and on conceptualizing tools for harmonized processing and analyzing NGS data, as well as collecting associated epidemiological data. This initiative should lead to a more complete follow-up of the resistance

mechanisms of said MDRO, many of which are also followed as part of EARSBE surveillance, and as such contribute to strategies for their containment and prevention.

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