Short report

European antimicrobial resistance surveillance for Belgium (EARS-BE) 2020 – description of main findings.

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Introduction

This report describes main findings of the "EARS-BE 2020" survey, which covers annual national data collection for Belgium and 2020 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 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 2020 data on blood/CSF isolates were submitted in August 2021 to ECDC for inclusion in the Annual European report on antimicrobial resistance (to appear begin 2022) 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 EUCAST-interpreted results presented here. In turn, ECDC shares EARS-NET annual data (including those of BE collected by EARSBE) with the Global Antimicrobial surveillance system (GLASS, under coordination by the World Health Organization[3]), for inclusion in the annual WHO report on antimicrobial resistance in Europe[4],

The background and methodology of EARS-BE 2020 can be found elsewhere[2]. The results presented and discussed here are derived from the "EARS-BE 2020 statistical report"[5], which contains exhaustive EARS-BE 2020 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 (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 2020 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 almost similar.

Participation

Due to many (hospital) laboratories as well as Sciensano continuing to be overwhelmed in 2021 by the COVID-19 crisis, national collection of 2020 AST data took more efforts as compared to pre-pandemic years.

Blood/CSF isolates: Thirty-two laboratories submitted AST results on isolates from blood/CSF samples taken in 2020 (statistical report Table MAIN.1); thirty-one of these were associated to an acute care hospital. Compared to 2019, the overall number of labs reporting results of blood/CSF samples increased (with 29 hospitals labs having submitted 2019 data). Annual participation of hospital laboratories to EARSBE for blood/CSF isolates (being the default option) is stable at around 30 labs during the last 5 years, 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 2020 data, Flanders (18/31 labs = 55%) and Brussels (4/31 labs = 13%) were only slightly overrepresented, with Wallonia (9/31 labs=29%) being underrepresented by about 5% when compared to the national distribution of hospital laboratories. In terms of type of hospitals, participating laboratories from primary hospitals were underrepresented by about 5-10% as compared to the national distribution.

Figure PART.EVO.1,
Laboratory participation for BLOOD/CSF isolates, EARS-BE, 2011-2020

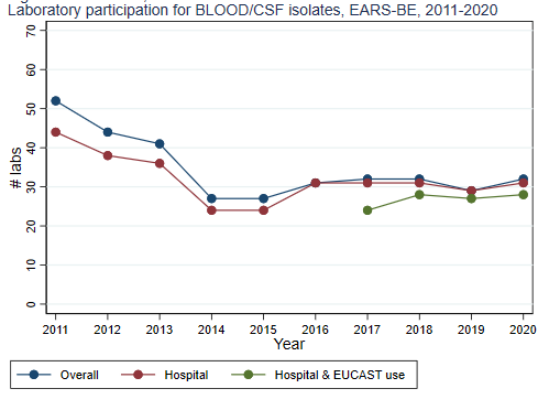
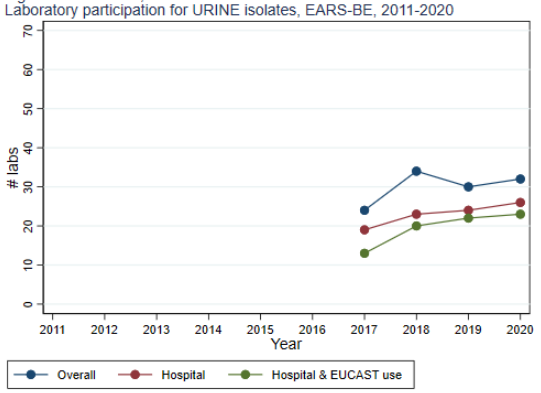


Figure PART.EVO.2,
Laboratory participation for URINE isolates, EARS-BE, 2011-2020



Urine isolates: Thirty-two laboratories submitted results for urine samples taken in 2020, 6 of these were not associated to an acute care hospital. Distribution of the 26 participating hospital laboratories over the three regions and hospital types was similar to the distribution for blood/CSF samples. However, the 6 non-hospital laboratories submitting results on urine samples were all situated in Flanders. Because of this, the results on urine isolates from the non-hospital setting for 2020 presented in this and the statistical report cannot be viewed as representing the national situation. Reporting of results of urine isolates by hospital laboratories is steadily increasing since its introduction in 2017, while this remains stable for non-hospital laboratories, see figure PART.EVO.2 above.

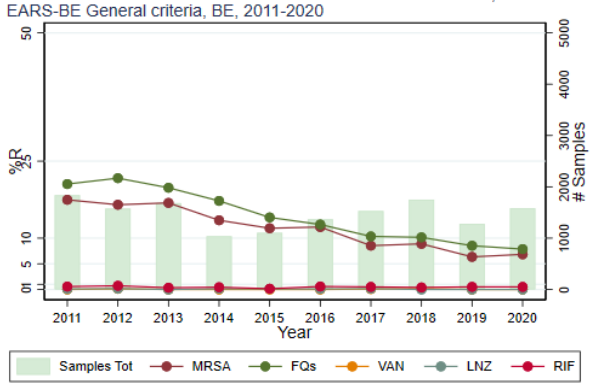
Use of EUCAST guidelines: For blood/CSF samples taken in 2020, 28 out 31 (92%) hospital labs and all 6 non-hospital labs reported the use of EUCAST guidelines for interpretation of ASTs, this represents a stabilization as compared to 2019. Four laboratories reported the use of EUCAST V10 guidelines in 2020, implementing the new definition of *intermediate resistance* categorization as 'susceptible, increased exposure'[6].

The statistical report still shows 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 *Staphylococcus aureus*

Blood/CSF isolates: in 2020, 6.8% (108/1580) of *S. aureus* isolates were resistant to methicillin (MRSA), while 7.9% (118/1499) of isolates were resistant to fluoroquinolones. While this represents a stabilization for MRSA as compared to 2019, for both indicators these results were the lowest since follow-up started in 2000, see also figure STA.EVO.0.1.1. No resistance was observed for vancomycin and linezolid, and very low resistance was observed for rifampicin.

Figure STA.EVO.0.1.1 *Staphylococcus aureus*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
EARS-BE General criteria, BE, 2011-2020



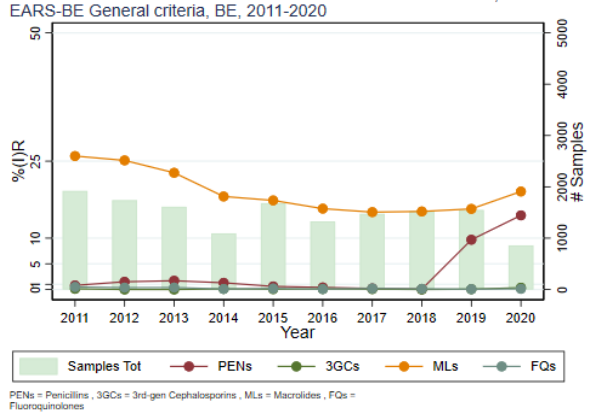
Results for *Streptococcus pneumoniae*

Results obtained from the national surveillance on invasive pneumococcal infections 2020

Results for AMR in *S. pneumoniae* isolates are based on 2020 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 (see the dedicated annual report[7] for complete results of this national surveillance). The data included AST results on blood/CSF isolates submitted by 89 labs, with susceptibility results interpreted according to EUCAST guidelines. The criteria for non-susceptibility (%IR) to penicillins were as follows: (1) for CSF isolates: Minimal Inhibitory Concentration (MIC)>0.06mg/L; (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 resistance in 2019 as compared to 2018. The NRC changed its method for susceptibility testing Mid-2020 from E-test to broth microdilution in response to EUCAST recommendations. 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 2020, non-wild type resistance to penicillins was 14.4% (124/859), a further increase as compared to 2019, partially attributed to the change in AST method in 2020 and the substantial decrease of collected isolates relative to the previous year (thought to be due to lower circulation of strains during COVID19-installed containment measures). Resistance levels to 3rd-generation cephalosporins (3GC) and fluoroquinolones were very low, ie 0.3% (3/859), and 0.1% (1/859) respectively, while resistance to macrolides was 19.1% (164/859), resistance among all three classes remaining stable compared to 2019.

Figure STRN.EVO.0.1.1 *Streptococcus pneumoniae* (NRC),
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
EARS-BE General criteria, BE, 2011-2020



Results obtained from the EARS-BE 2020 data collection

The results of the EARS-BE 2019 data collection of *S. pneumoniae* blood/CSF isolates (31 labs submitting results) are shown in Statistical report Table MAIN.1. For EUCAST-interpreted ASTs, non-wild-type resistance to penicillins was 13.7% (41/300), macrolide resistance was 15% (55/367), resistance to fluoroquinolones was 1.4% (5/350) and resistance to 3GC was 0.7% (2/287).

Results for Enterococci

Blood/CSF isolates: *E. faecalis* isolates showed no resistance to vancomycin (out of 654 isolates) and very low resistance to aminopenicillins (0.4%, 3/698), teicoplanin (0.9%, 5/582), and linezolid (0.4%, 2/553). It should be noted that absence of vancomycin resistance in combination with observed resistance to teicoplanin contradicts the resistance mechanisms of VanA and VanB- *E. faecalis* and/or *faecium* genotypes, therefore the reported %R against teicoplanin might be due to mis-identification of species and/or resistance pattern.

In *E. faecium* isolates, we observed 86.5%R (460/532) to aminopenicillins, 3.6% (19/533) to vancomycin, 2.8%R (12/436) to teicoplanin, and 0.2%R (1/430) to linezolid. Because teicoplanin and linezolid susceptibility results were not submitted for all *E. faecium* and *E. faecalis* isolates, the 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 VRE, see figures ENCFAE.EVO.1.1.b and ENCFAE.EVO.1.1.b below.

Figure ENCFAE.EVO.1.1.b *Enterococcus faecalis*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
EARS-BE Hospital labs only, BE, 2011-2020

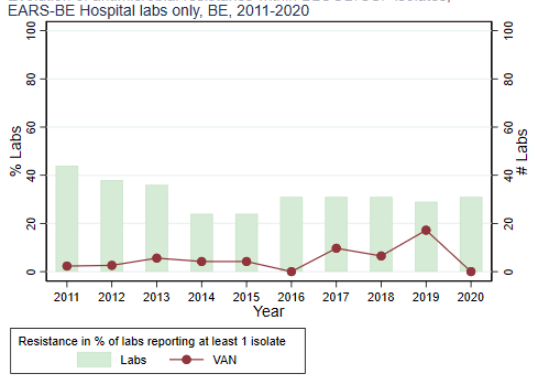
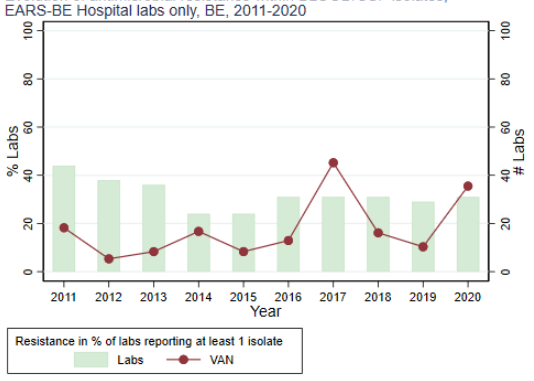


Figure ENCFAI.EVO.1.1.b *Enterococcus faecium*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
EARS-BE Hospital labs only, BE, 2011-2020



Urine isolates: in 2020, 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. Also for 2020, no difference was observed with resistance in blood/CSF isolates, see figure ENCFAI.COM.1 below.

In *E. faecium* urine isolates from hospital laboratories, resistance to vancomycin (1.8%, 33/1825), teicoplanin (1.8%, 26/1471) and linezolid (0.4%, 6/1418) were roughly similar to those of blood/CSF samples, see figure ENCFAI.COM.1 below. After 2019 being the first year since 2017 that vancomycin-resistant and teicoplanin-resistant *E. faecium* urine isolates were reported by non-hospital laboratories, this remained the case in 2020. However, the number of *E. faecium* urine isolates is very low, therefore %R are to be interpreted with caution.

Figure ENCFAE.COM..1 *Enterococcus faecalis*, Antimicrobial resistance in BLOOD/CSF vs URINE isolate EARS-BE Hospital labs only, BE, 2020

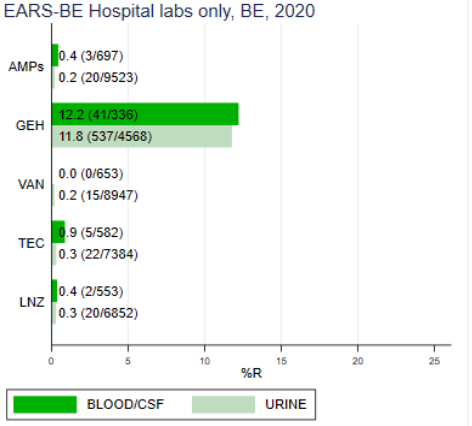


Figure ENCFAI.COM..1 *Enterococcus faecium*, Antimicrobial resistance in BLOOD/CSF vs URINE isolate EARS-BE Hospital labs only, BE, 2020

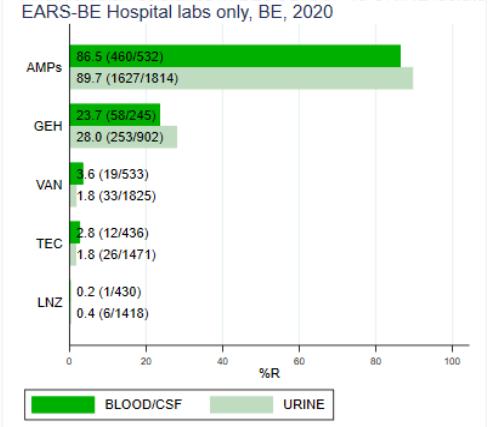


Figure ENCFAE.4.3.1 *Enterococcus faecalis*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2020

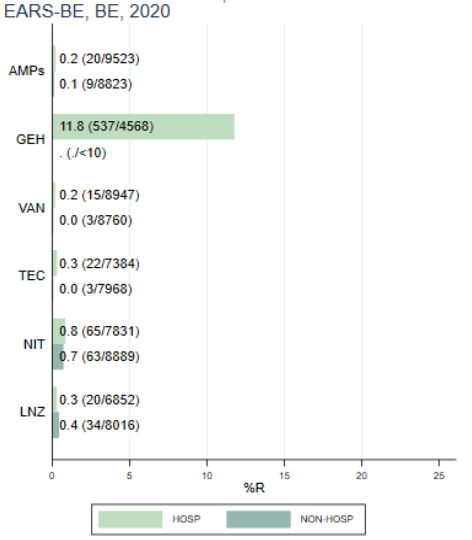
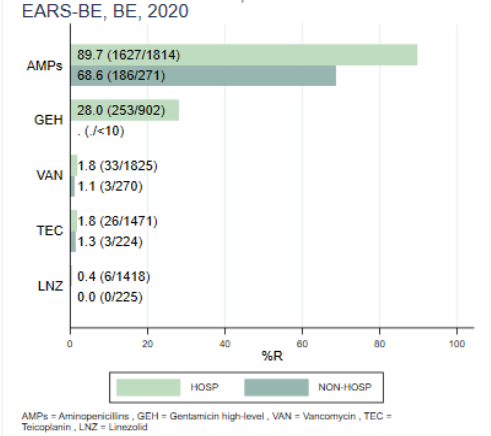


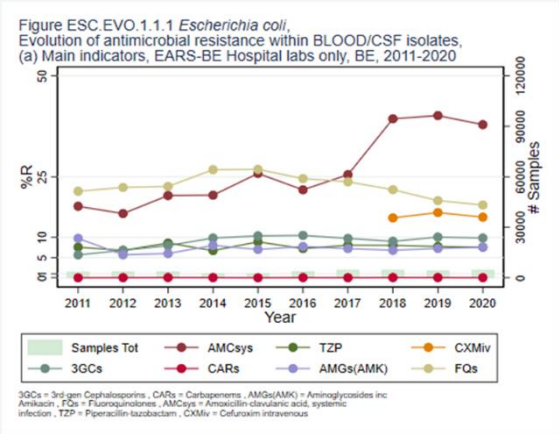
Figure ENCFAI.4.3.1 *Enterococcus faecium*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2020

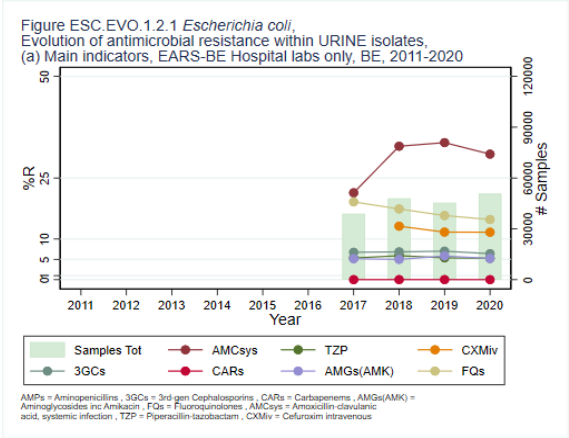


Results for *Escherichia coli*

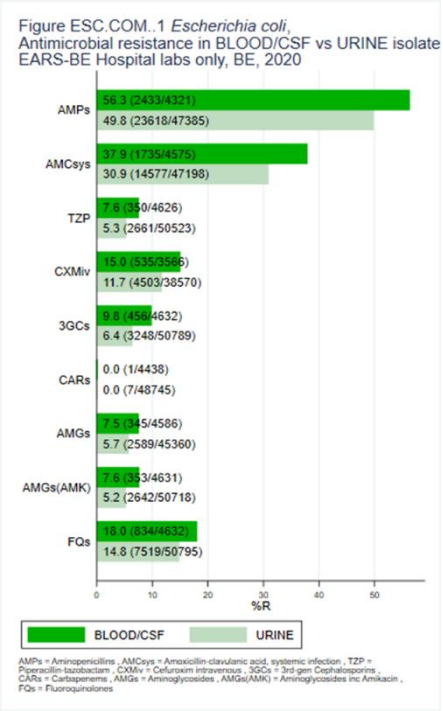
Blood/CSF isolates: For isolates obtained in 2020, we observed 37.9%R (1735/4575) to amoxicillin-clavulanic-acid, 18%R (834/4632) to fluoroquinolones, 15% (535/3566) to cefuroxime, 9.8%R (456/4632) to 3GC, 7.6%R (350/4626) to piperacillin-tazobactam, 7.6%R (353/4631) to aminoglycosides, and almost no resistance to

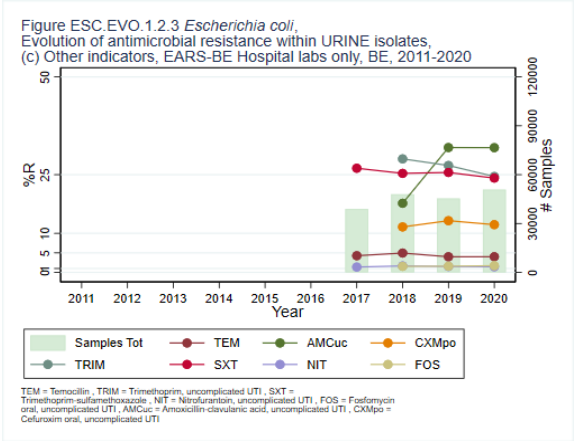
carbapenems. A steadily decreasing trend was detected for fluoroquinolones resistance (above 25%R in 2014-15), see also figure ESC.EVO.1.1.1 below, and an upwards shift in resistance to amoxicillin-clavulanic acid in 2018, which was documented in a previous EARSBE annual report[8], ie due to the introduction of a new card in Vitek systems (BioMérieux) for AMC susceptibility detection in relation to the changes of breakpoints implemented by EUCAST. Note that resistance to 3GC remained stable since 2014.





Urine isolates from hospital laboratories: Within urine isolates obtained in 2020, levels of **main indicators** for resistance were generally lower as compared to blood/CSF isolates, see figure ESC.COM.1 below. Also here, a steadily decreasing trend (over 4 years) of resistance to fluoroquinolones was observed (19.1%R in 2017, see figure ESC.EVO.1.2.1 above).



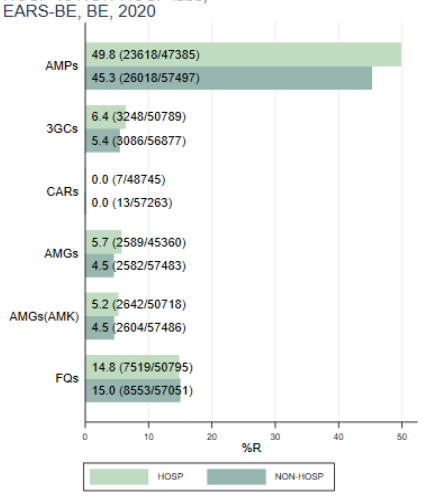


For other antimicrobials typically used for treatment of **urinary tract infection (UTI)**, we observed 24.1%R (10830/44903) to trimethoprim-sulfamethoxazole, 4%R (1902/47483) to temocillin, 1.5%R (573/39506) to nitrofurantoin and 1.7% (618/36020) to oral fosfomycin. For these, no major trends were detected since data collection of results from urine isolates started (in 2017, see ESC.EVO.1.2.3 above).

Urine isolates from non-hospital laboratories: Resistance levels in this group were mostly similar 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, 38.3%R versus 30.9%R in hospital laboratories).

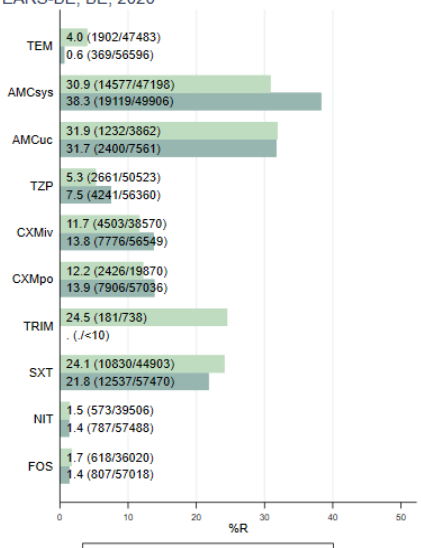
Resistance trends were generally stable (see figures ESC.EVO.3.2.1 and 3.2.3 below), except for an increase of resistance to piperacillin-tazobactam (3.8% in 2017 vs 7.5% in 2020).

Figure ESC.4.3.1 *Escherichia coli*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs,
EARS-BE, BE, 2020



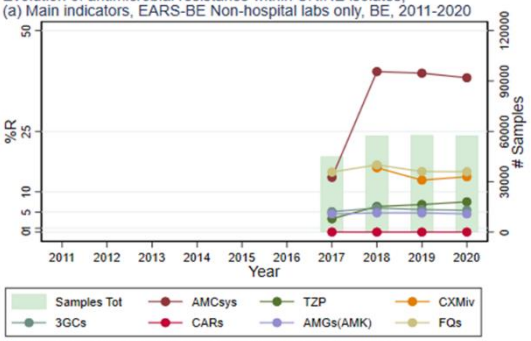
AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure ESC.4.3.2 *Escherichia coli*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs (b),
EARS-BE, BE, 2020



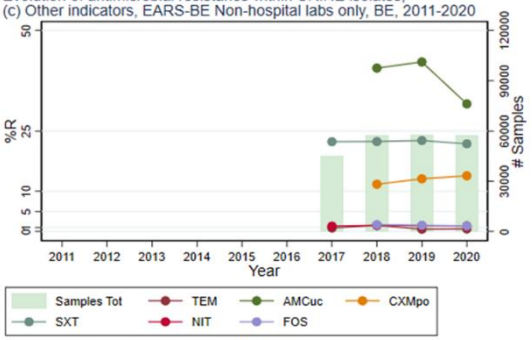
TEM = Temocillin , AMCsys = Amoxicillin-clavulanic acid, systemic infection , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous , CXMpo = Cefuroxim oral, uncomplicated UTI , TRIM = Trimethoprim, uncomplicated UTI , SXT = Trimethoprim-sulfamethoxazole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

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, 2011-2020



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 ESC.EVO.3.2.3 *Escherichia coli*,
Evolution of antimicrobial resistance within URINE isolates,
(c) Other indicators, EARS-BE Non-hospital labs only, BE, 2011-2020



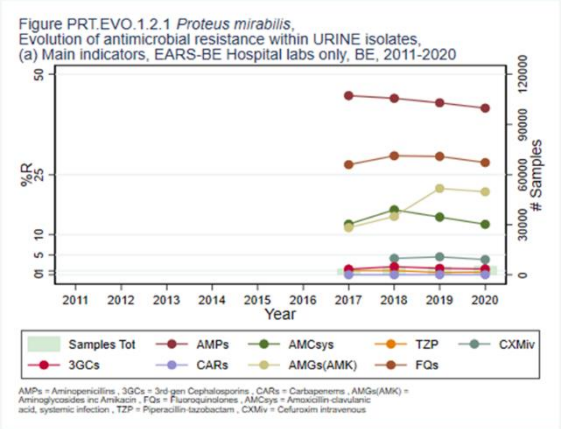
TEM = Temocillin , SXT = Trimethoprim-sulfamethoxazole , NIT = Nitrofurantoin, uncomplicated UTI , FOS = Fosfomycin oral, uncomplicated UTI , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , CXMpo = Cefuroxim oral, uncomplicated UTI

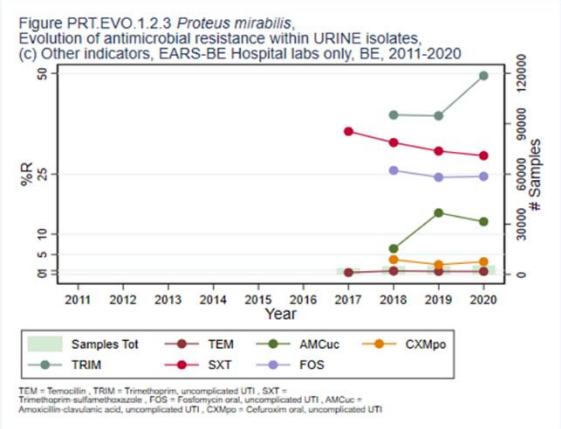
Results for *Proteus mirabilis*

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**.

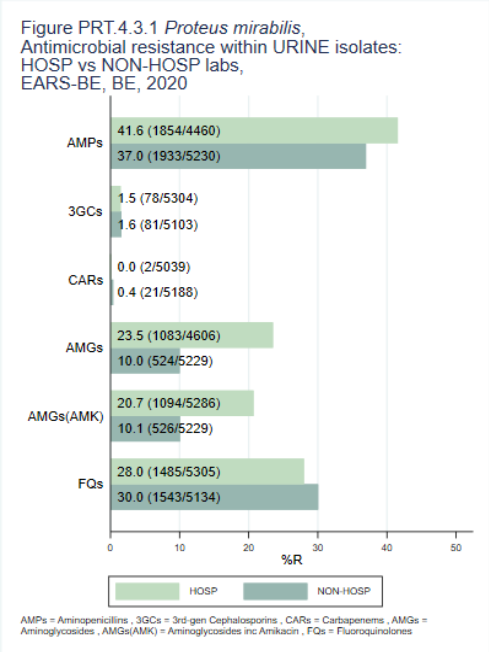
Urine isolates from hospital labs: In 2020, we observed 41.6%R (1854/4460) to aminopenicillins, 28%R (1485/5305) to fluoroquinolones, 20.7%R (1094/5286) to aminoglycosides, 12.6%R (620/4920) to amoxicillin-clavulanic acid, 3.8%R (147/3858) to cefuroxime, 1.5%R (78/5304) to 3GC, very low resistance (0.7%R) to piperacillin-tazobactam and almost no resistance to carbapenems. Over the 4 observed years of follow-up, an increase was observed in resistance to aminoglycosides (13.6% in 2017), see also figure PRT.EVO.1.2 below.

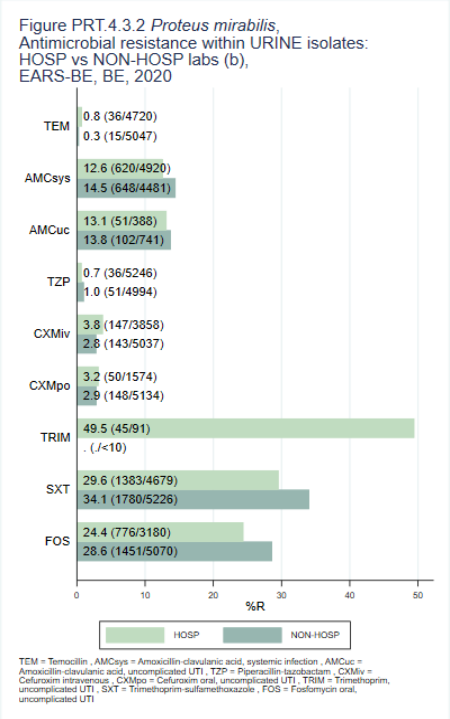
For other antimicrobials for treatment of UTI, resistance was 29.6%R (1383/4679) to trimethoprim-sulfamethoxazole, 24.4%R (776/3180) to oral fosfomycin, and very low resistance (0.8%R) to temocillin. Of these, a steady decrease was observed for resistance to trimethoprim-sulfamethoxazole (35.6%R in 2017)

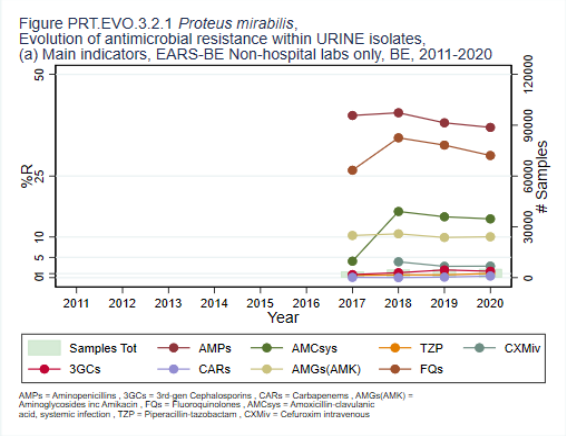


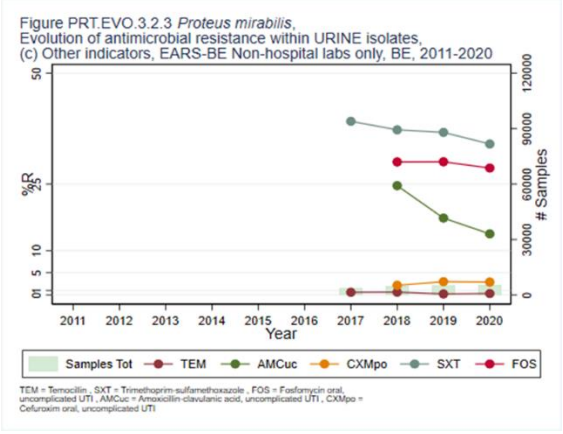


Urine isolates from non-hospital labs: Overall, resistance levels were similar (within 10% relative difference) between isolates from hospital and non-hospital laboratories, see figures PRT.4.3.1 and PRT.4.3.2 below. Exceptions were the lower resistance observed against aminoglycosides (10.1%R vs 20.7%R in hospital labs) and the higher resistance against trimethoprim-sulfamethoxazole (34.1%R vs 29.6%R in hospital labs) and fosfomycin (28.6%R vs 24.4%R in hospital labs) in isolates of non-hospital laboratories. Decreasing trends were observed for fluoroquinolones (34.4%R in 2018) and trimethoprim-sulfamethoxazole (39.2%R in 2017), see figures PRT.EVO.3.2.1 and PRT.EVO.3.2.3 below.





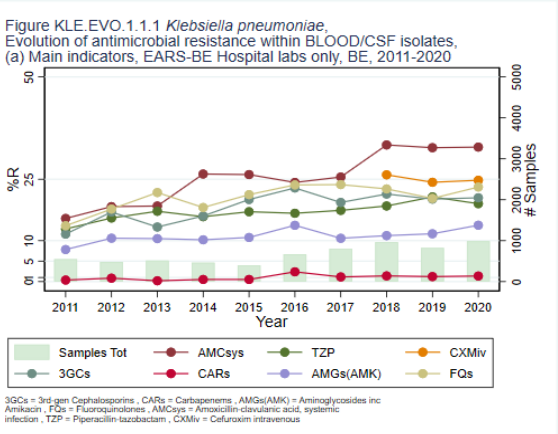


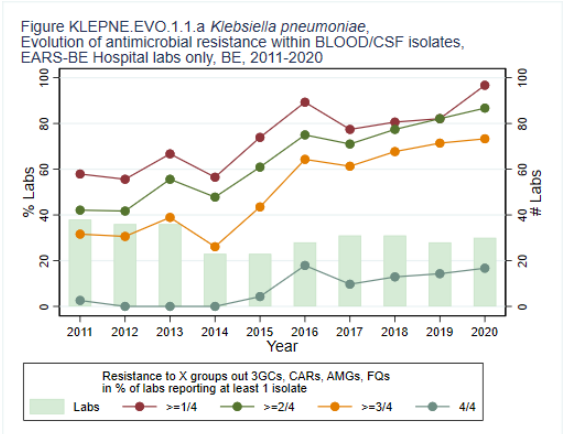


Results for *Klebsiella pneumoniae*

Blood/CSF isolates: In 2020, we observed 32.8% (320/974) resistance to amoxicillin-clavulanic acid, 24.8%R (195/788) to cefuroxime, 19%R (188/988) to piperacillin-tazobactam, 23.1%R (228/987) to fluoroquinolones, 20.5%R (202/987) to 3GC, 13.8%R (136/988) to aminoglycosides and 1.4%R (13/957) to carbapenems. Over the last 4-5 years, no clear trends were observed for followed antimicrobials except for resistance to amoxicillin-clavulanic acid (see comments for *E. coli*), see also figure KLE.EVO.1.1.1 below. Also, since the level of resistance to carbapenems first exceeded 1% in 2016, this level was steadily maintained up to 2020, see table MAIN.1 in the statistical report.

Interestingly, while typical indicators of multi-resistance (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, clearly 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.





Urine isolates from hospital laboratories: Levels of resistance for these isolates to **main resistance indicators** were generally lower than those observed in blood/CSF isolates, see figure KLE.COM.1 below. Steadily decreasing 4-year trends were observed for resistance to 3GC (from 19.5%R in 2017 to 15.4%R in 2020) and fluoroquinolones (from 23%R to 18%R), see figure KLE.EVO.1.2.1 below, as well as the indicators for combined resistance in the statistical report[3]. However, it should be noted that representativeness was not optimal in the 1st year of data collection of results from urine isolates (2017).

As for **other antimicrobials** used for treatment of UTI, we observed 35.1%R (1839/5240) to oral fosfomycin, 16.9%R (1162/6891) to trimethoprim-sulfamethoxazole, and 3.4%R (251/7289) to temocillin. Compared to previous years, an upward shift was observed for resistance to fosfomycin (25% in 2019), while a steadily

decreasing trend is observed for resistance to trimethoprim-sulfamethoxazole (24%R in 2017), see figure KLE.EVO.1.2.3 below.

Figure KLE.COM..1 *Klebsiella pneumoniae*,
Antimicrobial resistance in BLOOD/CSF vs URINE isolate
EARS-BE Hospital labs only, BE, 2020

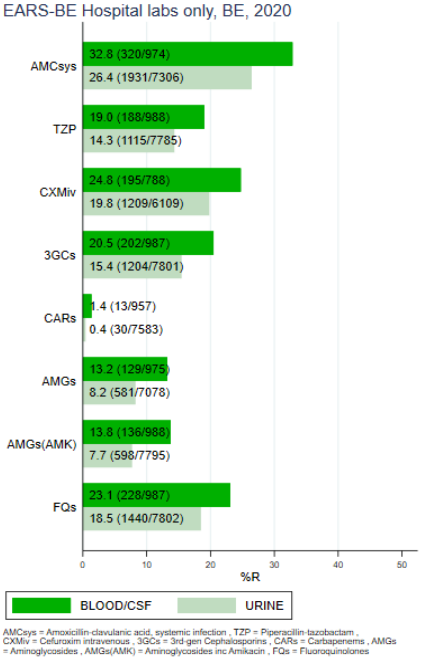


Figure KLE.EVO.1.2.1 *Klebsiella pneumoniae*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Hospital labs only, BE, 2011-2020

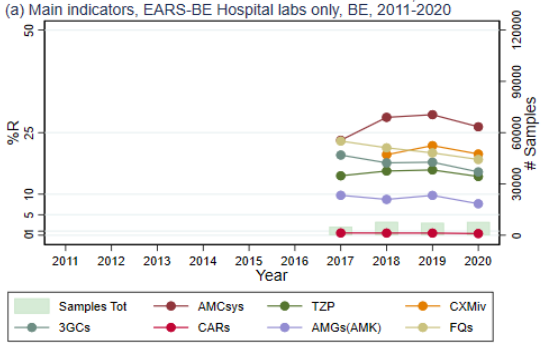
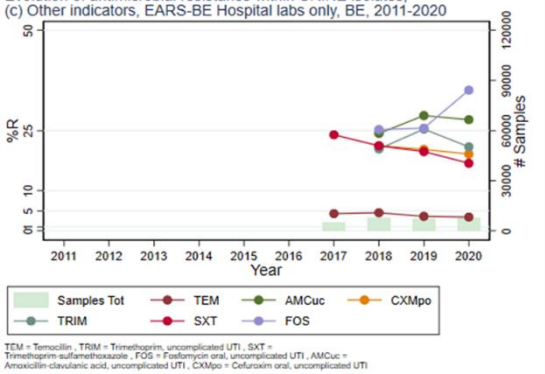
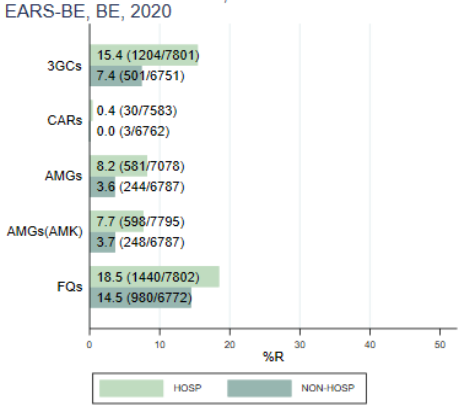


Figure KLE.EVO.1.2.3 *Klebsiella pneumoniae*,
Evolution of antimicrobial resistance within URINE isolates,
(c) Other indicators, EARS-BE Hospital labs only, BE, 2011-2020



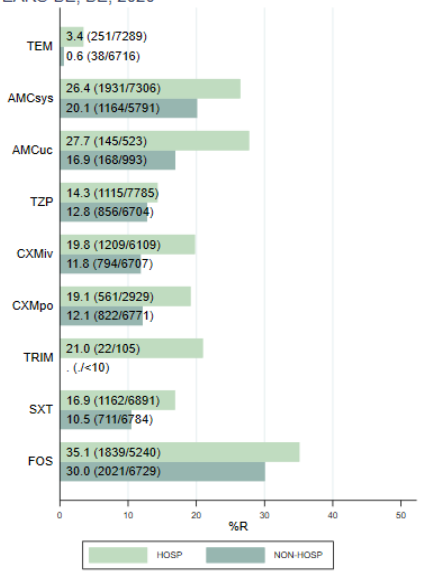
Urine isolates from non-hospital laboratories: Substantially lower levels of resistance were observed in this group, ie about 50-30% less of levels of resistance observed as compared to urine isolates from hospital laboratories, see figures KLE.4.3.1 and KLE.4.3.2 below. No meaningful trends could be detected for this group, most probably due to the low & variable number of laboratories participating over the years.

Figure KLE.4.3.1 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2020



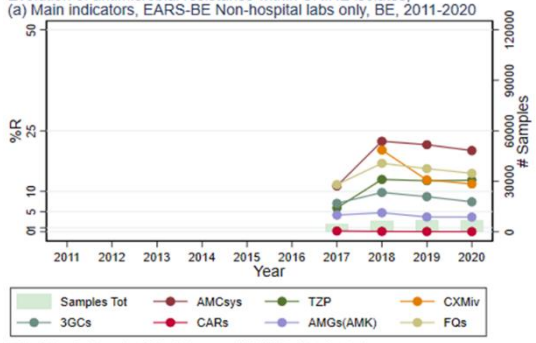
3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure KLE.4.3.2 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs (b), EARS-BE, BE, 2020



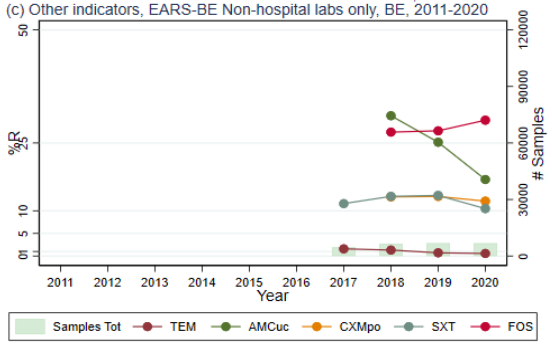
TEM = Temocillin , AMCsys = Amoxicillin-clavulanic acid, systemic infection , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous , CXMpo = Cefuroxim oral, uncomplicated UTI , TRIM = Trimethoprim, uncomplicated UTI , SXT = Trimethoprim-sulfamethoxazole , 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, 2011-2020



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 KLE.EVO.3.2.3 *Klebsiella pneumoniae*, Evolution of antimicrobial resistance within URINE isolates, (c) Other indicators, EARS-BE Non-hospital labs only, BE, 2011-2020



TEM = Temocillin , SXT = Trimethoprim-sulfamethoxazole , FOS = Fosfomycin oral, uncomplicated UTI , AMCuc = Amoxicillin-clavulanic acid, uncomplicated UTI , CXMpo = Cefuroxim oral, uncomplicated UTI

Results for *Pseudomonas aeruginosa*

Blood/CSF isolates: We observed 10.9%R (59/544) to piperacillin-tazobactam, 8.7%R (46/530) to ceftazidime, 12.1%R (62/514) to carbapenems, 9.4%R (51/544) to aminoglycosides, and 14.1%R (77/544) 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.

Similar to multi-resistance patterns in *K. pneumoniae* invasive isolates, increasing trends were observed when *P. aeruginosa* Blood/CSF multi-resistance is expressed as the % of laboratories reporting at least one multi-resistant Blood/CSF isolate, see figure KLE.EVO.1.1.b below.

Figure PSE.EVO.1.1.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
EARS-BE Hospital labs only, BE, 2011-2020

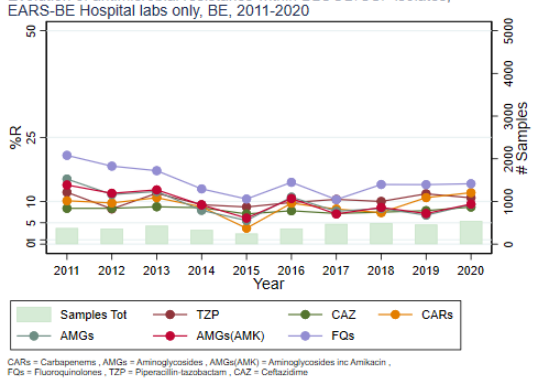
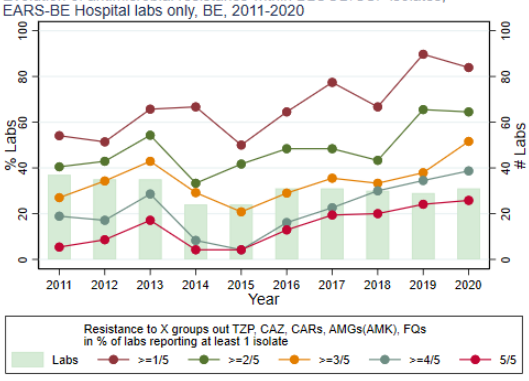


Figure PSEAER.EVO.1.1.b *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
EARS-BE Hospital labs only, BE, 2011-2020



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 (6.9%R), ceftazidime (5.1%R) and carbapenems (5.8%R), similar levels were observed for aminoglycosides (8.3%R) and (slightly) higher levels for fluoroquinolones (16.2%R), see figure PSE.COM.1. As compared to Blood/CSF isolates, trends in resistance were more clearly distinguishable within *P. aeruginosa* urine isolates, with fluoroquinolones resistance increasing (13.7%R in 2017), and resistance against other antimicrobials remaining stable between 5 and 10% during the last 4 years.

Figure PSE.COM..1 *Pseudomonas aeruginosa*,
Antimicrobial resistance in BLOOD/CSF vs URINE isolate
EARS-BE Hospital labs only, BE, 2020

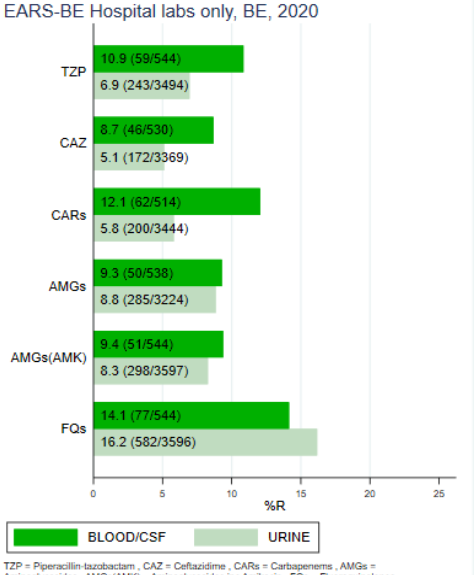
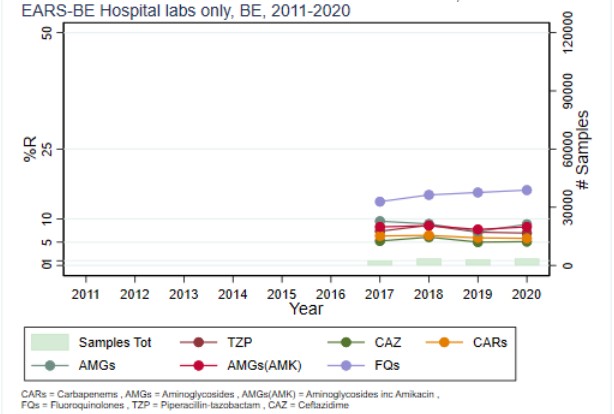
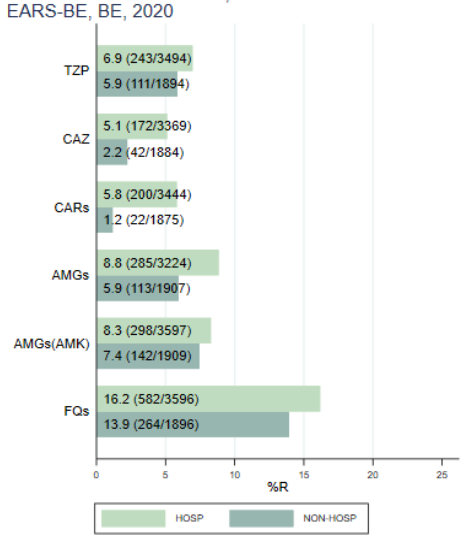


Figure PSE.EVO.1.2.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within URINE isolates,
EARS-BE Hospital labs only, BE, 2011-2020



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.

Figure PSE.4.3.1 *Pseudomonas aeruginosa*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2020



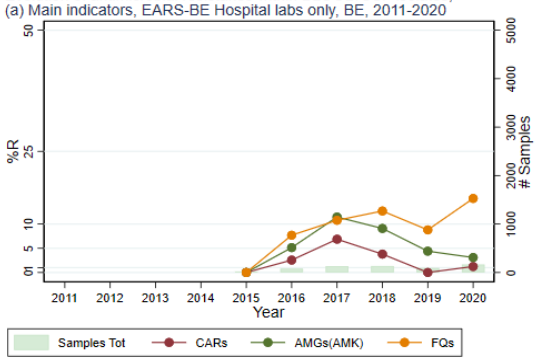
TZP = Piperacillin-tazobactam , CAZ = Ceftazidime , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Results for *Acinetobacter* species

Blood/CSF isolates: For 2020, results were obtained from 24 labs on 164 isolates. For those, we observed 1.2%R (2/163) to carbapenems, 2.7%R (4/151) to aminoglycosides, and 15.3%R (22/144) to fluoroquinolones. As compared to 2019, these levels remained at a similar level, see figure ACISPP.EVO.1.1 below.

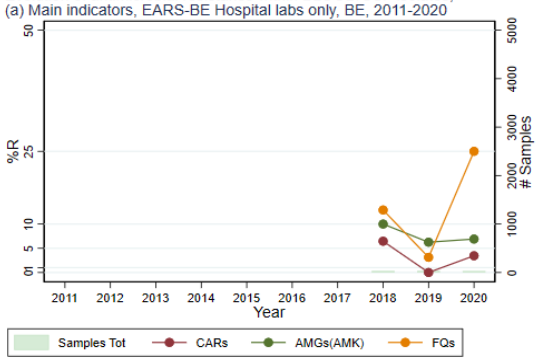
For *A. baumannii* isolates (results on 29 isolates available), we observed 3.5%R (1/29) to carbapenems, 7.1%R (2/28) to aminoglycosides, and 25%R (7/28) to fluoroquinolones. Of these, resistance to fluoroquinolones increased substantially as compared to previous years (10% in 2018 and 6.3% in 2019), however detection of meaningful trends is difficult given such small number of isolates, see figure ACIBAU.EVO.1.1.1.

Figure ACISPP.EVO.1.1.1 *Acinetobacter* spp, Evolution of antimicrobial resistance within BLOOD/CSF isolates, (a) Main indicators, EARS-BE Hospital labs only, BE, 2011-2020



CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure ACIBAU.EVO.1.1.1 *Acinetobacter baumannii*, Evolution of antimicrobial resistance within BLOOD/CSF isolates, (a) Main indicators, EARS-BE Hospital labs only, BE, 2011-2020



CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

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[9]. The resistance rates reported here therefore come with the above limitations, and need confirmation from national microbiological surveillance[10].

Restricting the analysis to hospital laboratories, colistin testing rates on blood/CSF isolates varied from 55.6% in *E. coli* (of 20 labs reporting), 66.3% in *K. pneumoniae* (of 16 labs reporting), to 52.3% in *P. aeruginosa* (of 18 labs reporting). In urine isolates, these rates were 35.2% in *E. coli* (23 labs reporting), 57.3% in *K. pneumoniae* (16 labs reporting), and 57.5% in *P. aeruginosa* (17 labs reporting). In *E. coli*, resistance to colistin in 2020 was 0.9% in blood/CSF isolates and 1.1% urine isolates. In *K. pneumoniae* isolates, resistance was 1.5% in blood/CSF isolates and 1.6% in urine isolates. In *P. aeruginosa*, resistance was 4.9% in blood/CSF and 2.6% in urine isolates. But again, due to selective testing, these rates are most likely biased upwards.

Conclusions and recommendations

For the EARS-BE 2020 surveillance, thirty-one hospital laboratories submitted results to Sciensano on isolates from blood or cerebrospinal fluid (CSF) samples taken in 2020, while 26 hospital labs submitted results on urine isolates taken in 2020. Furthermore, six laboratories not associated to an acute care hospital submitted results on urine isolates.

In *Staphylococcus aureus* isolates from blood or cerebrospinal fluid (CSF) samples taken in 2020, resistance to methicillin (MRSA) remained stable as compared to 2019, while resistance to fluoroquinolones continued to decrease. In Enterococci blood/CSF isolates, no vancomycin resistance was observed in *E. faecalis* isolates, while this reached 3.8% in *E. faecium* isolates. For both isolates, variability in vancomycin resistance increased in the last couple of years.

For *Streptococcus pneumoniae* blood/CSF isolates, a substantial decrease in observed positive isolates was observed in 2020 compared to 2019, which can be attributed to reduced circulation of strains as a result of COVID19-imposed distancing measures. Non-susceptibility to penicillins further increased to 14.4%, which is partly due to a change in susceptibility test method (E-test replaced by microdilution) within the NRC in 2020.

For *Escherichia coli* blood/CSF and urine isolates, a steadily decreasing trend was observed for resistance to fluoroquinolones since 2015, while trends for other main resistance indicators such as amoxicillin-clavulanic acid, piperacillin-tazobactam, cefuroxime, 3rd-generation cephalosporins (3GC), carbapenems, and aminoglycosides remained stable. In *Klebsiella pneumoniae* blood/CSF isolates, clear trends were difficult to observe for many resistance indicators due to variable rates during the last couple of years, however in urine *K. pneumoniae* isolates from hospital labs, decreasing trends were observed for resistance to 3GC and fluoroquinolones. Resistance to carbapenems was (almost) not observed in *E. coli* and very low (around 1%) in *K. pneumoniae*.

For antimicrobials used for treatment of urinary tract infection, resistance in *E. coli* urine isolates to amoxicillin-clavulanic acid was high (above 30%), moderate to high (around 25%) for trimethoprim-sulfamethoxazole, and low to very low (between 1-5%) for temocillin, nitrofurantoin, and oral fosfomycin. Within *K. pneumoniae* urine isolates, resistance to oral fosfomycin was observed to be higher (above 30%) but lower for trimethoprim-sulfamethoxazole (below 20%), while this last antimicrobial also showed a decreasing 4-year trend.

Pseudomonas aeruginosa blood/CSF isolates showed resistance to almost all studied antibiotic groups (piperacillin-tazobactam, ceftazidime, carbapenems, aminoglycosides, fluoroquinolones), however it remains difficult to detect meaningful trends due to a relatively low number of isolates. In urine *P aeruginosa* isolates, an increase was observed of fluoroquinolones resistance, while other indicators remained stable. In *Acinetobacter* spp blood/CSF isolates (including those of *A. baumannii*), resistance to carbapenems remained low, but the number of labs submitting results should further increase to improve trend detection.

Interestingly, for *K. pneumoniae* and *P. aeruginosa* blood/CSF isolates since 2014-15, indicators for multi-resistance show a clearly increasing trend when expressed as the % of laboratories reporting at least one (multi-resistant) isolate. This result is indicative of the historical emergence on a national scale of multi-resistance for these species within invasive isolates, and is especially troublesome for isolates reported as extensive drug resistant (XDR), ie those being resistant to all antimicrobials under follow-up.

Despite all efforts by participating laboratories and Sciensano, a database with moderate (hospital laboratories) or insufficient (non-hospital laboratories) representativeness could be obtained, with resistance indicators also being insufficiently precise for pathogens such as *P. aeruginosa* and *Acinetobacter* spp. Because these issues persist since several years, it should be noted that EARS-BE data collection proceeds without official regulation

nor funding, not on the level of participating laboratories nor of Sciensano. The current COVID19 crisis did further highlight this structural lack of resources, by emphasizing even more the efforts needed to obtain qualitative and representative data from laboratories in timely fashion as well as to organize the follow-up & analysis of this project within Sciensano. This lack of structure and funding is in contradiction with international recommendations to organize national surveillance of AMR up to the level of the susceptibility test, as done by EARS-NET and GLASS surveillances. It is also in contradiction with the 2013 MDRO plan[11], which called for extension of current national AMR surveillance towards the non-hospital environment. In recent years, the EARSBE surveillance has tried to answer these calls, both by extending its scope to urine isolates as well as to non-hospital laboratories, but the current crisis shows that structural funding and prioritization is needed to improve data representativeness and quality as well as reduce reporting delays.

National AMR and Bloodstream infection surveillance in BE is organized through the Royal Decree for funding of acute care hospitals[12], the current version of which is restricted and prioritized on surveillances for AMR and Bloodstream infection (BSI) that are incompatible with the inclusion criteria and AST-level data specification of EARS-NET and GLASS. Modification of this legislation to include and prioritize EARS-NET and GLASS surveillance is therefore a first important step, even if this will not acknowledge calls to establish AMR surveillance within the non-hospital sector. In 2019, a harmonized data collection protocol[13] was proposed for the EARS-BE and the AMR national surveillances (i.e. for harmonized collection of 2019 data), its main objectives being to improve the quality of data for AMR national surveillances collecting detailed antimicrobial susceptibility tests (AST) data instead of aggregated data, to reduce workload for laboratories, and to increase the number of participants to the EARS-BE project.

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