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HEALTHCARE-ASSOCIATED INFECTIONS AND ANTIMICROBIAL RESISTANCE

European antimicrobial resistance surveillance for Belgium (EARS-BE) 2022

Descriptive report

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WHO WE ARE

SCIENSANO can count on more than 700 staff members who commit themselves, day after day, to achieving our motto: Healthy all life long. As our name suggests, science and health are central to our mission. Sciensano's strength and uniqueness lie within the holistic and multidisciplinary approach to health. More particularly we focus on the close and indissoluble interconnection between human and animal health and their environment (the "One health" concept). By combining different research perspectives within this framework, Sciensano contributes in a unique way to everybody's health.
For this, Sciensano builds on the more than 100 years of scientific expertise of the former Veterinary and Agrochemical Research Centre (CODA-CERVA) and the ex-Scientific Institute of Public Health (WIV-ISP).

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Epidemiology and public health – Healthcare-associated infections and antimicrobial resistance

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LIST OF ABBREVIATIONS

3CG	Third generation cephalosporines
AMR	Antimicrobial resistance
AST	Antimicrobial Susceptibility Test
CSF	Cerebrospinal fluid
EARS-NET	European Antimicrobial Resistance Surveillance Network
EARS-BE	European Antimicrobial Resistance Surveillance for Belgium
ECDC	European Centre for Disease Prevention and Control
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GLASS	Global Antimicrobial surveillance system
I	Susceptible, increased exposure
MRGN	Multidrug-resistant gram-negative bacteria
MRSA	Methicillin-resistant Staphylococcus aureus.
NRC	National reference center
NSIH	Service of National Surveillance of Infections in Healthcare settings, Sciensano
NSIH-AMR	Mandatory national AMR surveillance (MRSA, MRGN, VRE) coordinated by NSIH
UTI	Urinary tract infection
S	Susceptible, standard dosing regimen
R	Resistant
VRE	Vancomycin- or linezolid-resistant enterococci
WHO	World Health Organization

INTRODUCTION

This report describes the main findings of the "EARS-BE 2022" survey, i.e. the annual collection of data on antimicrobial resistance in Belgium as part 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 the occurrence of antimicrobial resistance (AMR) in human pathogens isolated from invasive samples (blood and cerebrospinal fluid (CSF)) across Europe. EARS-BE differs from EARS-NET by the additional collection of antimicrobial susceptibility testing (AST) results from urinary samples. EARS-BE 2022 data on blood/CSF isolates were submitted in June 2023 to ECDC for inclusion in the annual EARS-NET report[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 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 2022 can be found in the EARS-BE 2022 reporting protocol[2]. The results presented and discussed here can be found in details in the "EARS-BE 2022 statistical report"[6] in Excel format, which contains the exhaustive EARS-BE 2022 results, 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 bacterium-AST combination, the number of laboratory 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 the following sets of inclusion criteria and subgroups:

(1) general EARS-BE 2022 inclusion criteria, as defined in the surveillance protocol;

(2) Same as (1), but restricted to hospital laboratories;

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

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

(5) Same as (2), but 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-four laboratories submitted AST results on isolates from blood/CSF samples taken in 2022 (statistical report Table MAIN.1); thirty-two of these were associated to an acute care hospital. This is very close to the participation in last year's surveillance (35 laboratories); and to the level of participation prior to COVID-19 (Figure PART.EVO.1). 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 2022 data, Flanders (21/32 labs = 65.6%) and Brussels (4/32 labs = 12.5%) continue to be overrepresented (as in previous years), with Wallonia (7/32 labs = 21.9%) being underrepresented by about 10% when compared to the national distribution of hospital laboratories.

Figure PART.EVO.1,
Laboratory participation for BLOOD/CSF isolates, EARS-BE, 2013-2022

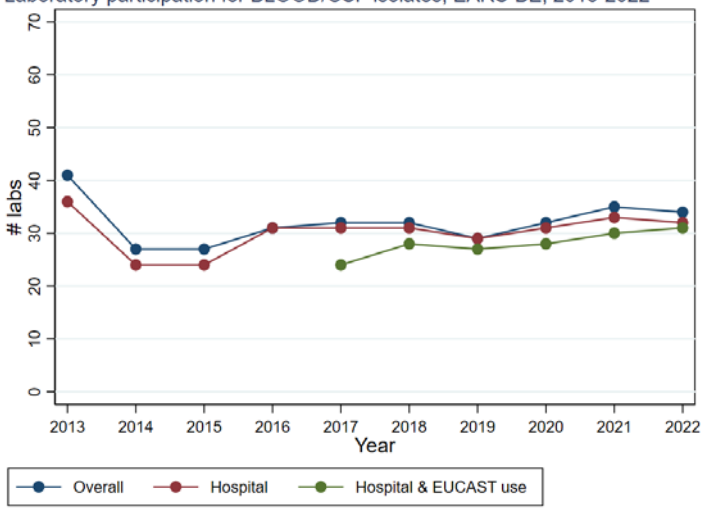
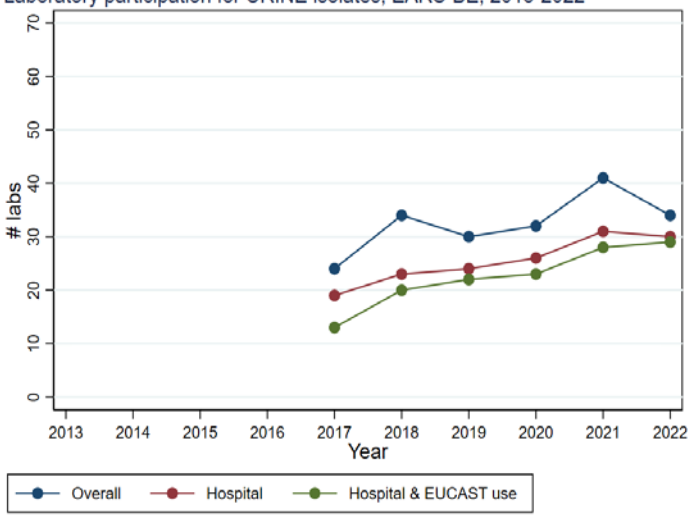


Figure PART.EVO.2,
Laboratory participation for URINE isolates, EARS-BE, 2013-2022



Urine isolates:

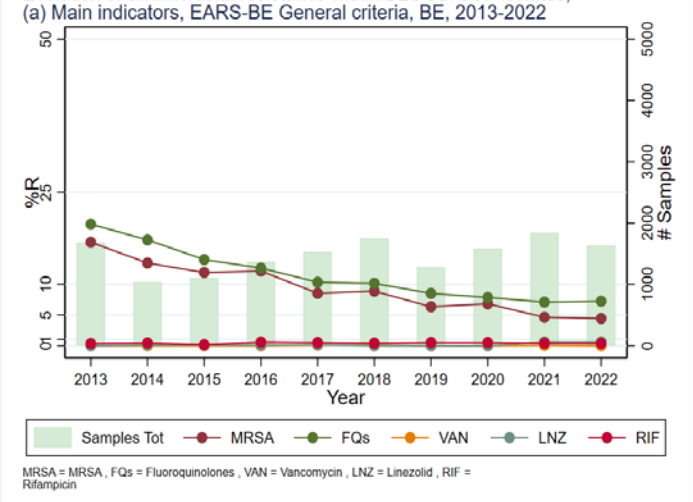
Thirty-four laboratories participated in the EARS-BE URI 2022 surveillance. Four of them were not associated to an acute care hospital. The distribution of the 30 participating hospital laboratories over the three regions and hospital types was similar to the distribution for blood/CSF samples. The four non-hospital laboratories were all located in Flanders. Because of the latter, the results on urine isolates from the non-hospital setting for 2022 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. Participation of non-hospital laboratories remains low and variable (Figure PART.EVO.2).

Use of EUCAST guidelines: Of all laboratories submitting results, only one reported the use of another guideline than EUCAST for the interpretation of ASTs. Among laboratories reporting blood/CSF results, 27 (79%) reported the use of EUCAST V10 (or later) guidelines in 2022, implementing the new definition of the "I" category of EUCAST: 'susceptible, increased exposure'[7].

RESULTS FOR *S. AUREUS*

Blood/CSF isolates: In 2022, 4.4% (72/1625) of *S. aureus* isolates were resistant to methicillin (MRSA), while 7.3% (117/1613) of isolates were resistant to fluoroquinolones. This represents a stabilization as compared to 2021 for both indicators, it remains the lowest result since EARS-NET follow-up started in 2000 (Figure STA.EVO.0.1.1). No resistance was observed for vancomycin, and very low resistance was observed for linezolid and rifampicin. Combined resistance against two or more of these groups remains low (3.7% ; 48/1311) (statistical report Table MAIN).

Figure STA.EVO.0.1.1 *Staphylococcus aureus*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



RESULTS FOR *S. PNEUMONIAE*

Results obtained from the national surveillance on invasive pneumococcal infections 2022

The results for AMR in *S. pneumoniae* isolates in this report are based on 2022 AST data obtained from the National Reference Centre's (NRC UZ Leuven) national surveillance of invasive pneumococcal infections, and shown in the statistical report, Table STRN.1. The full results of this national surveillance can be found in the NRC's dedicated annual report [8]. The data included AST results on blood/CSF isolates submitted by 80 labs, with susceptibility results interpreted according to EUCAST guidelines.

In line with the new definitions of resistance introduced by EUCAST in 2019, ECDC uses the term "penicillin non-wild-type" to refer to isolates reported as "I" or "R" by local laboratories, that is, isolates with a minimum inhibitory concentration (MIC) to benzylpenicillin above those of wild-type isolates (>0.06 mg/L) [3].

The EUCAST criteria for the SIR categorization for penicillins in *S. pneumoniae* are as follows[7]:

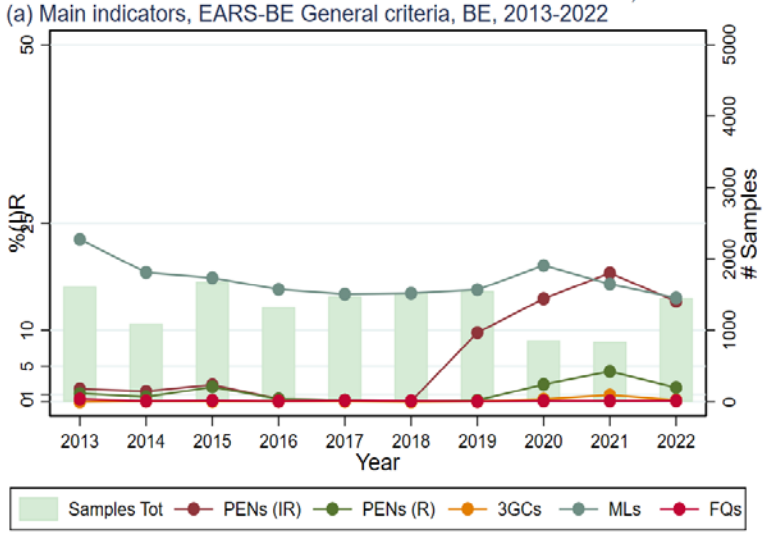
(1) for CSF isolates: Minimal Inhibitory Concentration (MIC)>0.06 mg/L: R;
(2) for blood isolates: MIC<=0.06 mg/L: S; 0.06<MIC≤2 mg/L: I; >2 mg/L: R.

For blood isolates these interpretation criteria were applied as of 2019 (up to 2018 the criteria were for blood isolates: MIC>2 mg/L: IR), causing the substantial artificial increase in penicillin "I" and "R" categories in 2019 as compared to 2018 (Figure STRN.EVO.0.1.1 below) .
In 2020, the NRC changed its AST method from E-test to broth microdilution in response to a warning from EUCAST that the E-test was underestimating penicillin MIC values. This change could therefore potentially also have led to an increase in the number of I and R in 2020.

Finally, ECDC requested that results from invasive isolates from 2021 onwards reported to EARS-NET be interpreted according to EUCAST V11 breakpoints for non-meningitis (i.e. the above criteria for blood) irrespective of the specimen type (blood or CSF), which implied re-interpreting some CSF penicillin-R AST results as "I".

In 2022, the number of sample tested is back to the pre-COVID levels. The percentage of penicillin non-wild type (%IR) was 14.1% (205/1457), a decrease for the first time since 2018 (Figure STRN.EVO.0.1.1). Resistance to penicillin (%R) was 2.0% (29/1457), also a decrease compared to 2021. Resistance levels to 3rd-generation cephalosporins (3GC) and fluoroquinolones were both very low (<1%), while resistance to macrolides was 14.6% (212/1457). The resistance among all three classes remains stable as compared to pre-COVID19 years.

Figure STRN.EVO.0.1.1 *Streptococcus pneumoniae* (NRC),
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



PENs (IR) = Penicillins , PENs (R) = Penicillins , 3GCs = 3rd-gen Cephalosporins , MLs = Macrolides , FQs = Fluoroquinolones

Results obtained from the EARS-BE 2022 data collection

The results of the EARS-BE 2022 data collection of *S. pneumoniae* blood/CSF isolates (32 labs submitting results) are shown in the Statistical report, Table MAIN.1. The percentage of penicillin non-wild-type was 10.5% (60/573), macrolide resistance was 14.8% (94/634), resistance to fluoroquinolones was 2.3% (12/532) and resistance to 3GC was 0%.

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

Blood/CSF isolates: In 2022, *E. faecalis* isolates showed no resistance to vancomycin and teicoplanin (out of 687 and 429 isolates, respectively) and very low resistance (<1%) to aminopenicillins and linezolid. In *E. faecium* isolates, we observed 86.9%R (378/435) to aminopenicillins, 1.4%R (6/444) to vancomycin, 1.1%R (3/260) 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 (Figure ENCFAE EVO.0.1.1 and ENCFAI EVO.0.1.1)
About a third (30%) of the tested isolates are resistant to 2 or more antimicrobial groups under surveillance.

Figure ENCFAE.EVO.0.1.1 *Enterococcus faecalis*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022

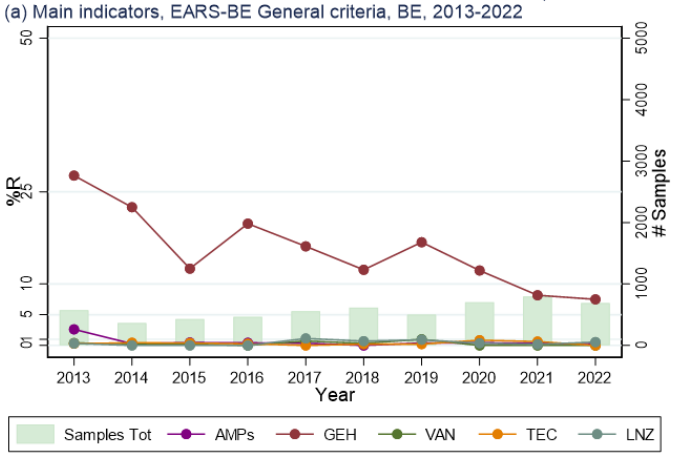
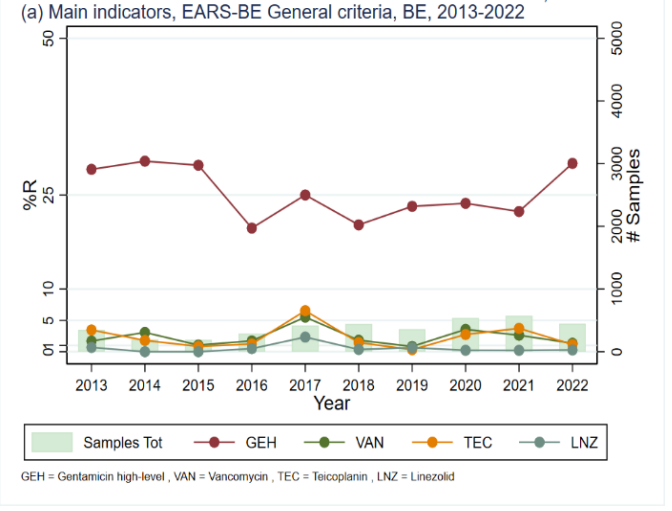


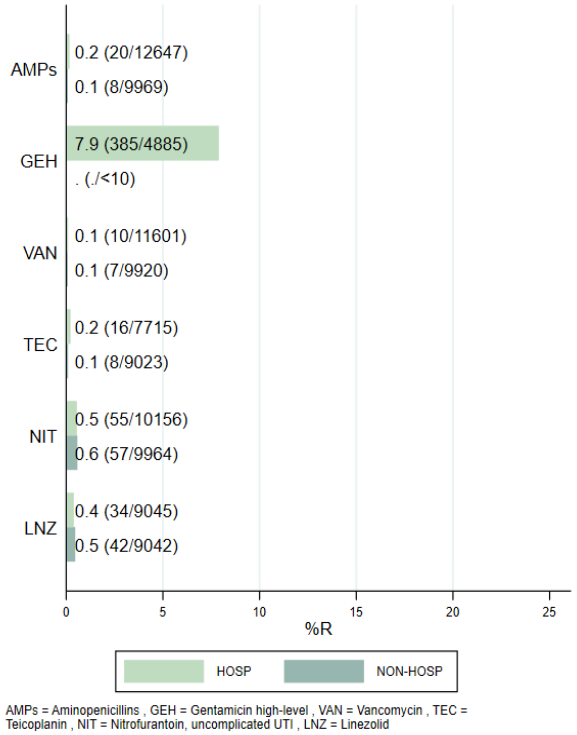
Figure ENCFAI.EVO.0.1.1 *Enterococcus faecium*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



Urine isolates: In 2022, 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 (Figure ENCFAE.4.3.1). No difference was observed with the resistance in blood/CSF isolates.

In *E. faecium* urine isolates from hospital laboratories taken in 2022, resistance to vancomycin, teicoplanin and linezolid was very low (<1%). No AST results on *E. faecium* from urine isolates were received from non-hospital labs.

Figure ENCFAE.4.3.1 *Enterococcus faecalis*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2022

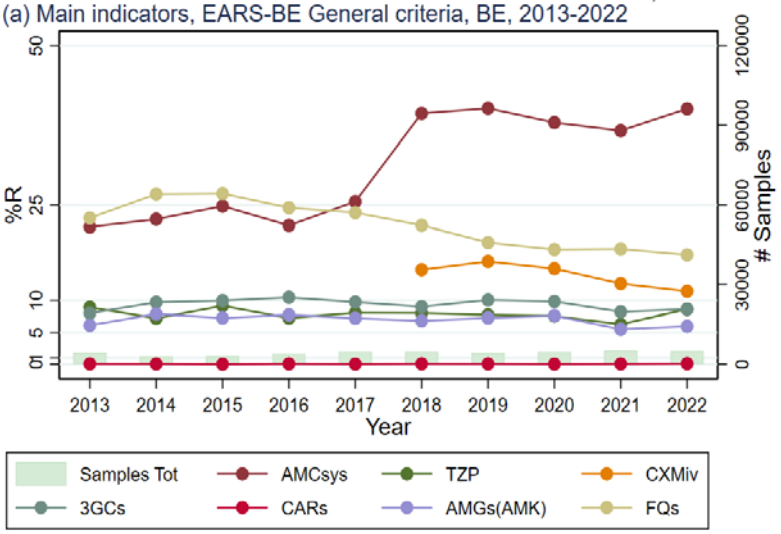


AMPs = Aminopenicillins , GEH = Gentamicin high-level , VAN = Vancomycin , TEC = Teicoplanin , NIT = Nitrofurantoin, uncomplicated UTI , LNZ = Linezolid

RESULTS FOR *E. COLI*

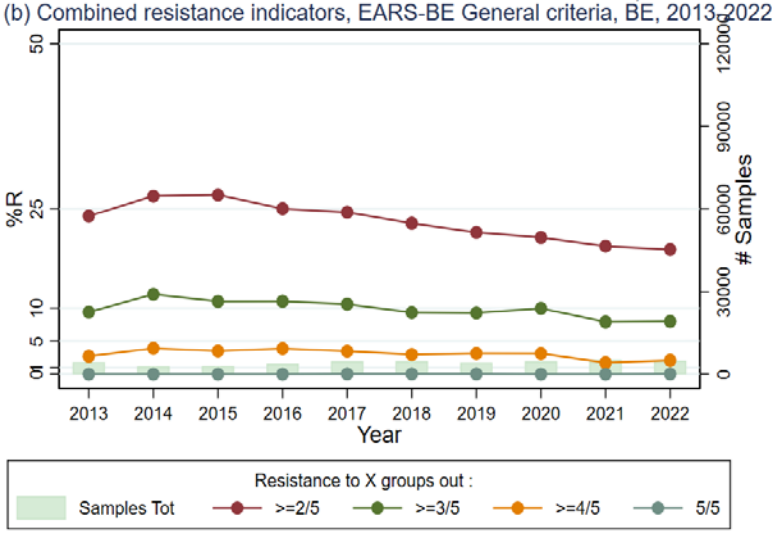
Blood/CSF isolates: For isolates obtained in 2022, we observed 40.1%R (1862/4646) to amoxicillin-clavulanic-acid, 17.2%R (844/4916) to fluoroquinolones, 11.4%R (472/4127) to cefuroxime, 8.6%R (421/4880) to 3GC, 8.6%R (406/4699) to piperacillin-tazobactam, 6.0%R (293/4919) to aminoglycosides, and almost no resistance to carbapenems (0.1%R).
For amoxicillin-clavulanic acid, this is a return to the level of resistance seen in 2019, the highest since 2013. For the other antimicrobials, the trends are either stable or decreasing over the past four years (Figure ESC.EVO.0.1.1).
As such, multidrug resistance rates were observed to decline as well (Figure ESC.EVO.0.1.2). The percentage of isolates resistant to at least one of the antimicrobials under surveillance, although high (59.3%R), remains stable over the last four years.

Figure ESC.EVO.0.1.1 *Escherichia coli*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



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

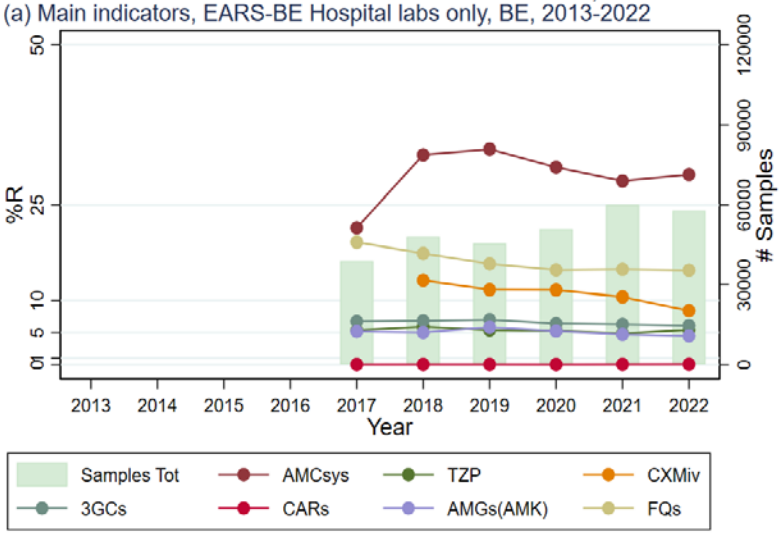
Figure ESC.EVO.0.1.2 *Escherichia coli*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(b) Combined resistance indicators, EARS-BE General criteria, BE, 2013-2022



Included groups: aminopenicillins, 3rd-gen cephalosporins, carpabenems, aminoglycosides, fluoroquinolones

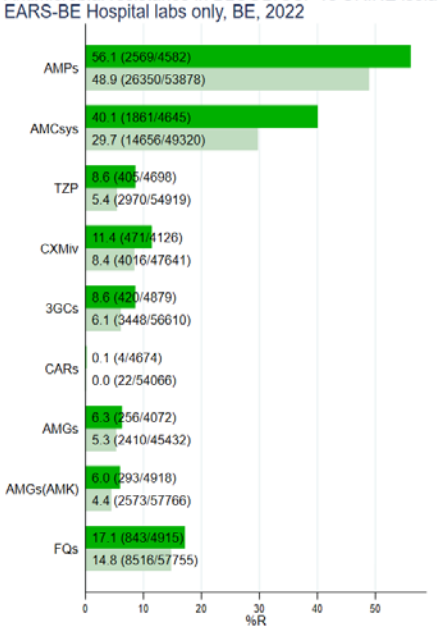
Urine isolates from hospital laboratories: Within urine isolates obtained in 2022, levels of **main indicators for resistance** were generally lower as compared to blood/CSF isolates (Figure ESC.COM.1). Also here, decreasing or stable 4-years trends of resistance to main antimicrobials were observed (Figure ESC.EVO.1.2.1), and as such also for multidrug resistance.

Figure ESC.EVO.1.2.1 *Escherichia coli*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Hospital labs only, BE, 2013-2022



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.COM..1 *Escherichia coli*,
Antimicrobial resistance in BLOOD/CSF vs URINE isolat
EARS-BE Hospital labs only, BE, 2022



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

For other antimicrobials typically used for treatment of **urinary tract infection (UTI)**, we observed 23.4%R (11283/48155) to trimethoprim-sulfamethoxazole, 2.6%R (1313/50360) to temocillin, 1.3%R (541/40794) to nitrofurantoin and 2.5%R (886/35693) to oral fosfomycin (interpretation criteria for per os formulation; PO), and 9.4%R for oral cefuroxium. Among these, some slight decreasing trends were observed over the last four years, including resistance against trimethoprim-sulfamethoxazole, temocillin and oral cefuroxim (see ESC.EVO.1.2.3)

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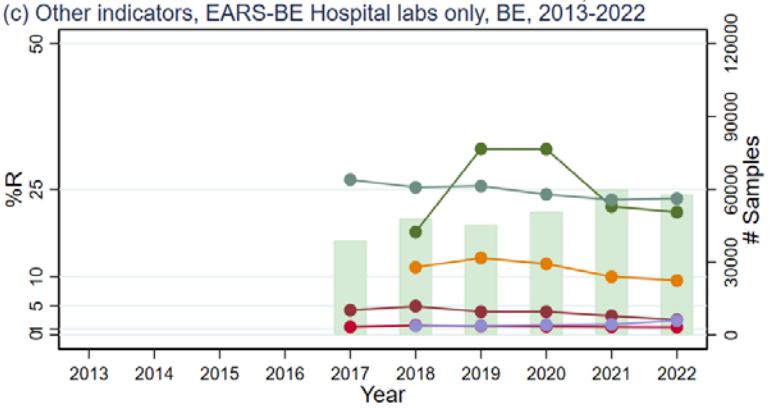
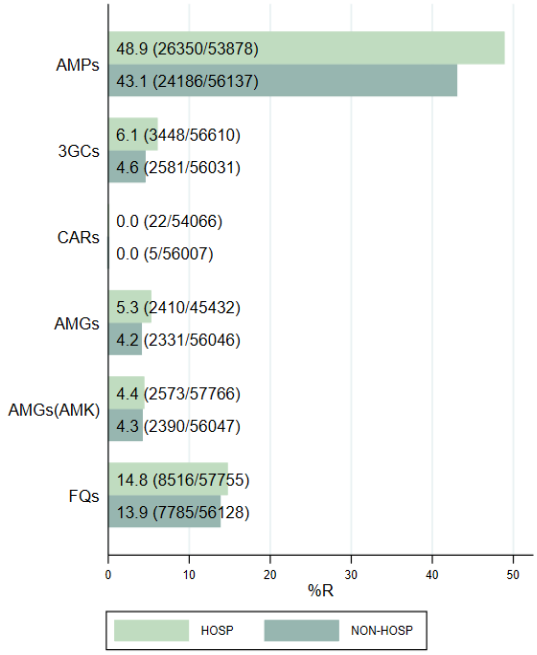
Figure ESC.EVO.1.2.3 *Escherichia coli*,
Evolution of antimicrobial resistance within URINE isolates,
(c) Other indicators, EARS-BE Hospital labs only, BE, 2013-2022



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

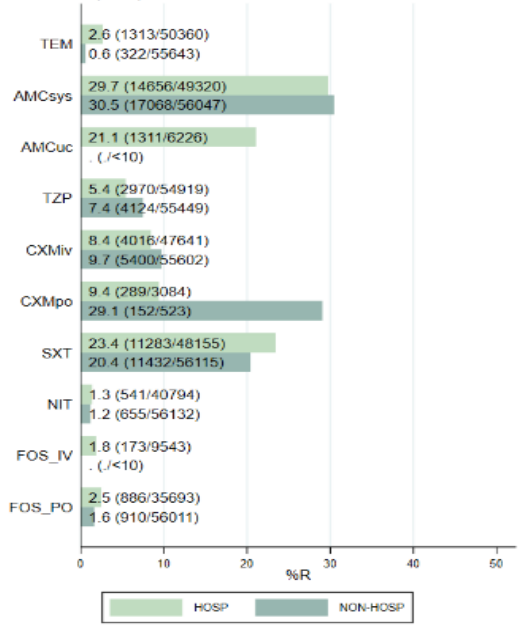
Urine isolates from non-hospital laboratories: Resistance levels in this group were mostly similar to those of hospital laboratories, with the exception of temocillin for which it was much lower in non-hospital laboratories, and oral cefuroxime for which it was much higher in non-hospital laboratories (Figures ESC.4.3.1 and ESC.4.3.2). Except for TZP, for which resistance is back to nearly the highest level since 2017 (7.4%, 4124/55449), the trends are stable or decreasing for most of the antimicrobials (Figure ESC.EVO.3.2.1)

Figure ESC.4.3.1 *Escherichia coli*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2022



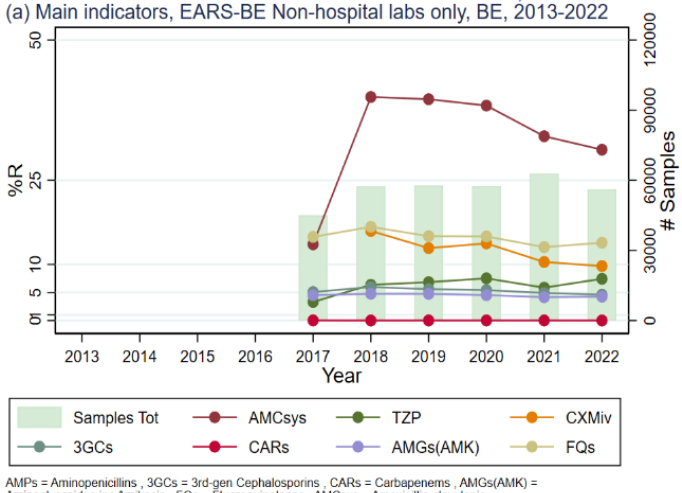
AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure ESC.4.3.2 *Escherichia coli*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs EARS-BE, BE, 2022



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 , SXT = Trimethoprim-sulfamethoxazole , NIT = Nitrofurantoin, uncomplicated UTI , FOS_IV = Fosfomycin intravenous , FOS_PO = 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, 2013-2022



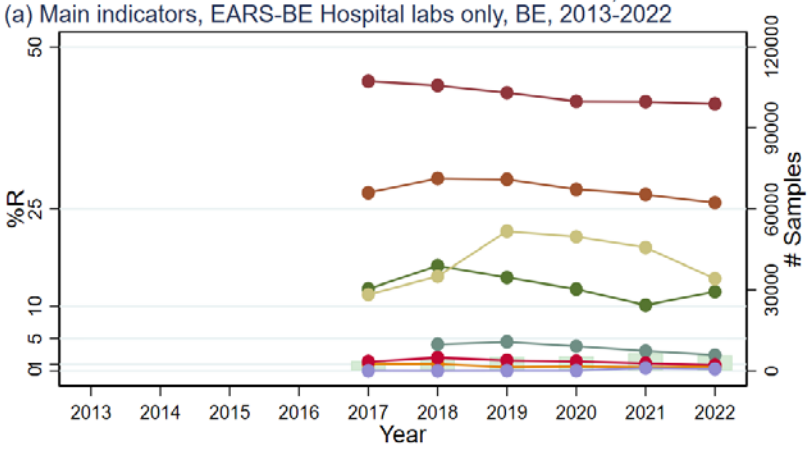
AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , AMCsys = Amoxicillin-clavulanic acid, systemic infection , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous

RESULTS FOR *P. MIRABILIS*

Data on this pathogen were collected for the first time by EARS-BE for the year 2017 to cover the most frequent pathogens isolated from **urine samples**.

Urine isolates from hospital labs: In 2022, we observed 41.2%R (2186/5307) to aminopenicillins, 25.9%R (1475/5686) to fluoroquinolones, 14.2%R (809/5686) to aminoglycosides, 12.2%R (581/4753) to amoxicillin-clavulanic acid, 2.4%R (100/4128) to cefuroxime, 0.9%R (50/5559) to 3GC and very low resistance to piperacillin-tazobactam (0.7%R) and to carbapenems (0.3%R). For all those antibiotics, the general trend over the past four years is stable or decreasing (Figure PRT.EVO.1.2.1).

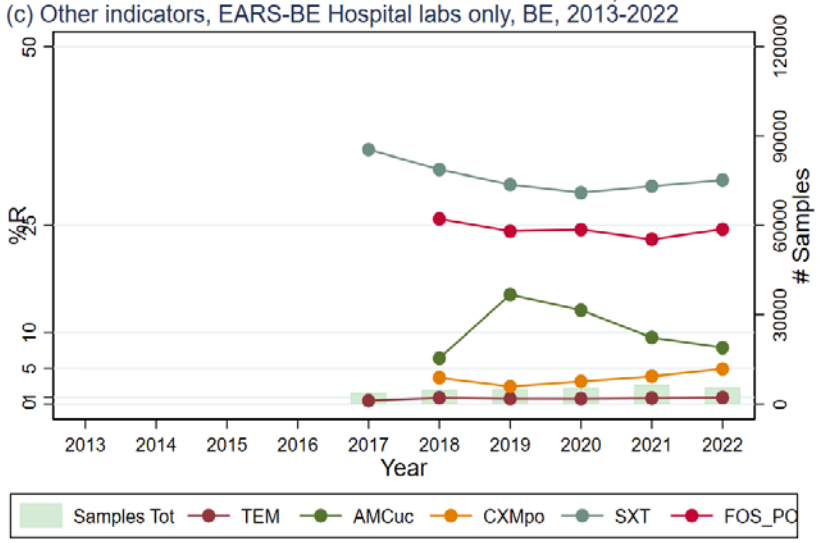
Figure PRT.EVO.1.2.1 *Proteus mirabilis*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Hospital labs only, BE, 2013-2022



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

For other antimicrobials for treatment of UTI, resistance was 31.3%R (1358/4334) to trimethoprim-sulfamethoxazole, 24.4%R (699/2860) to oral fosfomycin, and very low resistance (0.9%R) to temocillin. Except for the resistance to amoxicillin-clavulanic acid, which keeps decreasing, trends over the past few years are stable or slightly increasing (Figure PRT.EVO.1.2.3).

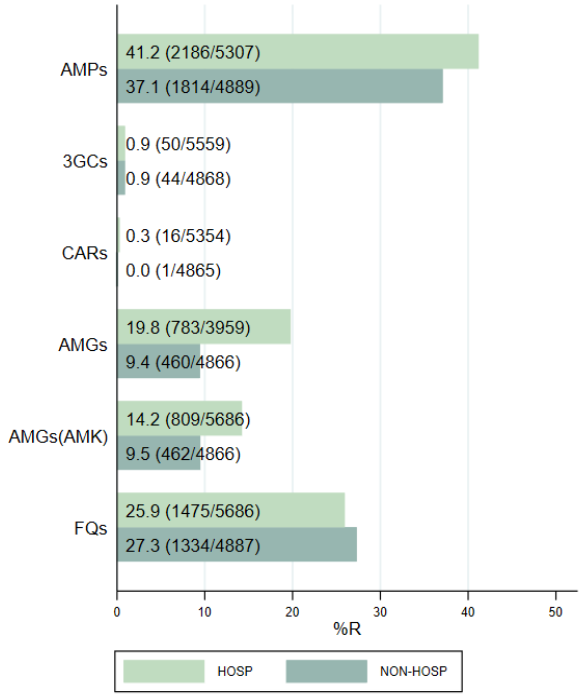
Figure PRT.EVO.1.2.3 *Proteus mirabilis*,
Evolution of antimicrobial resistance within URINE isolates,
(c) Other indicators, EARS-BE Hospital labs only, BE, 2013-2022



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

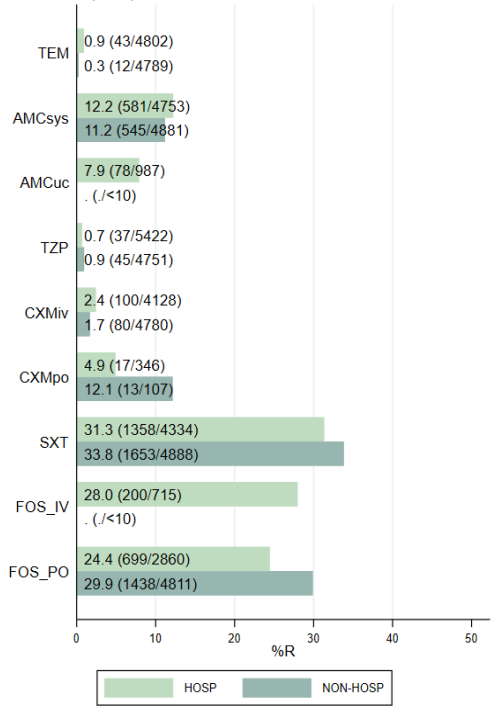
Urine isolates from non-hospital labs: Overall, resistance levels were similar (within 10% relative difference) between isolates from hospital and non-hospital laboratories, except for the much lower resistance to aminoglycosides (9.5%R) and the higher resistance to oral fosfomycin (29.9%R) and to oral cefuroxime observed in isolates of non-hospital laboratories (Figures PRT.4.3.1 and PRT.4.3.2).

Figure PRT.4.3.1 *Proteus mirabilis*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2022



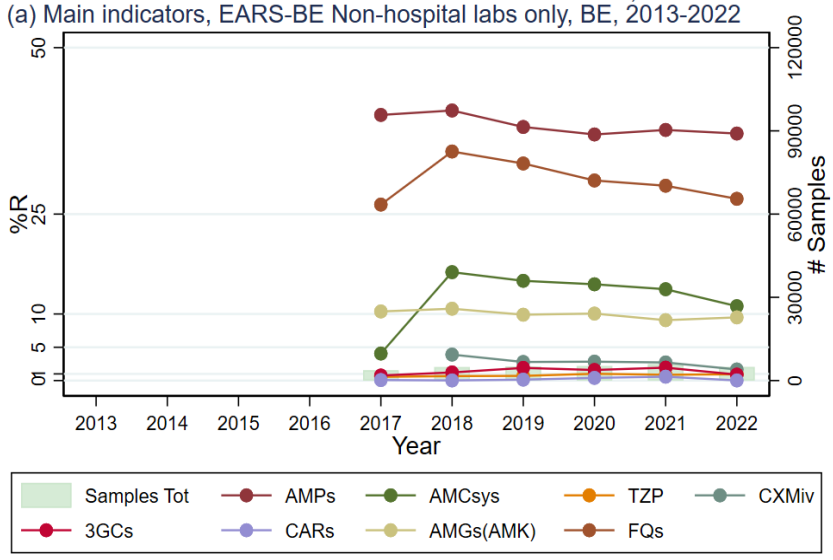
AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure PRT.4.3.2 *Proteus mirabilis*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs (b), EARS-BE, BE, 2022



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 , SXT = Trimethoprim-sulfamethoxazole , FOS_IV = Fosfomycin intravenous , FOS_PO = Fosfomycin oral, uncomplicated UTI

Figure PRT.EVO.3.2.1 *Proteus mirabilis*, Evolution of antimicrobial resistance within URINE isolates, (a) Main indicators, EARS-BE Non-hospital labs only, BE, 2013-2022



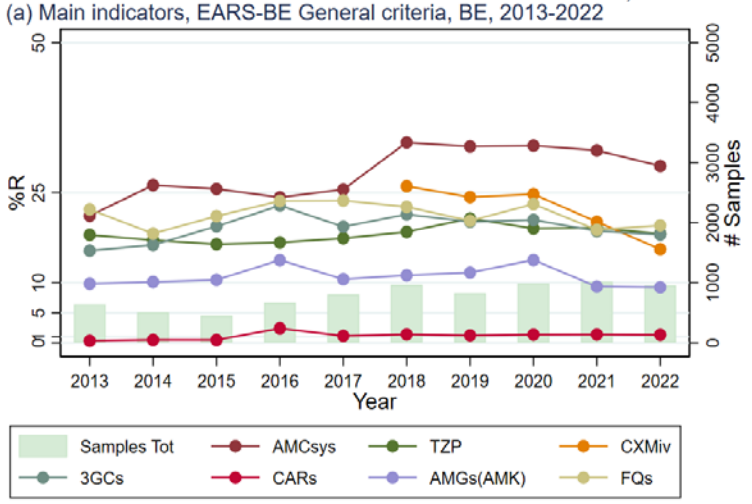
AMPs = Aminopenicillins , 3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , AMCsys = Amoxicillin-clavulanic acid, systemic infection , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous

Resistance to fluoroquinolones and amoxicillin-clavulanic acid has been decreasing over the past four years (Figure PRT.EVO.3.2.1).

RESULTS FOR *K. PNEUMONIAE*

Blood/CSF isolates: In 2022, we observed 29.4%R (265/900) resistance to amoxicillin-clavulanic acid, 15.6%R (128/822) to cefuroxime, 18.1%R (173/953) to piperacillin-tazobactam, 19.5%R (186/952) to fluoroquinolones, 18.0%R (170/944) to 3GC, 9.2%R (88/953) to aminoglycosides and 1.3%R (12/900) to carbapenems. Except for a decreasing trend for resistance to cefuroxime (26.1%R in 2018), no clear trends could be observed for the other antimicrobials, although 3GC and aminoglycosides showed the lowest resistance levels of the last 4 years (Figure KLE.EVO.0.1.1). Furthermore, resistance to carbapenems remained stable at just over 1.0%R.

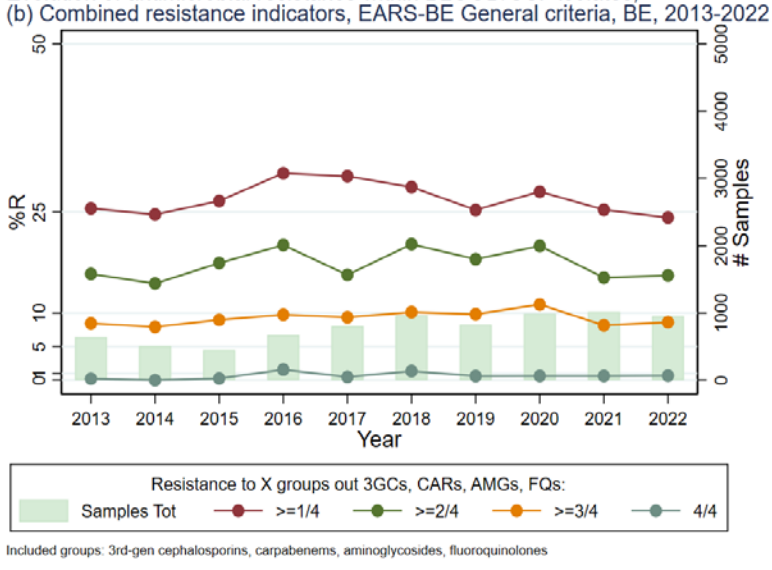
Figure KLE.EVO.0.1.1 *Klebsiella pneumoniae*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



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

Indicators of multi-resistance (to one or more of main antimicrobials, i.e. 3GC, carbapenems, aminoglycosides, fluoroquinolones)in *K. pneumoniae* blood/CSF isolates do not show much change over the last four years (Figure KLE.EVO.0.1.2)

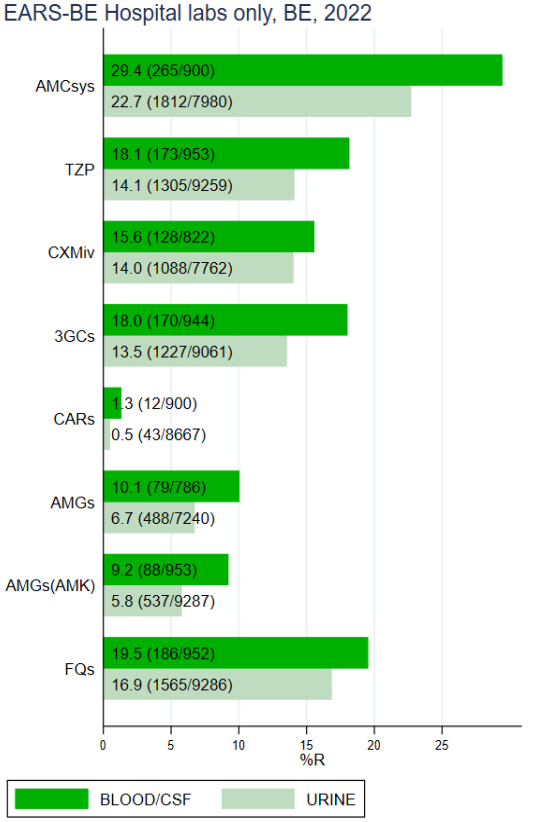
Figure KLE.EVO.0.1.2 *Klebsiella pneumoniae*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(b) Combined resistance indicators, EARS-BE General criteria, BE, 2013-2022



Included groups: 3rd-gen cephalosporins, carpabenems, aminoglycosides, fluoroquinolones

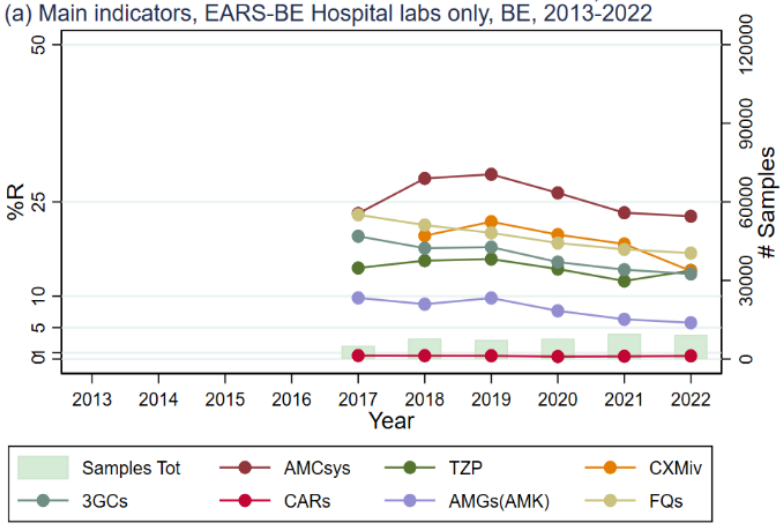
Urine isolates from hospital laboratories: Levels of resistance of these isolates to **main resistance indicators** were generally lower than those observed in blood/CSF isolates (Figure KLE.COM.1). Decreasing four-year trends were observed for many of the antimicrobials under surveillance (Figure KLE.EVO.1.2.1), especially for amoxicillin-clavulanic acid (29.4%R in 2019 vs 22.7%R in 2022), cefuroxime (21.8%R in 2019 vs 14.0%R in 2022), 3GC (17.8%R in 2019 vs 13.5%R in 2022) and fluoroquinolones (20.1%R in 2018 vs 16.9%R in 2022).

Figure KLE.COM..1 *Klebsiella pneumoniae*,
Antimicrobial resistance in BLOOD/CSF vs URINE isolat
EARS-BE Hospital labs only, BE, 2022



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

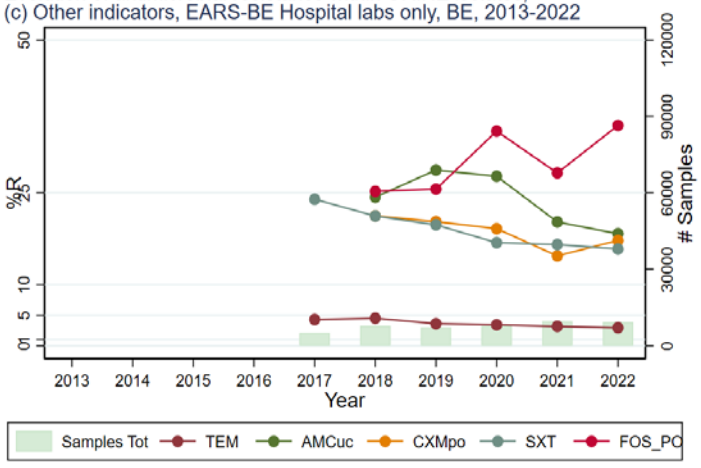
Figure KLE.EVO.1.2.1 *Klebsiella pneumoniae*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Hospital labs only, BE, 2013-2022



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

As for **other antimicrobials** used for treatment of UTI, we observed 36.0%R (1973/5478) to oral fosfomycin, 15.8%R (1214/7671) to trimethoprim-sulfamethoxazole, and 3.0%R (241/8136) to temocillin. Resistance to oral fosfomycin is increasing over the 4 previous year, while resistance to amoxicillin-clavulanic acid and trimethoprim-sulfamethoxazole is decreasing (Figure KLE.EVO.1.2.3).

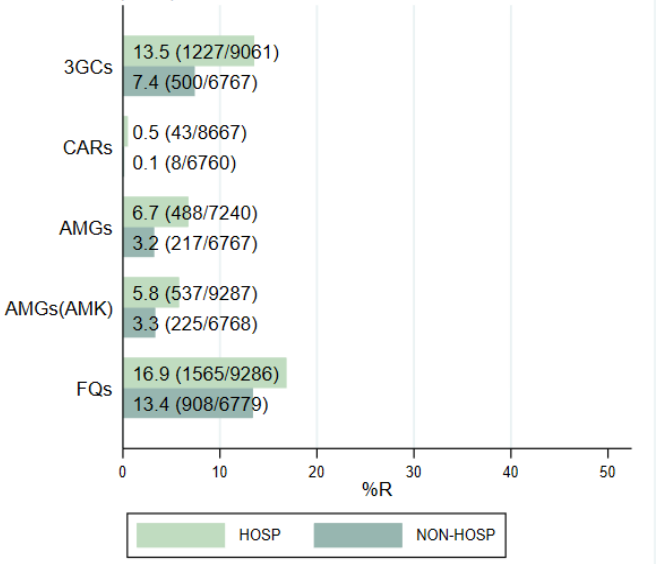
Figure KLE.EVO.1.2.3 *Klebsiella pneumoniae*,
Evolution of antimicrobial resistance within URINE isolates,
(c) Other indicators, EARS-BE Hospital labs only, BE, 2013-2022



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

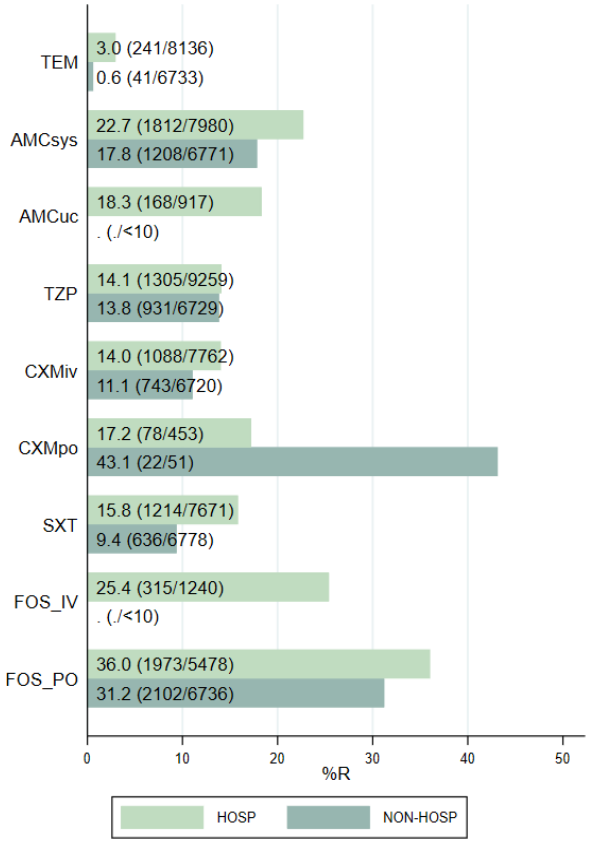
Urine isolates from non-hospital laboratories: Substantially lower levels of resistance, i.e. 30 to 50% lower, were observed in this group compared to urine isolates from hospital laboratories (Figures KLE.4.3.1 and KLE.4.3.2). For main antimicrobials, similar decreasing trends could be observed as for urine isolates from hospital laboratories (Figure KLE.EVO.3.2.1).

Figure KLE.4.3.1 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs, EARS-BE, BE, 2022



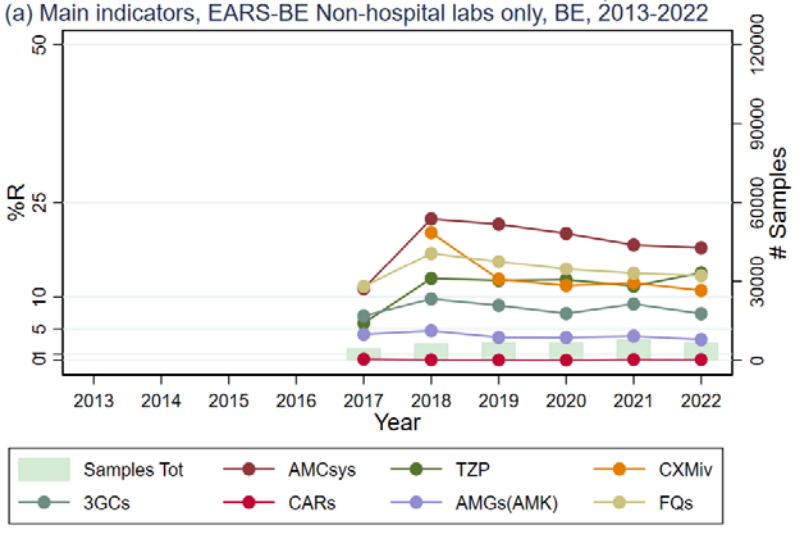
3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs = Aminoglycosides , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones

Figure KLE.4.3.2 *Klebsiella pneumoniae*, Antimicrobial resistance within URINE isolates: HOSP vs NON-HOSP labs (b), EARS-BE, BE, 2022



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 , SXT = Trimethoprim-sulfamethoxazole , FOS_IV = Fosfomycin intravenous , FOS_PO = 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, 2013-2022

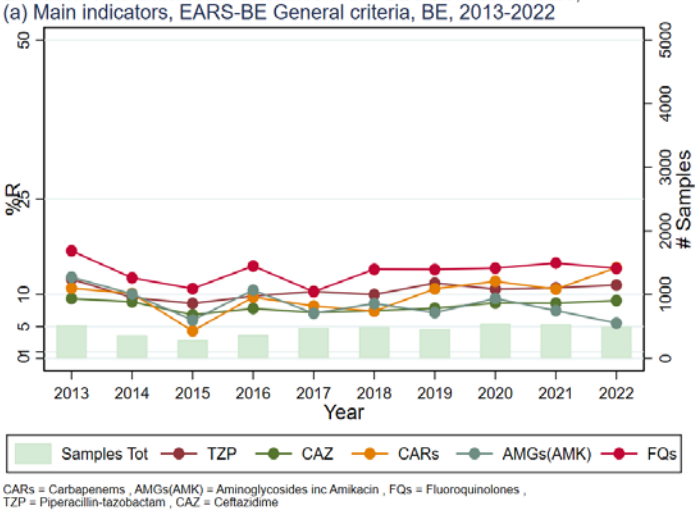


3GCs = 3rd-gen Cephalosporins , CARs = Carbapenems , AMGs(AMK) = Aminoglycosides inc Amikacin , FQs = Fluoroquinolones , AMCsys = Amoxicillin-clavulanic acid, systemic infection , TZP = Piperacillin-tazobactam , CXMiv = Cefuroxim intravenous

RESULTS FOR *P. AERUGINOSA*

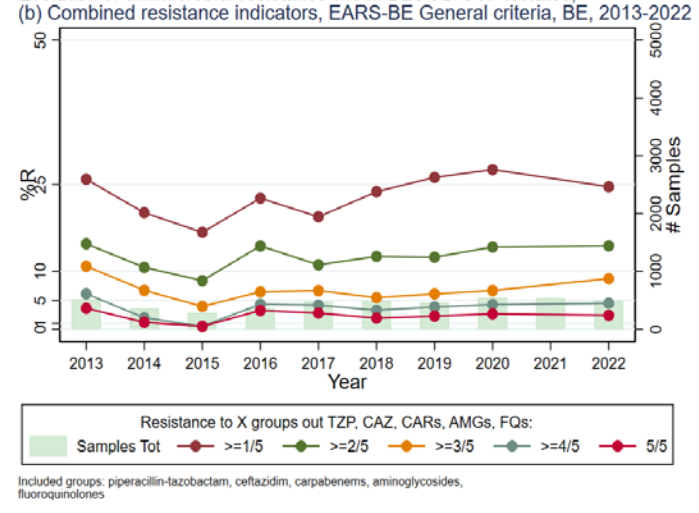
Blood/CSF isolates: We observed 11.5%R (54/470) to piperacillin-tazobactam, 9.1%R (41/453) to ceftazidime, 14.2%R (69/485) to carbapenems, 5.5%R (27/489) to aminoglycosides, and 14.1%R (69/489) to fluoroquinolones (Figure PSE.EVO.0.1.1) .
There has been no clear change in the resistance trends over the last four years for these antimicrobials. We can nevertheless note that the resistance to carbapenems tends to be rising again since 2018 (7.4%R) and has reached its highest level since the beginning of the surveillance in 2013 (11.0%R), while resistance to aminoglycosides, although fluctuating, tends to decrease.
In multidrug-resistant *P. aeruginosa*, no clear four-year trends could be observed.

Figure PSE.EVO.0.1.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



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

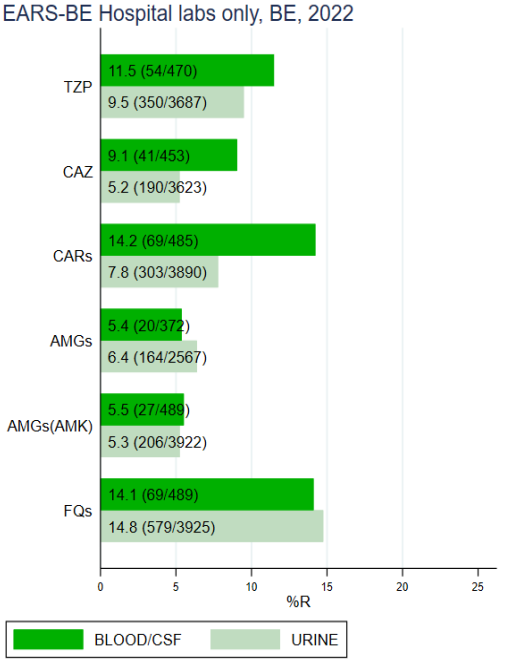
Figure PSE.EVO.0.1.2 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(b) Combined resistance indicators, EARS-BE General criteria, BE, 2013-2022



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

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 (9.5% vs 11.5%R), ceftazidime (5.2% vs 9.1%R) and carbapenems (7.8% vs 14.2%R), while similar levels were observed for fluoroquinolones and aminoglycosides (Figure PSE.COM.1).

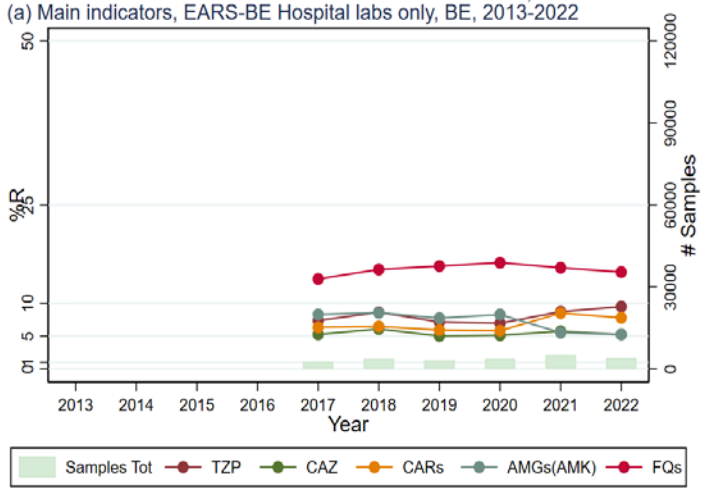
Figure PSE.COM..1 *Pseudomonas aeruginosa*,
Antimicrobial resistance in BLOOD/CSF vs URINE isolat
EARS-BE Hospital labs only, BE, 2022



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

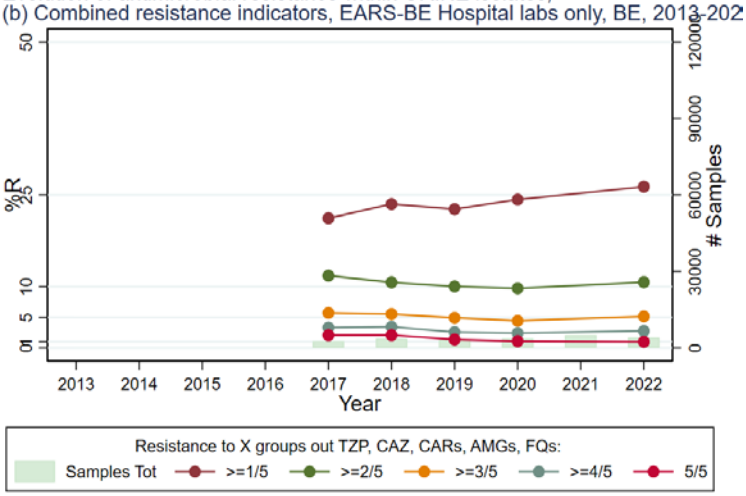
The trends of resistance over the period 2019 - 2022 are increasing for piperacillin-tazobactam (7.2% to 9.5%R) and carbapenems (5.9% to 7.8%R) and decreasing for aminoglycosides (7.7% to 5.3%R).
The number of isolates resistant to at least one antimicrobial group has increased over the past four years, but the combined resistances to several antimicrobial group remain stable (Figure PSE.EVO.1.2.2) .

Figure PSE.EVO.1.2.1 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within URINE isolates,
(a) Main indicators, EARS-BE Hospital labs only, BE, 2013-2022



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

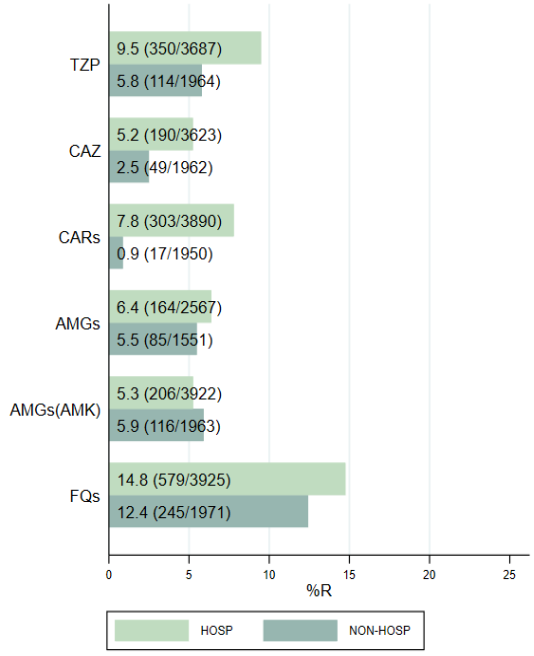
Figure PSE.EVO.1.2.2 *Pseudomonas aeruginosa*,
Evolution of antimicrobial resistance within URINE isolates,
(b) Combined resistance indicators, EARS-BE Hospital labs only, BE, 2013-202



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

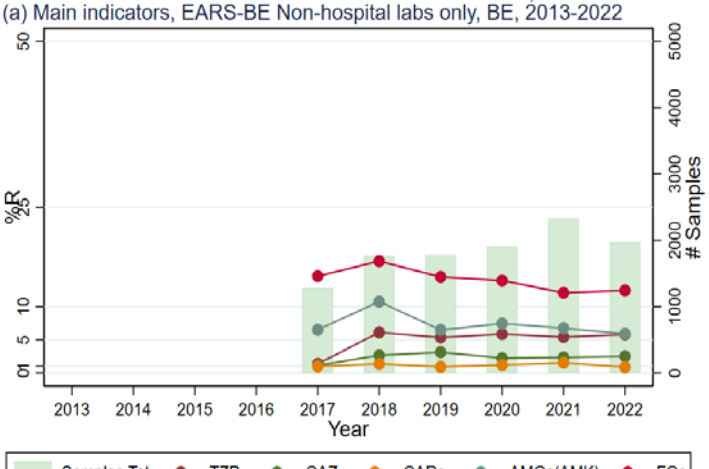
<u>Urine isolates from non-hospital laboratories</u>: Levels of antimicrobial resistance in urine isolates were generally lower in this group compared to those of hospital laboratories, particularly for ceftazidime and carbapenems (Figure PSE.4.3.1). Trends in resistance are relatively stable (Figure PSE.EVO.3.2.1).

Figure PSE.4.3.1 *Pseudomonas aeruginosa*,
Antimicrobial resistance within URINE isolates:
HOSP vs NON-HOSP labs,
EARS-BE, BE, 2022



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, 2013-2022



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

RESULTS FOR *ACINETOBACTER* SPECIES

Blood/CSF isolates: For 2022, results were obtained from 29 labs on 189 isolates. For those, we observed 2.7%R (5/187) to carbapenems, 2.1%R (4/189) to aminoglycosides, and 8%R (15/188) to fluoroquinolones. Over the past four years, resistance trends were relatively stable (Figure ACISPP.EVO.0.1.1).

For *A. baumannii* isolates (results on 26 isolates from 14 labs available), we observed 11.5%R (3/262) to carbapenems, 7.7%R (2/26) to aminoglycosides, and 11.5%R (3/26) to fluoroquinolones (Figure ACIBAU.EVO.0.1.1). Given the very small number of isolates, it is very difficult to detect any meaningful trends. Resistance rates vary greatly from one year to the next, but the absolute numbers of resistant isolates are quite stable (see the statistical report, Table MAIN, for detailed numbers).

Figure ACISPP.EVO.0.1.1 *Acinetobacter* spp,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022

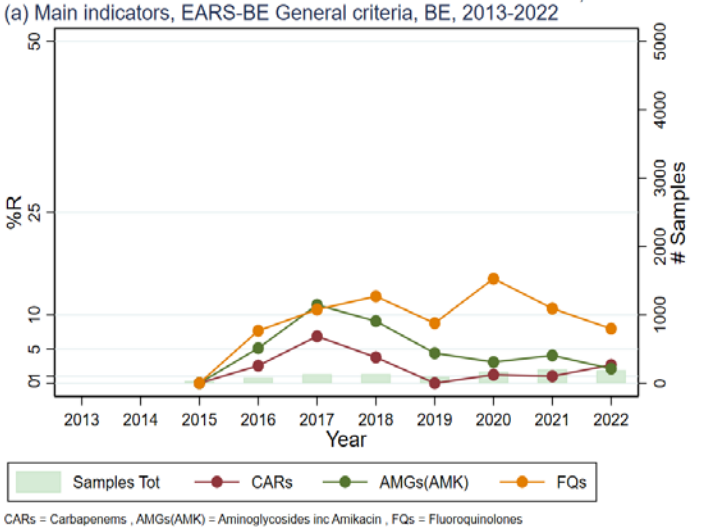
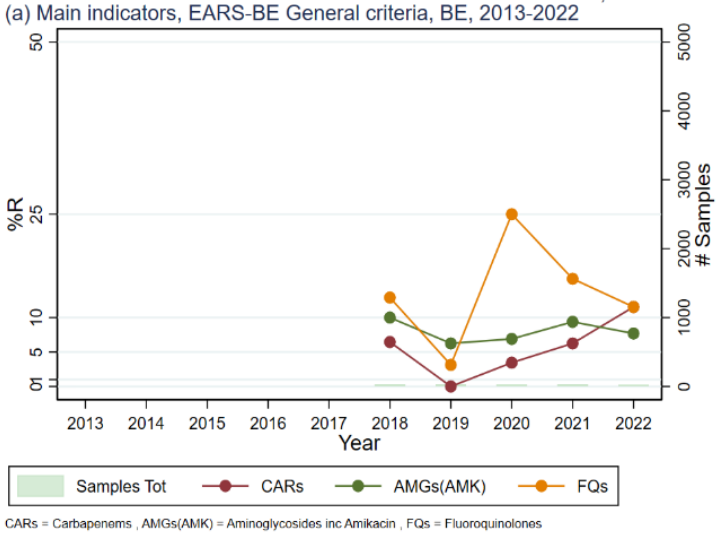


Figure ACIBAU.EVO.0.1.1 *Acinetobacter baumannii*,
Evolution of antimicrobial resistance within BLOOD/CSF isolates,
(a) Main indicators, EARS-BE General criteria, BE, 2013-2022



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) it is likely that not all laboratories rely on broth microdilution for colistin resistance testing, i.e. 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.

Restricting the analysis to hospital laboratories, colistin testing rates on blood/CSF isolates (number of samples tested for colistin resistance/all the samples)varied from 76.4% in *E. coli* (17 labs reporting), 68.7% in *K. pneumoniae* (17 labs reporting), to 70.3% in *P. aeruginosa* (17 labs reporting). In urine isolates, these rates were 56.1% in *E. coli* (19 labs reporting), 58.0% in *K. pneumoniae* (18 labs reporting), and 60.7% in *P. aeruginosa* (18 labs reporting). In *E. coli*, resistance to colistin was 0.7% (11/1529) in blood/CSF isolates in 2022 and 1.1% (199/18258) in urine isolates. In *K. pneumoniae* isolates, resistance was 1.8% (5/283) in blood/CSF isolates and 1.4% (36/2533) in urine isolates. In *P. aeruginosa*, resistance was 2.9% (2/175) in blood/CSF and 3.2% (44/1385) in urine isolates. But again, due to selective testing, these rates are most likely biased upwards.

CONCLUSIONS AND RECOMMENDATIONS

For the EARS-BE 2022 surveillance, 32 hospital laboratories and 2 non-hospital laboratories submitted results for isolates coming from blood or cerebrospinal fluid (CSF) samples, and 32 hospital labs and 4 non-hospital labs submitted results for isolates originating from urine samples. This level of participation is similar to that of 2021 for hospital laboratories, but is lower for the non-hospital laboratories (4 vs 10 in 2021).

All laboratories but one used EUCAST guidelines, and 27 of them used V10 or a more recent version, implementing the new EUCAST definition of the “S” and “I” categories.

When comparing invasive isolates versus urinary tract results, substantial higher rates of insusceptibility have been found for the vast majority of tested bacterium-antimicrobial combinations retrieved from blood/CSF samples. When overall comparing hospital versus non-hospital strains, the hospital isolates tend to show only moderate higher levels of resistance. Exceptions are fluoroquinolone and trimethoprim – sulfamethoxazole resistance in *P. mirabilis* and cefuroxime resistance in coliforms *(E. coli/K. pneumoniae)* both from urinary tract samples.

In *S. aureus* isolates from blood/CSF samples, resistance to methicillin (MRSA, 4.4%) and fluoroquinolones (7.3%) remains stable compared to 2021, remaining at the lowest level observed since the start of EARS-BE surveillance in 2000.

In enterococci, there was no resistance to vancomycin or teicoplanin, and only very low resistance to linezolid or aminopenicillins in *E. faecalis* in blood/CSF samples. In urine samples, the resistances to those antimicrobials were all very low. *E. faecium* displayed a decrease in resistance to vancomycin and teicoplanin (1.4% and 1.1%R, respectively) in blood/CSF samples, and similar levels in urine samples.

In *S. pneumoniae* blood/CSF isolates, the percentage of penicillin non-wild type was 14.1 %, a decrease for the first time since 2018. Resistance to 3CG and fluoroquinolones remains very low, and the resistance to macrolide returned to the pre-COVID19 level.

In *E. coli* blood/CSF isolates, resistance to amoxicillin-clavulanic acid has returned to 2019 levels, the highest since 2013. On the other hand, resistances to the other antimicrobials are stable or decreasing, leading to a decrease of the multidrug resistance rates as well. In urinary samples, the rise of amoxicillin-clavulanic acid resistance was less pronounced, the rest was also decreasing, including multidrug resistance.
In *K. pneumoniae* blood/CSF isolates, except for a decrease in cefuroxime resistance over the past two years, no clear trends of resistance could be observed. However, in urine *K. pneumoniae* isolates from hospital labs, decreasing trends in resistance for many antimicrobials were observed.
In *P. mirabilis*, resistance against the main indicators were decreasing over the past 4 years, and resistance to other antimicrobials used for treatment of UTI were stable or slightly increasing. Resistance to carbapenems was almost not observed in *E. coli* and very low in *K. pneumoniae* from blood/CSF samples, and in *P. mirabilis* from urine samples

P. aeruginosa blood/CSF isolates showed resistance to almost all studied antibiotic groups (piperacillin-tazobactam, ceftazidime, carbapenems, aminoglycosides, fluoroquinolones). Although it remains difficult to detect meaningful trends of resistance due to wide fluctuation over time, resistance to carbapenems tends to increase since 2018 (from 7.4% in 2018 to 14.2%R in 2022). In urine isolates from hospital labs, an increasing trend was detectable in resistance to piperacillin-tazobactam and carbapenems, and a decreasing trend in resistance to aminoglycosides. In urine isolates from non-hospital laboratories, resistance to fluoroquinolone showed a slight decrease since 2018.

In *Acinetobacter* spp blood/CSF isolates (including those of *A. baumannii*), with 2022 results being available for 189 isolates reported by 29 laboratories, resistance levels remained stable, with resistance to carbapenems remaining very 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 to several antimicrobials were observed, including amoxicillin-clavulanic acid and fluoroquinolones. Compared to previous years, the number of participating non-hospital laboratories however decreased, which can influence the results.

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*.

Participation to EARS-BE was stable over the last couple of years. However the administrative burden of registration remains high. Current initiatives for the development of national EARS-BE surveillance focus on harmonizing data collection with other AMR and healthcare-associated infections surveillance[10] in order to avoid parallel data flows, to reduce the administrative burden, and increase participation to EARS-BE surveillance[11]. 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.
To this end, for the past 2 years there has been an EARS/AMR option in EARS-BE surveillance, which includes the collection of additional data enabling the comparison of data collected via EARS with that collected via the mandatory national NSIH-AMR surveillance[12] for labs that choose this option. This helps to identify mismatches and harmonize the two types of monitoring. In 2022, five laboratories participated in the EARSBE-AMR data collection. Major discrepancies are sometimes observed, and more in-depth analyses are needed to explain the differences found and how to correct them for the harmonization.

Since 2017, EARS-BE 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, EARS-BE results on uropathogens might only have limited clinical relevance. A new project focusing on *clinical surveillance* of AMR within primary care (SARPRIC-UTI[13]) has started in 2023. Preliminary results are expected by the end of 2024. It will give the opportunity to validate EARS-BE results on urine isolates.

REPORT APPROVAL OF VARIOUS ENTITIES

Table. Dates that the different entities were invited for review and sent their comments

Entity	Invited for review	Comments received
Sciensano	NA	23/04/2024
NRC for resistant Gram-negative bacilli	26/04/2024	None received so far
NRC for resistant enterococci	26/04/2024	None received so far
NRC for *Staphylococcus aureus* and other S*taphylocci*	26/04/2024	None received so far
NRC *Streptococcus pneumoniae*	26/04/2024	30/04/2024
BAPCOC	31/05/2024	None received so far
TC-MDRO	31/05/2024	None received so far
Regional authorities	31/05/2024	None received so far

**includes passive approval*

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