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HEALTHCARE-ASSOCIATED INFECTIONS AND ANTIMICROBIAL RESISTANCE

SURVEILLANCE OF ANTIMICROBIAL RESISTANT BACTERIA IN BELGIAN HOSPITALS

Report 2019 - 2020

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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EXECUTIVE SUMMARY

Introduction

Antibiotics have been one of the most important life-saving drugs, but unnecessary and inappropriate use reduces their ability to treat infections. Some bacteria have become tolerant to certain antibiotics or have found ways to break them down. This is called acquired antimicrobial resistance (AMR). The World Health Organization recognizes AMR as one of the top ten global health threats facing humanity.

In order to follow up the national evolution of the resistance proportion and incidence of multidrug resistant organisms (MDRO) in Belgian hospitals, Sciensano collects and analyzes AMR surveillance. By Royal Decree, all Belgian acute care hospitals mandatorily have to participate in the surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) and multiresistant Gram-negative bacilli (MRGN). The surveillance of vancomycin-resistant enterococci (VRE) is one of four additional programs from which hospitals must choose one for participation.

The current report presents the 2019 and 2020 results of the three surveillance programs and describes trends in AMR in Belgian acute and/or chronic care hospitals.

Because of the exceptional work load circumstances due to the COVID-19 pandemic, the Belgian Antibiotic Policy Coordination Committee declared that there was no legal obligation for hospitals to participate in the national surveillances (incl. MRSA, MRGN and VRE) in 2020 (collecting 2019 data) and 2021 (collecting 2020 data). For this reason and because of delayed data delivery, it was decided to combine the 2019 annual report with the 2020 report. When interpreting the results, it is important to keep in mind that the 2019 surveillance findings presented in this report reflect the pre-pandemic period. The 2020 data are however largely impacted by the altered hospital activities due to the COVID-19 crisis.

Methods

Surveillance data (year 2019 and 2020) were collected retrospectively in the following year by the microbiology laboratories and/or the infection prevention and control teams of the participating hospitals. It concerned data aggregated at hospital level. Hospitals could either provide annual figures or data for one semester, except for the VRE surveillance for which only annual data were allowed.

Data originating from acute and chronic care hospitals were presented separately. Acute care hospitals with an average length of stay of ≥ 16 days were classified as chronic care hospitals.

Following microorganisms and resistances were explored:

- *Staphylococcus aureus (S. aureus)* resistant to methicillin or oxacillin
- *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) non-susceptible* to 3rd generation cephalosporins (3GC I/R) and/or to meropenem (meropenem I/R)
- Meropenem I/R in *Acinetobacter baumannii* (*A. baumannii*)
- Multidrug-resistant (MDR) *Pseudomonas aeruginosa* (*P. aeruginosa*), i.e. non-susceptible* (2019) or resistant (2020) to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin or levofloxacin), aminoglycosides (gentamicin, tobramycin or amikacin), carbapenems (meropenem or imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime or cefepime)
- *Enterococcus faecalis* (*E. faecalis*) and *E. faecium* resistant to vancomycin (vanco-R)

** Non-susceptibility = reduced suceptibility (I) or resistance (R) (NB: EUCAST criterium for the "I" category before 2019)*

Only hospitals providing Type D data (i.e. de-duplication in which each patient is counted only once per period of hospitalisation and bacteria) were included in the analyses. In this report, analyses were solely based on data originating from clinical samples (unless otherwise stipulated). All sample types (e.g. blood, urine) were included. Faeces samples were considered as screening samples and were thus excluded from the category of clinical samples.

The potential healthcare-associated character was assessed for MRSA only. Healthcare-associated MRSA was defined as either colonization or infection with MRSA considered to be acquired in the hospital (first positive sample for MRSA collected more than 48 hours after admission), not present on admission and not known from the patient's history (in the past 12 months).

For each species, a resistance proportion, an incidence (number of cases per 1 000 hospital admissions) and/or incidence density (cases per 1 000 patient days) were calculated.
Historical data were used to present the evolution of resistance proportions and incidence (densities). We fitted a negative binomial regression model with hospital as cluster and year as fixed effect to explore and assess statistically significant ($p<0.05$) changes in the incidence. To assess whether trends observed in resistance proportions were statistically significant ($p<0.05$), we used linear regression with hospital as cluster.
Data were analysed in STATA 16 (StataCorp LP, College Station, Texas, USA) and presented by region and level of specialty care within the hospital. Differences were considered significant if $p<0.05$.

Results

Table 1 presents the resistance proportion and incidence per 1 000 admissions of the bacteria under surveillance (clinical samples only) in Belgian acute care hospitals in 2019 and 2020. In these years, 85.3% (n=87/102) and 94.1% (n=96/102) of all acute care hospital administrative groups (mergers) participated in the MRSA and MRGN surveillance with at least one hospital site, respectively. Despite the optional character of the VRE surveillance, 84.3% (n=86/102) and 91.2% (n=93/102) of all mergers participated with at least one hospital site in 2019 and 2020, respectively.

Since 2004, a significantly decreasing trend in the resistance proportion (-1.21% per year; $p<0.001$) and incidence (IRR=0.920, 95%CI: 0.917-0.923, $p<0.001$) of MRSA can be observed. The decrease in incidence was however not statistically significant between 2018 and 2020 (IRR=0.909, 95%CI: 0.791-1.045; p=0.179).
Due to the combined efforts of the infection prevention and control teams and a whole range of actions, the proportion of healthcare-associated MRSA on the total number of MRSA dropped from 78.8% in 1994 (start of the surveillance) to 43.1% in 2006 (year in which the surveillance became mandatory). Currently, the proportion is at its lowest: 22.4% in 2019 and 21.7% in 2020.

No significant trend (2014-2020) can be observed in the resistance proportion (-0.13% per year; p=0.292) and incidence (IRR=0.981, 95%CI: 0.920-1.047; p=0.569) of vanco-R *E. faecium*.

Between 2014 and 2020, a significant change in the resistance proportion (+0.25% per year; p=0.001) and incidence (IRR=1.018, 95%CI: 1.002-1.034; p=0.024) of 3GC I/R *E. coli* can be noted. Moreover, a small but significant increase in the resistance proportion (+0.01% per year; $p<0.001$) and incidence (IRR=1.140, 95%CI: 1.069-1.215; $p<0.001$) of meropenem I/R *E. coli* can also be observed between 2015 and 2020.

Table 1. Resistance proportion and incidence per 1 000 admissions of the bacteria included in the surveillance of antimicrobial resistance (clinical samples only), Belgian acute care hospitals, 2019 and 2020

		2019				2020			
		Resistance proportion (%)		Incidence per 1 000 admissions		Resistance proportion (%)		Incidence per 1 000 admissions	
		Crude	Median	Crude	Median	Crude	Median	Crude	Median
Staphylococcus aureus	Methicillin R	12.4	9.9	2.30	1.81	10.6	9.0	1.88	1.53
Healthcare-associated *Staphylococcus aureus*	Methicillin R	21.2	25.0	0.49	0.41	21.0	23.3	0.39	0.33
Enterococcus faecium	Vancomycin R	2.0	0.0	0.10	0.00	1.7	0.0	0.09	0.00
Enterococcus faecalis	Vancomycin R	0.0	0.0	0.01	0.00	0.1	0.0	0.01	0.00
Escherichia coli	3GC I/R	9.9	10.1	4.95	4.86	9.2	9.1	5.22	5.32
	Meropenem I/R	0.1	0.1	0.07	0.02	0.1	0.0	0.06	0.00
Klebsiella pneumoniae	3GC I/R	22.7	21.1	2.64	2.16	21.3	19.7	2.67	1.95
	Meropenem I/R	2.1	1.1	0.25	0.10	1.8	0.8	0.22	0.08
Acinetobacter baumannii	Meropenem I/R	6.7	0.0	0.03	0.00	7.3	0.0	0.03	0.00
Pseudomonas aeruginosa	MDR	6.7	4.3	0.73	0.44	6.7	4.2	0.77	0.40

R = resistant, I/R = intermediate susceptibility or resistant, 3GC = 3rd generation cephalosporins, MDR = reduced susceptibility (2019) or resistance (2020) to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin or levofloxacin), aminoglycosides (gentamicin, tobramycin or amikacin), carbapenems (meropenem or imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime or cefepime)

Between 2014 and 2020, the resistance proportion (+0.82% per year; p=0.002) and incidence (IRR=1.060, 95%CI: 1.040-1.080; p<0.001) of 3GC I/R *K. pneumoniae* significantly increased. Since 2018, a significant decrease in the resistance proportion (-1.62% per year; p<0.001) and a non-significant decline in incidence (IRR=0.961, 95%CI: 0.924-1.000; p=0.055) can however be observed.
A non-significant increase in the resistance proportion (+0.07% per year; p=0.295) and incidence (IRR=1.025, 95%CI: 0.977-1.075; p=0.311) of meropenem I/R *K. pneumoniae* can be observed between 2015 and 2020. Since 2018, there is however a significant decrease in the resistance proportion (-0.35% per year; p=0.010) and a non-significant decline in the incidence (IRR=0.919, 95%CI: 0.820-1.029; p=0.143).

Since 2013, no significant change in the evolution of the resistance proportion of meropenem I/R *A. baumannii* can be observed (-0.18%; p=0.545). The incidence however significantly decreased between 2013 and 2020 (IRR=0.912, 95%CI: 0.860-0.966; p=0.002).

Definition changes in 2017, 2018 and 2020 make it difficult to interpret the evolution of MDR *P. aeruginosa.* Since 2018, there is a stabilization in the resistance proportion (-0.08%; p=0.753) and incidence (IRR=0.941, 95%CI: 0.868-1.020; p=0.140).

Table 2 shows the resistance proportion and incidence density per 1 000 patient days of the bacteria under surveillance in Belgian chronic care hospitals in 2019 and 2020. These numbers should however be interpreted with caution as the number of participating chronic care hospitals was low (≤ 12).

Table 2. Resistance proportion and incidence density per 1 000 patient days of the bacteria included in the surveillance of antimicrobial resistance (clinical samples only), Belgian chronic care hospitals, 2019 and 2020

		2019				2020			
		Resistance proportion (%)		Incidence density per 1 000 patient days		Resistance proportion (%)		Incidence density per 1 000 patient days	
		Crude	Median	Crude	Median	Crude	Median	Crude	Median
Staphylococcus aureus	Methicillin R	14.3	8.5	0.16	0.10	16.2	13.5	0.16	0.06
Healthcare-associated *Staphylococcus aureus*	Methicillin R	53.8	49.3	0.09	0.07	23.1	6.3	0.04	0.01
Enterococcus faecium	Vancomycin R	0.0	0.0	0.00	0.00	0.0	0.0	0.00	0.00
Enterococcus faecalis	Vancomycin R	0.0	0.0	0.00	0.00	0.0	0.0	0.00	0.00
Escherichia coli	3GC I/R	8.4	5.6	0.27	0.18	11.1	6.6	0.33	0.10
	Meropenem I/R	0.4	0.0	0.01	0.00	0.0	0.0	0.00	0.00
Klebsiella pneumoniae	3GC I/R	23.1	12.3	0.25	0.14	27.2	21.7	0.24	0.12
	Meropenem I/R	2.5	1.7	0.03	0.02	3.1	1.3	0.03	0.02
Acinetobacter baumannii	Meropenem I/R	11.8	0.0	0.00	0.00	10.0	0.0	0.00	0.00
Pseudomonas aeruginosa	MDR	4.4	3.2	0.04	0.02	6.6	2.9	0.05	0.02

R = resistant, I/R = intermediate susceptibility or resistant, 3GC = 3rd generation cephalosporins, MDR = reduced susceptibility (2019) or resistance (2020) to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin or levofloxacin), aminoglycosides (gentamicin, tobramycin or amikacin), carbapenems (meropenem or imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime or cefepime)

Discussion

This report presents the 2019 and 2020 results of three national surveillance programs on AMR, i.e. the surveillance of (1) MRSA, (2) VRE and (3) MRGN. To our knowledge, our national AMR surveillance is one of the few programs that does not merely focus on invasive samples (e.g. cerebrospinal fluid and blood samples), but includes both invasive and non-invasive sample types (e.g. urine samples).

Although there was no legal obligation to participate due to the COVID-19 crisis, more than 85% of all mergers succeeded (with or without a considerable delay) in transmitting MRSA and MRGN data. Moreover, the participation rate for the VRE surveillance was above 84% in the relevant years. When interpreting the results, it is important to keep in mind that the 2019 findings reflect the pre-pandemic period, while the 2020 data can be impacted by altered hospital activities owing to the crisis.

Since 2004, a significantly decreasing trend in the resistance proportion and incidence of MRSA can be observed. No significant trend (2014-2020) can be observed in the resistance proportion and incidence of vanco-R *E. faecium*. Likewise, no noteworthy trend in the resistance proportion of meropenem I/R *A. baumannii* can be observed since 2013. The incidence however significantly decreased in the same time span. Since 2018, there seems to be a stabilization in the resistance proportion and incidence of MDR *P. aeruginosa*. Between 2014 and 2020, the resistance proportion and incidence of 3GC I/R *E. coli and K. pneumoniae* significantly increased.

The changes we observe in the 2020 data are in all likelihood influenced by the COVID-19 crisis and the associated altered hospital activities. Also indirectly ambulant care has altered and might have influenced the patient population in hospitals. More research is required in this area to find causal inference, but it is reasonable to believe that the answer will be multifactorial. There were significant changes in population-level behaviour (e.g. social distancing) and healthcare provision (reduced healthcare seeking and less referrals). Also within the hospitals many changes occurred such as enhanced infection prevention and control programs with renforcement

of hand hygiene and use of personal protective equipment, change in patient mix and cancellations of elective and non-urgent surgeries.

In 2019 and 2020, a limited number of hospitals participated in a pilot study and tested a harmonized AMR/EARS-BE protocol. For the AMR surveillance, this will imply abandoning an aggregated data collection and going for the collection of detailed laboratory data at isolate/antimicrobial susceptility testing level. This type of data collection will result in more detailed and standardized data as data validation will be possible and interpretation discrepancies will be minimized. Data analyses are pending and results will be included in the next report.

SAMENVATTING

Inleiding

Antibiotica zijn één van de belangrijkste levensreddende geneesmiddelen, maar onnodig en onjuist gebruik vermindert hun vermogen om infecties te behandelen. Sommige bacteriën zijn tolerant geworden voor bepaalde antibiotica of hebben manieren gevonden om ze af te breken. Dit wordt verworven antimicrobiële resistentie (AMR) genoemd. De Wereldgezondheidsorganisatie beschouwt AMR als één van de tien grootste bedreigingen voor de volksgezondheid.

Om de nationale evolutie van het resistentiepercentage en de incidentie van multidrug resistente organismen (MDRO) in Belgische ziekenhuizen op te volgen, verzamelt en analyseert Sciensano surveillancegegevens over AMR. Bij Koninklijk Besluit moeten alle Belgische acute ziekenhuizen verplicht deelnemen aan de surveillance van meticilline resistente *Staphylococcus aureus* (MRSA) en van multiresistente Gram-negatieve bacillen (MRGN). De surveillance van vancomycine resistente enterokokken (VRE) is één van de vier aanvullende programma's waaruit ziekenhuizen er één voor deelname moeten kiezen.

Het huidige rapport toont de resultaten voor 2019 en 2020 met betrekking tot de drie surveillanceprogramma's en beschrijft trends in AMR in Belgische acute en/of chronische ziekenhuizen.

Door de uitzonderlijke werklast als gevolg van de COVID-19 pandemie verklaarde de Belgische Commissie voor de Coördinatie van het Antibioticabeleid (BAPCOC) dat er in 2020 (gegevensverzameling voor 2019) en 2021 (gegevensverzameling voor 2020) geen wettelijke verplichting voor de ziekenhuizen was om deel te nemen aan de nationale surveillances (incl. MRSA, MRGN en VRE). Om deze reden en vanwege de laattijdige aanlevering van gegevens werd besloten om het jaarrapport voor 2019 te combineren met dat voor 2020. Bij de interpretatie van de resultaten is het echter belangrijk om in gedachten te houden dat de surveillanceresultaten van 2019 de pre-pandemische periode weerspiegelen. De gegevens van 2020 werden dan weer grotendeels beïnvloed door de gewijzigde ziekenhuisactiviteiten als gevolg van de COVID-19 crisis.

Methodologie

De surveillancegegevens (jaar 2019 en 2020) werden in het daaropvolgende jaar retrospectief verzameld door de laboratoria voor microbiologie al dan niet in samenwerking met de infectiepreventie en -bestrijdingsteam van de deelnemende ziekenhuizen. Het betrof geaggregeerde gegevens op ziekenhuisniveau. Ziekenhuizen konden ofwel jaarcijfers ofwel gegevens voor één semester verstrekken, behalve voor de VRE surveillance waarvoor alleen jaargegevens werden toegestaan.

Gegevens afkomstig van acute en chronische ziekenhuizen werden afzonderlijk voorgesteld. Acute ziekenhuizen met een gemiddelde verblijfsduur van ≥ 16 dagen werden als chronische ziekenhuizen beschouwd.

De volgende micro-organismen en resistenties werden onderzocht:

- *Staphylococcus aureus (S. aureus)* resistent tegen meticilline of oxacilline
- *Escherichia coli* (*E. coli*) en *Klebsiella pneumoniae* (*K. pneumoniae*) niet gevoelig* voor 3de generatie cefalosporines (3GC I/R) en/of voor meropenem (meropenem I/R)
- *Acinetobacter baumannii* (*A. baumannii*) niet gevoelig* voor meropenem (meropenem I/R)
- Multiresistente (MDR) *Pseudomonas aeruginosa* (*P. aeruginosa*), d.w.z. niet gevoelig* (2019) of resistent (2020) tegen minstens drie van de volgende antibioticaklassen: fluorochinolonen (ciprofloxacine of

levofloxacine), aminoglycosiden (gentamicine, tobramycine of amikacine), carbapenems (meropenem of imipenem), 3de en/of 4de generatie cefalosporines (ceftazidime of cefepime).

- *Enterococcus faecalis* (*E. faecalis*) en *E. faecium* resistent tegen vancomycine (vanco-R)

** Niet gevoelig = verminderde gevoeligheid (I) of resistentie (R) (NB: EUCAST-criterium voor de categorie "I" vóór 2019).*

Alleen ziekenhuizen die type D-gegevens (d.w.z. ontdubbeling waarbij elke patiënt slechts éénmaal per hospitalisatieperiode en per bacterie geteld wordt) verstrekten, werden in de analyses opgenomen. In dit rapport werden alleen gegevens afkomstig van klinische stalen in rekening gebracht (tenzij anders gespecificeerd). Alle staaltypes (vb. bloed, urine) werden geïncludeerd, met uitzondering van stoelgangstalen die als screeningsstalen beschouwd en bijgevolg ook geëxcludeerd moesten worden

Het potentieel zorggerelateerde karakter werd enkel voor MRSA beoordeeld. Zorggerelateerde MRSA werd gedefinieerd als kolonisatie of infectie met MRSA die geacht werd in het ziekenhuis verworven te zijn (eerste positief MRSA staal meer dan 48 uur na opname), niet aanwezig bij opname en geen gekend dragerschap van of infectie met MRSA in de voorgeschiedenis van de patiënt (tijdens de voorbije 12 maanden).

Voor elke bacterie werden de resistentieproportie, een incidentie (aantal gevallen per 1 000 ziekenhuisopnames) en/of een incidentiedensiteit (aantal gevallen per 1 000 hospitalisatiedagen) berekend.
Historische gegevens werden gebruikt om de evolutie van de resistentieproportie en de incidentie(densiteit) weer te geven. Een negatief binomiaal regressiemodel werd toegepast met het ziekenhuis als cluster en het jaar als vast effect om statistisch significante veranderingen ($p<0,05$) in de incidentie te onderzoeken en te beoordelen. Om na te gaan of de waargenomen trends in de resistentieproportie statistisch significant ($p<0,05$) waren, werd een lineaire regressie met het ziekenhuis als cluster gebruikt.
De gegevens werden geanalyseerd in STATA 16 (StataCorp LP, College Station, Texas, USA) en voorgesteld per regio en per specialisatietype van het ziekenhuis.

Resultaten

Tabel 1 geeft de resistentieproportie en de incidentie per 1 000 opnames van de bacteriën die deel uitmaken van de AMR surveillance (alleen klinische monsters) in de Belgische acute ziekenhuizen in 2019 en 2020 weer. In deze jaren namen respectievelijk 85,3% (n=87/102) en 94,1% (n=96/102) van alle acute ziekenhuisbestuursgroepen (fusies) met minstens één ziekenhuissite deel aan de MRSA en MRGN surveillance. Ondanks het optionele karakter van de VRE surveillance nam 84,3% (n=86/102) en 91,2% (n=93/102) van alle fusies in 2019 en 2020 met minstens één ziekenhuissite deel.

Sinds 2004 kan een significant dalende trend in de resistentieproportie (-1,21% per jaar; $p<0,001$) en de incidentie (IRR=0,920, 95%CI: 0,917-0,923; $p<0,001$) van MRSA worden waargenomen. De afname van de incidentie was echter niet statistisch significant tussen 2018 en 2020 (IRR=0,909, 95%CI: 0,791-1,045; p=0,179).
Dankzij de gezamenlijke inspanningen van de teams voor infectiepreventie en -bestrijding en een hele reeks acties is het aandeel van zorggerelateerde MRSA op het totale aantal MRSA gedaald van 78,8% in 1994 (begin van de surveillance) tot 43,1% in 2006 (jaar waarin de surveillance verplicht werd). Momenteel is het aandeel het laagst: 22,4% in 2019 en 21,7% in 2020.

Er kan geen significante trend (2014-2020) in de resistentieproportie (-0,13% per jaar; p=0,292) en de incidentie (IRR=0,981, 95%CI: 0,920-1,047; p=0,569) van vanco-R *E. faecium* worden waargenomen.

Tussen 2014 en 2020 kan echter wel een significante verandering in de resistentieproportie (+0,25% per jaar; p=0,001) en de incidentie (IRR=1,018, 95%CI: 1,002-1,034; p=0,024) van 3GC I/R *E. coli* worden vastgesteld.

Bovendien kan tussen 2015 en 2020 ook een kleine maar significante toename van de resistentieproportie (+0,01% per jaar; p<0,001) en de incidentie (IRR=1,140, 95%CI: 1,069-1,215; p<0,001) van meropenem I/R *E. coli worden waargenomen*.

Tabel 1. Resistentieproportie en incidentie per 1 000 opnames van de bacteriën opgenomen in de surveillance van antimicrobiële resistentie (alleen klinische stalen), Belgische acute ziekenhuizen, 2019 en 2020

		2019				2020			
		Resistentieproportie (%)		Incidentie per 1 000 opnames		Resistentieproportie (%)		Incidentie per 1 000 opnames	
		Crude	Mediaan	Crude	Mediaan	Crude	Mediaan	Crude	Mediaan
Staphylococcus aureus	Methicillin R	12.4	9.9	2.30	1.81	10.6	9.0	1.88	1.53
Zorggerelateerde *Staphylococcus aureus*	Methicillin R	21.2	25.0	0.49	0.41	21.0	23.3	0.39	0.33
Enterococcus faecium	Vancomycin R	2.0	0.0	0.10	0.00	1.7	0.0	0.09	0.00
Enterococcus faecalis	Vancomycin R	0.0	0.0	0.01	0.00	0.1	0.0	0.01	0.00
Escherichia coli	3GC I/R	9.9	10.1	4.95	4.86	9.2	9.1	5.22	5.32
	Meropenem I/R	0.1	0.1	0.07	0.02	0.1	0.0	0.06	0.00
Klebsiella pneumoniae	3GC I/R	22.7	21.1	2.64	2.16	21.3	19.7	2.67	1.95
	Meropenem I/R	2.1	1.1	0.25	0.10	1.8	0.8	0.22	0.08
Acinetobacter baumannii	Meropenem I/R	6.7	0.0	0.03	0.00	7.3	0.0	0.03	0.00
Pseudomonas aeruginosa	MDR	6.7	4.3	0.73	0.44	6.7	4.2	0.77	0.40

R = resistent, I/R = intermediaire gevoeligheid of resistentie, 3GC = 3de generatie cefalosporines, MDR = niet gevoelig (verminderde gevoeligheid (I) of resistentie (R); 2019) of resistentie (2020) voor minstens drie van de volgende antibioticaklassen: fluorochinolonen (ciprofloxacine of levofloxacine), aminoglycosiden (gentamicine, tobramycine of amikacine), carbapenems (meropenem of imipenem), 3de en/of 4de generatie cefalosporines (ceftazidime of cefepime)

Tussen 2014 en 2020 namen de resistentieproportie (+0,82% per jaar; p=0,002) en de incidentie (IRR=1,060, 95%CI: 1,040-1,080; p<0,001) van 3GC I/R *K. pneumoniae* significant toe. Sinds 2018 kan echter een significante daling van het resistentieaandeel (-1,62% per jaar; p<0,001) en een niet-significante daling van de incidentie (IRR=0,961, 95%CI: 0,924-1,000; p=0,055) worden waargenomen.
Tussen 2015 en 2020 kan een niet-significante toename van de resistentieproportie (+0,07% per jaar; p=0,295) en de incidentie (IRR=1,025, 95%CI: 0,977-1,075; p=0,311) van meropenem I/R *K. pneumoniae* worden waargenomen. Sinds 2018 is er echter een significante daling van de resistentieproportie (-0,35% per jaar; p=0,010) en een niet-significante daling van de incidentie (IRR=0,919, 95%CI: 0,820-1,029; p=0,143).

Sinds 2013 kan er geen significante verandering in de evolutie van de resistentieproportie van meropenem I/R *A. baumannii* worden waargenomen (-0,18%; p=0,545). De incidentie nam echter significant af tussen 2013 en 2020 (IRR=0,912, 95%CI: 0,860-0,966; p=0,002).

Definitiewijzigingen in 2017, 2018 en 2020 maken het moeilijk om de evolutie van MDR *P. aeruginosa te* interpreteren. Sinds 2018 is er een stabilisatie in de resistentieproportie (-0,08%; p=0,753) en de incidentie (IRR=0,941, 95%CI: 0,868-1,020; p=0,140).

Tabel 2 toont de resistentieproportie en de incidentiedensiteit per 1 000 hospitalisatiedagen van de bacteriën geïncludeerd in de surveillance (alleen klinische stalen) in Belgische chronische ziekenhuizen in 2019 en 2020. Deze cijfers moeten echter met enige voorzichtigheid worden geïnterpreteerd, aangezien het aantal deelnemende chronische ziekenhuizen beperkt was (≤ 12).

Tabel 2. Resistentieproportie en incidentiedensiteit per 1 000 hospitalisatiedagen van de bacteriën opgenomen in de surveillance van antimicrobiële resistentie (alleen klinische stalen), Belgische chronische ziekenhuizen, 2019 en 2020

		2019				2020			
		Resistentieproportie (%)		Incidentie per 1 000 opnames		Resistentieproportie (%)		Incidentie per 1 000 opnames	
		Crude	Mediaan	Crude	Mediaan	Crude	Mediaan	Crude	Median
Staphylococcus aureus	Methicillin R	14.3	8.5	0.16	0.10	16.2	13.5	0.16	0.06
Healthcare-associated *Staphylococcus aureus*	Methicillin R	53.8	49.3	0.09	0.07	23.1	6.3	0.04	0.01
Enterococcus faecium	Vancomycin R	0.0	0.0	0.00	0.00	0.0	0.0	0.00	0.00
Enterococcus faecalis	Vancomycin R	0.0	0.0	0.00	0.00	0.0	0.0	0.00	0.00
Escherichia coli	3GC I/R	8.4	5.6	0.27	0.18	11.1	6.6	0.33	0.10
	Meropenem I/R	0.4	0.0	0.01	0.00	0.0	0.0	0.00	0.00
Klebsiella pneumoniae	3GC I/R	23.1	12.3	0.25	0.14	27.2	21.7	0.24	0.12
	Meropenem I/R	2.5	1.7	0.03	0.02	3.1	1.3	0.03	0.02
Acinetobacter baumannii	Meropenem I/R	11.8	0.0	0.00	0.00	10.0	0.0	0.00	0.00
Pseudomonas aeruginosa	MDR	4.4	3.2	0.04	0.02	6.6	2.9	0.05	0.02

R = resistent, I/R = intermediaire gevoeligheid of resistentie, 3GC = 3de generatie cefalosporines, MDR = niet gevoelig (verminderde gevoeligheid (I) of resistentie (R); 2019) of resistentie (2020) voor minstens drie van de volgende antibioticaklassen: fluorochinolonen (ciprofloxacine of levofloxacine), aminoglycosiden (gentamicine, tobramycine of amikacine), carbapenems (meropenem of imipenem), 3de en/of 4de generatie cefalosporines (ceftazidime of cefepime)

Discussie

Dit rapport toont de resultaten van 2019 en 2020 van de drie nationale AMR surveillanceprogramma's, namelijk de surveillance van (1) MRSA, (2) VRE en (3) MRGN. Voor zover wij weten, is onze nationale AMR surveillance één van de weinige programma's die zich niet alleen richten op invasieve monsters (vb. cerebrospinaal vocht en bloed), maar ook niet-invasieve staaltypes (vb. urinestalen) includeert.

Hoewel er als gevolg van de COVID-19-crisis geen wettelijke verplichting tot deelname bestond, slaagde meer dan 85% van alle fusies erin (al dan niet met aanzienlijke vertraging) MRSA en MRGN gegevens in te dienen. Bovendien lag het deelnamepercentage voor de VRE surveillance in de betrokken jaren boven 84%. Bij de interpretatie van de resultaten moet rekening gehouden worden dat de resultaten van 2019 de pre-pandemische periode weerspiegelen, terwijl de gegevens van 2020 beïnvloed kunnen zijn door gewijzigde ziekenhuisactiviteiten als gevolg van de crisis.

Sinds 2004 kan een significant dalende trend in de resistentieproportie en de incidentie van MRSA worden waargenomen. Er kan geen significante trend (2014-2020) worden waargenomen in de resistentieproportie en de incidentie van vanco-R *E. faecium*. Evenzo kan sinds 2013 geen opmerkelijke trend in de resistentieproportie van meropenem I/R *A. baumannii worden waargenomen*. De incidentie daalde echter aanzienlijk in dezelfde periode. Sinds 2018 lijkt er sprake te zijn van een stabilisatie van de resistentieproportie en de incidentie van MDR *P. aeruginosa*. Tussen 2014 en 2020 zijn de resistentieproportie en de incidentie van 3GC I/R *E. coli en K. pneumoniae* significant toegenomen.

De veranderingen die we in de gegevens van 2020 waarnemen, zijn naar alle waarschijnlijkheid beïnvloed door de COVID-19 crisis en de daarmee samenhangende gewijzigde ziekenhuisactiviteiten. Ook de ambulante zorg is indirect veranderd en kan de patiëntenpopulatie in ziekenhuizen hebben beïnvloed. Er is meer onderzoek nodig

om causale conclusies te kunnen trekken, maar redelijkerwijs mag worden aangenomen dat het antwoord multifactorieel zal zijn. Er waren significante veranderingen in het gedrag van de bevolking (vb. sociale afstand) en het zorgaanbod (minder zorg zoeken en minder doorverwijzingen). Ook binnen de ziekenhuizen vonden veel veranderingen plaats, zoals verbeterde programma's voor infectiepreventie en -bestrijding met meer handhygiëne en gebruik van persoonlijke beschermingsmiddelen, veranderingen in de patiëntenpopulatie en annulatie van electieve en niet-urgente operaties.

In 2019 en 2020 heeft een beperkt aantal ziekenhuizen deelgenomen aan een pilootstudie en een geharmoniseerd AMR/EARS-BE protocol getest. Voor de AMR surveillance houdt dit in dat wordt afgestapt van een geaggregeerde gegevensverzameling en wordt overgestapt op de verzameling van gedetailleerde laboratoriumgegevens op het niveau van isolaten/antimicrobiële gevoeligheidstesten. Dit type gegevensverzameling zal leiden tot meer gedetailleerde en gestandaardiseerde gegevens, aangezien gegevensvalidatie mogelijk zal zijn en discrepanties in interpretatie tot een minimum zullen worden beperkt. De gegevens worden nog geanalyseerd. De resultaten zullen in het volgende rapport worden opgenomen.

RÉSUMÉ

Introduction

Les antibiotiques sont l'un des médicaments les plus importants pour sauver des vies, mais leur utilisation inutile et inappropriée réduit leur capacité à traiter les infections. Certaines bactéries sont devenues tolérantes à certains antibiotiques ou ont trouvé des moyens de les décomposer. C'est ce qu'on appelle la résistance aux antimicrobiens (AMR) acquise. L'Organisation mondiale de la Santé reconnaît l'AMR comme l'une des dix principales menaces pour la santé de l'humanité.

Afin de suivre l'évolution nationale de la proportion de résistance et de l'incidence des organismes multirésistants (MDRO) dans les hôpitaux belges, Sciensano collecte et analyse les données de la surveillance AMR. L'Arrêté Royal du 8 Janvier 2015 stipule que les hôpitaux de soins aigus doivent participer obligatoirement à la surveillance de *Staphylococcus aureus* résistant à la méticilline (MRSA) et des bactéries à Gram-négatif multirésistantes (MRGN). La surveillance des entérocoques résistants à la vancomycine (VRE) est un des quatre programmes supplémentaires parmi lesquels les hôpitaux doivent choisir pour participer à l'un d'entre eux.

Le présent rapport vise à présenter les résultats 2019 et 2020 des trois programmes de surveillance et à décrire les tendances de l'AMR dans les hôpitaux belges de soins aigus et/ou chroniques belges.

En raison de la charge de travail exceptionnelle due à la pandémie COVID-19, la Commission belge de coordination de la politique antibiotiques (BAPCOC) a déclaré qu'il n'y avait aucune obligation légale pour les hôpitaux de participer aux surveillances nationales (y compris MRSA, MRGN et VRE) en 2020 (collecte des données de 2019) et 2021 (collecte des données de 2020). Pour cette raison et en raison de la livraison tardive des données, il a été décidé de combiner le rapport annuel 2019 avec le rapport 2020. Lors de l'interprétation des résultats, il est important de garder en tête que les résultats de la surveillance 2019 présentés dans ce rapport reflètent la période pré-pandémique. Les données de 2020 sont cependant largement impactées par les activités hospitalières modifiées en raison de la crise du COVID-19.

Méthodes

Les données de surveillance (année 2019 et 2020) ont été collectées rétrospectivement l'année suivante par les laboratoires de microbiologie seuls ou avec la collaboration des équipes de prévention et contrôle des infections des hôpitaux participants. Il s'agissait de données agrégées au niveau hospitalier. Les hôpitaux pouvaient fournir soit des chiffres annuels, soit des données pour un semestre, sauf pour la surveillance VRE pour laquelle seules les données annuelles étaient autorisées.

Les données provenant des hôpitaux de soins aigus et de soins chroniques ont été présentées séparément. Les hôpitaux de soins aigus ayant une durée moyenne de séjour de ≥ 16 jours ont été classés comme hôpitaux de soins chroniques.

Les micro-organismes et résistances suivants ont été étudiés :
o *Staphylococcus aureus* (*S. aureus*) résistant à la méthicilline ou à l'oxacilline
o *Escherichia coli* (*E. coli*) et *Klebsiella pneumoniae* (*K. pneumoniae*) non-sensibles* aux céphalosporines de 3ème génération (3GC I/R) et/ou au méropénème (méropénème I/R)
o *Acinetobacter baumannii* (*A. baumannii*) non-sensible* au méropénème (méropénème I/R)

o *Pseudomonas aeruginosa* (*P. aeruginosa*) multirésistant (MDR), c'est-à-dire non-sensible* (2019) ou résistant (2020) vis-à-vis d'au moins trois des classes d'antibiotiques parmi les suivantes : fluoroquinolones (ciprofloxacine ou lévofloxacine), aminoglycosides (gentamicine, tobramycine ou amikacine), carbapénèmes (méropénème ou imipénème), céphalosporines de 3ème et/ou 4ème génération (ceftazidime ou céfépime)
o *Enterococcus faecalis* (*E. faecalis*) et *E. faecium* résistant à la vancomycine (vanco-R)

* Non-sensibilité = une sensibilité intermédiaire (I) ou résistance (R) (NB : critère EUCAST pour la catégorie "I" avant 2019)

Seuls les hôpitaux ayant fourni des données de type D (soit des données dédupliquées) ont été inclus dans les analyses, c'est-à-dire que chaque patient n'a été compté qu'une seule fois par période d'hospitalisation et par bactérie. Dans ce rapport, les analyses incluent uniquement des basées provenant d'échantillons cliniques (sauf indication contraire). Tous les types d'échantillons (p.ex. sang, urine) ont été inclus à l'exception des selles considérés comme des échantillons de dépistage pour les surveillances MRGN et VRE et qui ont donc été exclues pour les surveillances MRGN et VRE.

Le caractère potentiellement lié aux soins n'a été évalué que pour le MRSA. Un MRSA lié aux soins a été défini comme une colonisation ou une infection par le MRSA, considérée comme acquise à l'hôpital (premier échantillon positif pour MRSA dans les 48 heures ayant suivi l'admission), non présente à l'admission et sans portage/infection de MRSA dans les antécédents du patient (au cours des 12 derniers mois).

Pour chaque bactérie, la proportion de résistance, l'incidence (nombre de cas pour 1 000 admissions) et/ou la densité d'incidence (nombre de cas pour 1 000 jours-patients) ont été calculées. Les données historiques ont été utilisées pour présenter l'évolution des proportions de résistance et de l'incidence (densités). Nous avons ajusté un modèle de régression binomiale négative avec l'hôpital comme cluster et l'année comme effet fixe pour explorer et évaluer les changements statistiquement significatifs ($p<0,05$) de l'incidence. Pour évaluer si les tendances observées dans les proportions de résistance étaient statistiquement significatives ($p<0,05$), nous avons utilisé une régression linéaire avec l'hôpital comme cluster.
Les données ont été analysées dans STATA 16 (StataCorp LP, College Station, Texas, USA) et présentées par région et par niveau de soins spécialisés au sein de l'hôpital.

Résultats

Le Tableau 1 présente la proportion de résistance et l'incidence pour 1 000 admissions des bactéries faisant partie de la surveillance (échantillons cliniques uniquement) dans les hôpitaux de soins aigus belges en 2019 et 2020. Au cours de ces années, 85,3% (n=87/102) et 94,1% (n=96/102) de tous les groupes administratifs d'hôpitaux de soins aigus (fusions) ont respectivement participé à la surveillance MRSA et MRGN avec au moins un site hospitalier. Malgré le caractère facultatif de la surveillance VRE, 84,3% (n=86/102) et 91,2% (n=93/102) de tous les regroupements ont respectivement participé avec au moins un site hospitalier en 2019 et 2020.

Depuis 2004, on observe une tendance à la baisse significative de la proportion de résistance (-1,21% par an ; $p<0,001$) et de l'incidence (IRR=0,920, 95%CI : 0,917-0,923 ; $p<0,001$) du MRSA. La diminution de l'incidence n'est toutefois pas statistiquement significative entre 2018 et 2020 (IRR=0,909, 95%CI : 0,791-1,045 ; $p=0,179$).
Grâce aux efforts combinés des équipes de prévention et contrôle des infections et à toute une série d'actions, la proportion de MRSA lié aux soins sur le nombre total de MRSA est passée de 78,8 % en 1994 (début de la surveillance) à 43,1 % en 2006 (année où la surveillance est devenue obligatoire). Actuellement, la proportion est à son plus bas niveau : 22,4% en 2019 et 21,7% en 2020.

Tableau 1. La proportion de résistance et l'incidence par 1 000 admissions des bactéries incluses dans la surveillance de la résistance aux antimicrobiens (uniquement les échantillons cliniques), hôpitaux de soins aigus belges, 2019 et 2020

		2019				2020			
		Proportion de résistance (%)		Incidence par 1 000 admissions		Proportion de résistance (%)		Incidence par 1 000 admissions	
		Brute	Médiane	Brute	Médiane	Brute	Médiane	Brute	Médiane
Staphylococcus aureus	Méticilline R	12.4	9.9	2.30	1.81	10.6	9.0	1.88	1.53
Staphylococcus aureus lié aux soins	Méticilline R	21.2	25.0	0.49	0.41	21.0	23.3	0.39	0.33
Enterococcus faecium	Vancomycine R	2.0	0.0	0.10	0.00	1.7	0.0	0.09	0.00
Enterococcus faecalis	Vancomycine R	0.0	0.0	0.01	0.00	0.1	0.0	0.01	0.00
Escherichia coli	3GC I/R	9.9	10.1	4.95	4.86	9.2	9.1	5.22	5.32
	Méropénème I/R	0.1	0.1	0.07	0.02	0.1	0.0	0.06	0.00
Klebsiella pneumoniae	3GC I/R	22.7	21.1	2.64	2.16	21.3	19.7	2.67	1.95
	Méropénème I/R	2.1	1.1	0.25	0.10	1.8	0.8	0.22	0.08
Acinetobacter baumannii	Méropénème I/R	6.7	0.0	0.03	0.00	7.3	0.0	0.03	0.00
Pseudomonas aeruginosa	MDR	6.7	4.3	0.73	0.44	6.7	4.2	0.77	0.40

R = résistance, I/R = sensibilité intermédiaire ou résistante, 3GC =céphalosporines de 3ème génération, MDR = sensibilité réduite (I ou R) vis-à-vis d'au moins trois classes d'antibiotiques parmi les suivantes: fluoroquinolones (ciprofloxacine ou lévofloxacine), aminoglycosides (gentamicine, tobramycine ou amikacine), les carbapénèmes (méropénème ou imipénème), céphalosporines de 3ème ou 4ème génération (ceftazidime ou céfépime)

Aucune tendance significative (2014-2020) ne peut être observée dans la proportion de résistance (-0,13% par an ; p=0,292) et l'incidence (IRR=0,981, 95%CI : 0,920-1,047 ; p=0,569) d'*E. faecium* vanco-R.

Entre 2014 et 2020, on note un changement significatif de la proportion de résistance (+0,25% par an ; p=0,001) et de l'incidence (IRR=1,018, 95%CI : 1,002-1,034 ; p=0,024) d'*E. coli* 3GC I/R. De plus, une augmentation faible mais significative de la proportion de résistance (+0,01% par an ; p<0,001) et de l'incidence (IRR=1,140, 95%CI : 1,069-1,215 ; p<0,001) d'*E. coli* méropénème I/R peut également être observée entre 2015 et 2020.

Entre 2014 et 2020, la proportion de résistance (+0,82% par an ; p=0,002) et l'incidence (IRR=1,060, 95%CI : 1,040-1,080 ; p<0,001) de *K. pneumoniae* 3GC I/R ont significativement augmenté. Depuis 2018, on observe toutefois une diminution significative de la proportion de résistance (-1,62% par an ; p<0,001) et une diminution non significative de l'incidence (IRR=0,961, 95%CI : 0,924-1,000 ; p=0,055).
Une augmentation non significative de la proportion de résistance (+0,07% par an ; p=0,295) et de l'incidence (IRR=1,025, 95%CI : 0,977-1,075 ; p=0,311) de *K. pneumoniae* méropénème I/R peut être observée entre 2015 et 2020. Depuis 2018, on observe cependant une diminution significative de la proportion de résistance (-0,35% par an ; p=0,010) et une diminution non significative de l'incidence (IRR=0,919, 95%CI : 0,820-1,029 ; p=0,143).

Depuis 2013, aucun changement significatif dans l'évolution de la proportion de résistance d'*A. baumannii* méropénème I/R ne peut être observé (-0,18% ; p=0,545). L'incidence a cependant significativement diminué entre 2013 et 2020 (IRR=0,912, 95%CI : 0,860-0,966 ; p=0,002).

Les changements de définition en 2017, 2018 et 2020 rendent difficile l'interprétation de l'évolution de *P. aeruginosa* MDR. Depuis 2018, on observe une stabilisation de la proportion de résistance (-0,08% ; p=0,753) et de l'incidence (IRR=0,941, 95%CI : 0,868-1,020 ; p=0,140).

Le Tableau 2 montre la proportion de résistance et la densité d'incidence par 1 000 jours-patients des bactéries sous surveillance (uniquement les échantillons cliniques) dans les hôpitaux de soins chroniques belges en 2019 et 2020. Ces chiffres doivent toutefois être interprétés avec prudence étant donné le taux de participation faible (≤ 12).

Tableau 2. La proportion de résistance et la densité d'incidence par 1 000 jours-patients des bactéries incluses dans la surveillance de la résistance aux antimicrobiens (uniquement les échantillons cliniques), hôpitaux de soins chroniques belges, 2019 et 2020

		2019				2020			
		Proportion de résistance (%)		Incidence par 1 000 admissions		Proportion de résistance (%)		Incidence par 1 000 admissions	
		Brute	Médiane	Brute	Médiane	Brute	Médiane	Brute	Médiane
Staphylococcus aureus	Méticilline R	14.3	8.5	0.16	0.10	16.2	13.5	0.16	0.06
Staphylococcus aureus lié aux soins	Méticilline R	53.8	49.3	0.09	0.07	23.1	6.3	0.04	0.01
Enterococcus faecium	Vancomycine R	0.0	0.0	0.00	0.00	0.0	0.0	0.00	0.00
Enterococcus faecalis	Vancomycine R	0.0	0.0	0.00	0.00	0.0	0.0	0.00	0.00
Escherichia coli	3GC I/R	8.4	5.6	0.27	0.18	11.1	6.6	0.33	0.10
	Méropénème I/R	0.4	0.0	0.01	0.00	0.0	0.0	0.00	0.00
Klebsiella pneumoniae	3GC I/R	23.1	12.3	0.25	0.14	27.2	21.7	0.24	0.12
	Méropénème I/R	2.5	1.7	0.03	0.02	3.1	1.3	0.03	0.02
Acinetobacter baumannii	Méropénème I/R	11.8	0.0	0.00	0.00	10.0	0.0	0.00	0.00
Pseudomonas aeruginosa	MDR	4.4	3.2	0.04	0.02	6.6	2.9	0.05	0.02

R = résistance, I/R = sensibilité intermédiaire ou résistante, 3GC =céphalosporines de 3ème génération, MDR = sensibilité réduite (I ou R) vis-à-vis d'au moins trois classes d'antibiotiques parmi les suivantes: fluoroquinolones (ciprofloxacine ou lévofloxacine), aminoglycosides (gentamicine, tobramycine ou amikacine), les carbapénèmes (méropénème ou imipénème), céphalosporines de 3ème ou 4ème génération (ceftazidime ou céfépime)

Discussion

Ce rapport présente les résultats 2019 et 2020 de trois programmes nationaux de la surveillance AMR, c'est-à-dire la surveillance (1) MRSA, (2) VRE et (3) MRGN. À notre connaissance, notre surveillance nationale de l'AMR est l'un des rares programmes qui ne se concentre pas simplement sur les échantillons invasifs (p.ex. les échantillons de liquide céphalorachidien et de sang), mais inclut des types d'échantillons invasifs et non invasifs (p.ex. les échantillons d'urine).

Bien qu'il n'y ait pas eu d'obligation légale de participer en raison de la crise du COVID-19, plus de 85 % de toutes les fusions ont réussi (avec ou sans un retard considérable) à transmettre des données MRSA et MRGN. En outre, le taux de participation à la surveillance VRE était supérieur à 84 % au cours des années concernées. Lors de l'interprétation des résultats, il est important de garder en tête que les résultats de 2019 reflètent la période pré-pandémique, tandis que les données de 2020 peuvent être influencées par des activités hospitalières modifiées en raison de la crise.

Depuis 2004, on observe une tendance à la baisse significative de la proportion de résistance et de l'incidence du SARM. Aucune tendance significative (2014-2020) ne peut être observée en ce qui concerne la proportion de résistance et l'incidence d'E*. faecium* vanco-R. De même, aucune tendance notable dans la proportion de résistance d'*A. baumannii* méropénème I/R ne peut être observée depuis 2013. L'incidence a cependant significativement diminué dans le même laps de temps. Depuis 2018, il semble y avoir une stabilisation de la

proportion de résistance et de l'incidence de *P. aeruginosa* MDR. Entre 2014 et 2020, la proportion de résistance et l'incidence d'*E. coli* et de *K. pneumoniae* 3GC I/R ont significativement augmenté.

Les changements que nous observons dans les données de 2020 sont selon toute vraisemblance influencés par la crise du COVID-19 et les activités hospitalières modifiées qui y sont associées. De même, les soins ambulatoires ont indirectement changé et pourraient avoir influencé la population de patients dans les hôpitaux. Des recherches supplémentaires sont nécessaires dans ce domaine pour trouver une inférence causale, mais il est raisonnable de croire que la réponse sera multifactorielle. Des changements significatifs ont été observés dans le comportement de la population (par exemple, la distanciation sociale) et dans l'offre de soins de santé (réduction de la recherche de soins et moins de références). De nombreux changements ont également eu lieu au sein des hôpitaux, tels que l'amélioration des programmes de prévention et de contrôle des infections avec le renforcement de l'hygiène des mains et l'utilisation d'équipements de protection individuelle, la modification de la composition des patients et l'annulation de chirurgies électives et non urgentes.

En 2019 et 2020, un nombre limité d'hôpitaux ont participé à une étude pilote et ont testé un protocole harmonisé AMR/EARS-BE. Pour la surveillance AMR, cela impliquera d'abandonner une collecte de données agrégées et d'opter pour la collecte de données de laboratoire détaillées au niveau des isolats/des tests de susceptibilité antimicrobienne. Ce type de collecte de données permettra d'obtenir des données plus détaillées et standardisées, car la validation des données sera possible et les divergences d'interprétation seront minimisées. Les analyses de données sont en cours et les résultats seront inclus dans le prochain rapport.

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ABBREVIATIONS

3GC	Third generation cephalosporins
4GC	Fourth generation cephalosporins
A. baumannii	*Acinetobacter baumannii*
AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
BSI	Bloodstream infection
CLSI	Clinical and Laboratory Standard Institute, USA
ColREC	Colistin-resistant *Escherichia coli*
CPE	Carbapenemase-producing *Enterobacteriaceae*
CRE	Carbapenem-resistant *Enterobacteriaceae*
E. coli	*Escherichia coli*
E. faecalis	*Enterococcus faecalis*
E. faecium	*Enterococcus faecium*
EARS-BE	European Antimicrobial Resistance Surveillance in Belgium
EARS-Net	European Antimicrobial Resistance Surveillance Network
ESBL	Extended spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
I	Intermediate category of susceptibility
IPC	Infection prevention and control
IQR	Inter Quartile Range
IRR	Incidence Rate Ratio
I/R	Non-susceptible (intermediate susceptible or resistant)
K. pneumoniae	*Klebsiella pneumoniae*
MDR	Multidrug-resistant
Meropenem I/R	Intermediate susceptibility or resistance to meropenem
MIC	Minimal inhibitory concentration
MRGN	Multiresistant Gram-negative bacteria
MRSA	Methicillin-resistant *Staphylococcus aureus*
NAP	National action plan
P. aeruginosa	*Pseudomonas aeruginosa*
R	Resistant or non-susceptible
S. aureus	*Staphylococcus aureus*
Type D	Data collection method with de-duplication of data: per period of hospitalisation and bacteria each patient is counted only once
Vanco-R	Resistance to vancomycin
VRE	Vancomycin-resistant enterococci

INTRODUCTION

Antibiotics have been one of the most important life-saving drugs, but unnecessary and inappropriate use reduces their ability to treat infections. Some bacteria have become tolerant to certain antibiotics or have found ways to break them down. This is called acquired antimicrobial resistance (AMR). The World Health Organization recognizes AMR as one of the top ten global health threats facing humanity. In addition to a considerable health impact (incl. prolonged illness, disability and death), the cost of AMR (among others due to longer hospital stays and the need for more expensive medicines) can also be significant.[1]

The service “Healthcare-associated infections and antimicrobial resistance” of Sciensano organizes, collects and analyzes AMR surveillance data originating from Belgian hospitals. The Royal Decree of 8 January 2015 stipulates that all Belgian non-psychiatric hospitals - with the exception of isolated Sp hospitals and services, isolated G hospitals and services, isolated and Sp hospitals for palliative care – mandatorily have to participate in the surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) and multiresistant Gram-negative bacteria (MRGN). Participation in the surveillance of vancomycin-resistant enterococci (VRE) is currently still optional.

The first national surveillance program for MRSA was initiated in 1994. This resistant Gram-positive bacterium causes difficult to treat infections, such as skin and soft tissue infections, surgical site infections, catheter infections, bloodstream infections and pneumonia. Initially, participation in this surveillance was voluntary, but became mandatory in 2006.
The second MRGN surveillance was set up in the late 1990s following the emergence of antimicrobial resistance in a wide range of Enterobacteriaceae as well as in nonfermenting Gram-negative bacteria (e.g. *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) . Multiresistant *Enterobacter aerogenes* was the first within the family of *Enterobacteriaceae* to be monitored (started in 2000, stopped in 2011) because it caused major healthcare-associated outbreaks with a subsequent endemic character in many Belgian hospitals. Because of the increased prevalence and incidence of extended-spectrum beta-lactamases (ESLBs) reported locally by several belgian hospitals, this surveillance program was subsequently extended to several other *Enterobacteriaceae* species, including *Escherichia coli* (2005)*, Klebsiella pneumoniae* (2005) and *Enterobacter cloacae* (2009, stopped in 2017)*,* as well as to nonfermenting Gram-negative bacteria (*Pseudomonas aeruginosa* and *Acinetobacter baumannii*). Owing to the upsurge of carbapenem-resistant and carbapenamase-producing Enterobacteriaceae (CRE and CPE, respectively), participation in the MRGN surveillance become compulsory in 2015.
The third surveillance program, VRE, was initiated in 2014 after multiple Belgian hospitals reported VRE outbreaks.

The primary objective of the three epidemiological AMR surveillances is to monitor the evolution of the resistance proportion and incidence of (multi)drug resistant bacteria in Belgian hospitals and thus to have national data on these resistant microorganisms. As a secondary objective, it may also encourage participating hospitals to monitor their own results over time.

The aim of the current report is to present the 2019 and 2020 results of the three AMR surveillance programs and to describe trends in AMR in Belgian acute and/or chronic care hospitals.

Attention: Due to the COVID-19 pandemic, there was no legal obligation for hospitals to participate in the national surveillances (incl. MRSA and MRGN) in 2020 (collecting 2019 data) and 2021 (collecting 2020 data). For this reason and because of delayed data delivery, it was decided to combine the 2019 annual report with the 2020 report. When interpreting the results, it is important to keep in mind that the 2019 surveillance findings presented in this report reflect the pre-pandemic period. The 2020 data are however largely impacted by the altered hospital activities due to the COVID-19 crisis.

METHODOLOGY

The modalities of the data collection for the AMR surveillance can be found in detail in the study protocol.[2]

The surveillance results were collected and reported by the microbiology laboratories and/or the infection prevention and control teams of the participating hospitals to the service "Healthcare-associated infections and antimicrobial resistance" of Sciensano.

The data (year 2019 and 2020) were collected retrospectively in the following year and were aggregated at hospital level. Hospitals could either provide annual figures or data for one semester, except for the VRE surveillance for which only annual data were allowed.

Following microorganisms and resistances were explored:

- **MRSA** — *Staphylococcus aureus (S. aureus)* resistant to methicillin or oxacillin

- **MRGN**

  1) *Enterobacteriaceae*:
  ***Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*)**

  Non-susceptible to 3rd generation cephalosporins (3GC I/R):
  i.e. reduced susceptibility (I) or resistance (R) to 3rd generation (cefotaxime, ceftriaxone, ceftazidime) according to EUCAST* or CLSI criteria.

  Non-susceptible to meropenem (meropenem I/R):
  i.e. reduced susceptibility (I) or resistance (R) to meropenem according to EUCAST* or CLSI criteria.

  2) Meropenem I/R *Acinetobacter baumannii* (*A. baumannii*):
  i.e. reduced susceptibility (I) or resistance (R) to meropenem according to EUCAST* or CLSI criteria.

  3) Multidrug-resistant (MDR) *Pseudomonas aeruginosa* (*P. aeruginosa*):
  2019: reduced susceptibility (I) or resistance (R) to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin or levofloxacin), aminoglycosides (gentamicin, tobramycin or amikacin), carbapenems (meropenem or imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime, cefepime)
  2020: resistance (R) to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin or levofloxacin), aminoglycosides (gentamicin, tobramycin or amikacin), carbapenems (meropenem or imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime, cefepime)

- **VRE** — *Enterococcus faecalis* (*E. faecalis*) and *Enterococcus faecium* (*E. faecium*) resistant to vancomycin (vanco-R) according to EUCAST* or CLSI criteria.

* Note: In 2019, EUCAST (European Committee on Antimicrobial Susceptibility Testing) changed the definitions of susceptibility testing categories S, I and R to 'S' being 'Susceptible, standard dosing regimen', 'I' being 'Susceptible, increased exposure' and 'R' being 'Resistant' (see https://www.eucast.org/newsiandr/). This change in approach implied that 'I' should be categorised as susceptible. Because the majority of Belgian hospital laboratories did not yet switch to use the new EUCAST guidelines, we still categorised 'I' (intermediary) as 'reduced susceptibility' for the 2019-2020 data.

All sample types (e.g. blood, urine) had to be included. For MRSA and VRE, a distinction had to be made between clinical samples (i.e. all samples taken for diagnostic purposes) and screening samples (i.e. samples taken - in the absence of clinical signs/symptoms - to detect colonization with resistant bacteria). **Faeces samples could not be considered as clinical samples in the MRGN and VRE surveillance programs, but had to be considered as screening samples.**

There were five possibilities for data collection:

- Type A: every positive sample was counted (screening samples and duplicates included)
- Type B: every positive clinical sample was counted (duplicates included)
- Type C: each sample originating for a different infection site was counted only once
- Type D: each patient was counted only once per period of hospitalisation (de-duplication)
- Type E: other

Duplicates were defined as isolates from the same patient of the same species with indistinguishable anti-biograms or with the same resistance mechanism, regardless of the purpose for which the sample was taken. **Only hospitals providing Type D data (with de-duplication) were included in the analyses reported here.**

The healthcare-associated character was explored for MRSA only. Healthcare-associated (or nosocomial) MRSA was defined as colonization or infection with MRSA, considered to be acquired in the hospital and not present on admission (first positive sample collected more than 48h after admission) or known in the patient's history (past 12 months).

Results are presented by hospital type (acute or chronic care hospitals), by region (Flanders, Wallonia or Brussels), and by level of specialty care within the hospital site (not of the merger). The latter is defined as follows:

Level of specialty care	Definition ECDC[3]	Definition FPS[4]
Primary	• Often referred to as 'district hospital' or 'first-level' referral • Few specialities (mainly internal medicine, obstetrics-gynaecology, paediatrics, general surgery or only general practice) • Limited laboratory services for general, but not specialised, pathological analysis • Often corresponds to general hospital without teaching function	• Algemeen ziekenhuis • Hôpital général • Allgemein krankenhaus
Secondary	• Often referred to as 'provincial hospital' or 'second-level referal' • The hospital is highly differentiated by function with five to ten clinical specialities, such as haematology, oncology, nephrology, ICU • Takes some referrals from other (primary) hospitals • Often corresponds to general hospital with teaching function/mission	• Algemeen ziekenhuis met universitair karakter • Hôpital général à caractère universitaire • A.Z. met univ. karakter - Hôpital général à caractère univ.
Tertiary	• Often referred to as 'central', 'regional' or 'tertiary-level' hospital • Highly specialised staff and technical equipment (ICU, haematology, transplantation, cardio-thoracic surgery, and neurosurgery) • Clinical services are highly differentiated by function • Specialised imaging units • Provides regional services and regularly takes referrals form other (primary and secondary) hospitals • Often a university hopsital or associated to a university	• Universitair ziekenhuis - Hôpital universitaire • Universitair ziekenhuis • Hôpital universitaire
Specialised	• Single clinical specialty, possibly with sub-specialties • Highly specialised staff and technical equipment	• Gespecialiseerd ziekenhuis • Geriatrisch- & Specialised • Hôpital spécialisé • Psychiatrisch ziekenhuis • Hôpital psychiatrique

ECDC = European Centre for Disease Prevention and Control; FPS = Federal Public Service Health, Food Chain Safety and Environment

For each bacterium, the resistance proportion was calculated by dividing the total number of resistant isolates by the total number of isolates reported by the hospital during the surveillance period. In addition, the incidence (number of cases per 1 000 hospital admissions) and incidence density (cases per 1 000 patient days) were calculated for each resistant bacteria under surveillance and this by dividing the total number of resistant isolates by the total number of admissions or patient days reported by the hospital during the surveillance period.

Following summary statistics were used in this report:

- Crude:
  - Crude resistance proportion: total number of bacterium X with resistance Y divided by the total number of bacterium X multiplied by 100
  - Crude incidence (density): total number of bacterium X with resistance Y divided by the total number of admissions (or patient days) multiplied by 1 000

- Mean: The sum of all scores (i.e. crude resistance proportions or crude incidences) divided by the number of scores

- Median (or P50): the score (i.e. crude resistance proportion or crude incidence) that divides the set of scores into two halves (middle score when scores are ranked in ascending/descending order)

- P25 (or Q1, first quartile): the 25th percentile is the score (i.e. crude resistance proportion or crude incidence) below which 25% of the cases fall

- P75 (or Q3, third quartile): the 75th percentile is the score (i.e. crude resistance proportion or crude incidence) below which 75% of the cases fall

- Between P25 and P75 lies half of all scores (= interquartile range (IQR) = P75 - P25)

Because the median is less affected by outliers (e.g. hospitals experiencing an outbreak) and skewed data (e.g. many hospitals reporting zero resistance cases) than the mean, we recommended hospitals to use the median as the preferred measure of central tendency.

Historical data were used to present the evolution of resistance proportions and incidence (densities). To assess whether trends observed in resistance proportions were statistically significant ($p<0.05$), we used linear regression with hospital as cluster. We fitted a negative binomial regression model with hospital as cluster and year as fixed effect to explore and assess statistically significant ($p<0.05$) changes in the incidence (density). The result was expressed as incidence rate ratio (IRR) and its 95% confidence interval (CI). An IRR of 1.20 means an 20% increase in the incidence, while a IRR of 0.80 points to a 20% decrease.

Data were analysed in STATA 16 (StataCorp LP, College Station, Texas, USA).

Hospitals that were part of an administrative hospital group could choose to participate as one hospital or to collect data by hospital site. Results were presented separately for acute care and chronic care hospitals. **In this report, acute care hospitals with an average length of stay of more than 16 days were considered as chronic care hospitals.**

The results presented in this report can slightly differ from the numbers reported in previous reports. Some hospitals modify or correct their data after publication of a report.

PART 1: METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)

In 2019 and 2020, 85.3% (n=87/102) and 94.1% (n=96/102) of all acute care hospital administrative groups (mergers) participated in the MRSA surveillance with at least one hospital site, respectively. In both years, two hospital administrative groups were considered as chronic care hospitals (length of stay > 16 days).

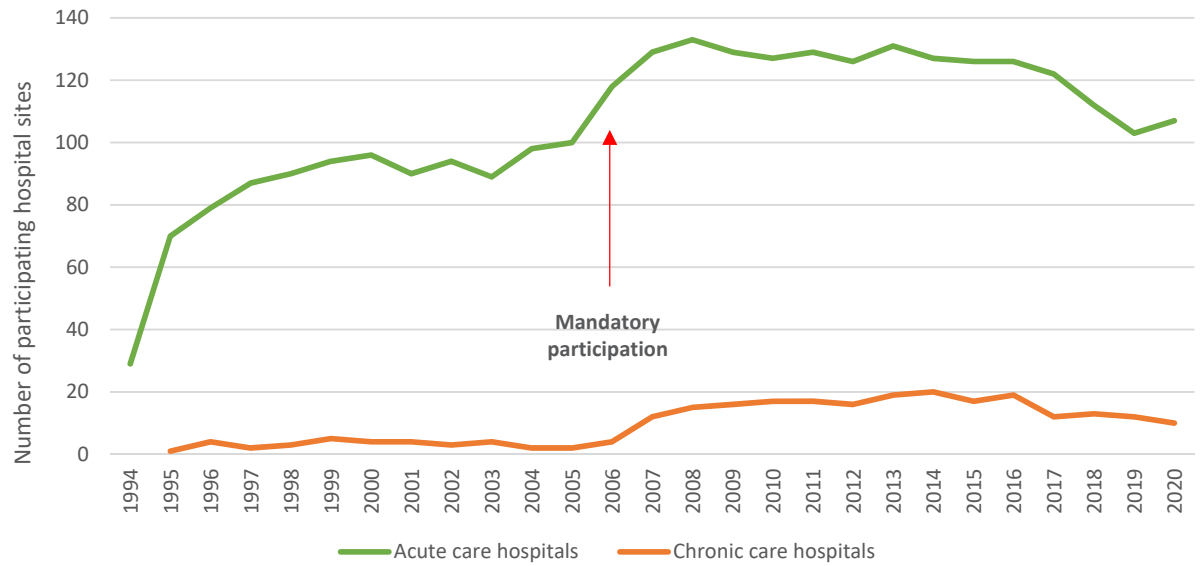
Table 3 presents the 2019 and 2020 participation in the MRSA surveillance by hospital care type, region and level of specialty care within the hospital. All hospitals provided Type D data and were therefore included.
Figure 1 shows the number of participating hospital sites since the beginning of the surveillance (1994).

Table 3. Participation in the surveillance of methicillin-resistant *Staphylococcus aureus* by hospital care type, region and level of specialty care within the hospital (for acute care hospitals only), Belgian acute and chronic care hospital sites, 2019 and 2020

	2019				2020			
	Flanders	Wallonia	Brussels	Belgium	Flanders	Wallonia	Brussels	Belgium
N of acute care hospitals (%)	**52**	**36**	**15**	**103**	**56**	**38**	**13**	**107**
Primary hospitals	42	30	8	80	47	30	8	85
Secondary hospitals	7	5	4	16	6	7	3	16
Tertiary hospitals	3	1	3	7	3	1	2	6
N of chronic care hospitals (%)	**4**	**6**	**2**	**12**	**3**	**6**	**1**	**10**

N = number

Figure 1. Evolution of the participation in the surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) based on the resistance proportion indicator, Belgian acute and chronic care hospital sites, 1994-2020



1. MRSA in acute care hospitals

1.1 RESISTANCE IN *STAPHYLOCOCCUS AUREUS*

In 2019, 12.4% of all *S. aureus* isolates (clinical samples only) were MRSA. This crude proportion dropped to 10.6% in 2020. The crude incidence of MRSA was 2.30 cases per 1 000 admissions or 0.35 cases per 1 000 patient days in 2019 and 1.88 cases per 1 000 admissions or 0.29 cases per 1 000 patient days in 2020 (Table 4).

The evolution of the median resistance proportion, incidence and incidence density is shown overall and by region in Figure 2, 3 and 4, respectively.

Between 2018 and 2020, the median resistance proportion decreased from 11.2% to 9.0% (-1.82% per year; p=0.001). Since 2004, a significant decrease in the resistance proportion can be observed overall (-1.21% per year; p<0.001) and in all three regions: -1.37% per year in Flanders (p<0.001), -0.92% per year in Wallonia (p<0.001) and -1.467% per year in Brussels (p<0.001).

The median incidence of MRSA dropped from 2.05 in 2018 to 1.53 cases per 1 000 admissions in 2020 (IRR=0.845, 95%CI: 0.797-0.897; p<0.001). Since 2004, the incidence of MRSA shows a decreasing trend overall (IRR=0.920, 95%CI: 0.917-0.923, p<0.001) and in all three regions: IRR=0.907 (95%CI: 0.903-0.912; p<0.001) in Flanders, IRR=0.945 (95%CI: 0.940-0.950; p<0.001) in Wallonia and IRR=0.919 (95%CI: 0.911-0.927; p<0.001) in Brussels.

Figure 2. Evolution of the median proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) on the total number of reported *S. aureus* by region (clinical samples only), Belgian acute care hospitals, 1994-2020

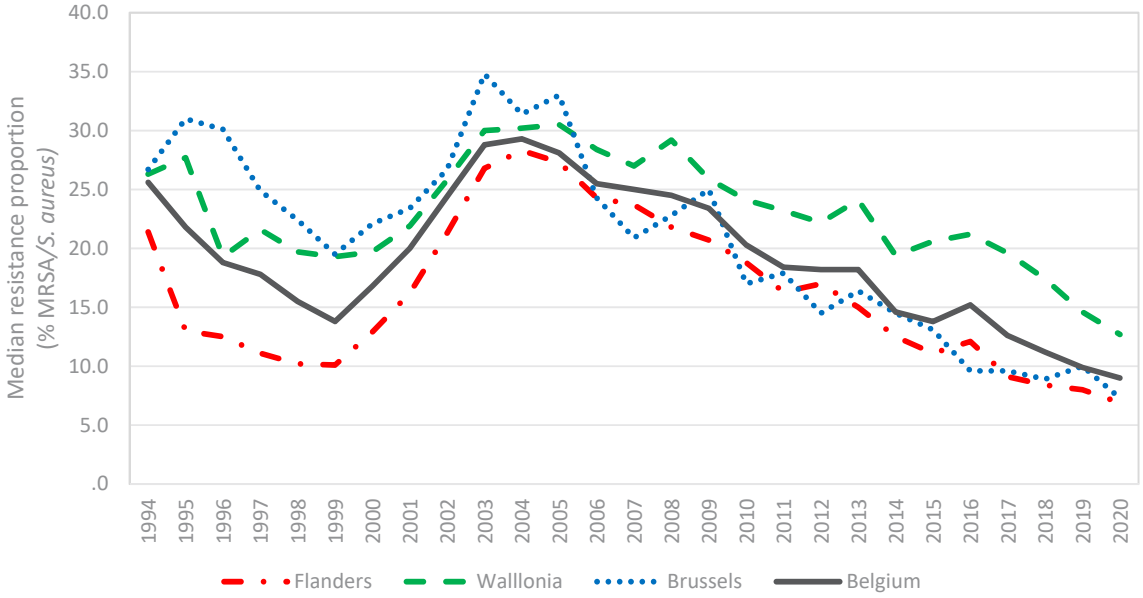


Table 4. Resistance proportion, incidence and incidence density of methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	MRSA (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**3 996**	**32 273**	**12.4**	**11.6**	**9.9**	**6.8-15.0**	**2 953**	**27 807**	**10.6**	**10.8**	**9.0**	**6.0-13.1**
Flanders	1 510	16 591	9.1	8.5	8.0	4.4-11.5	1 163	15 501	7.5	7.6	6.9	4.5-9.5
Wallonia	1 891	9 908	19.1	16.1	14.6	10.3-22.2	1 480	8 462	17.5	16.3	12.7	10.3-19.4
Brussels	595	5 774	10.3	11.2	10.0	7.4-14.4	310	3 844	8.1	8.7	7.3	5.9-9.2
Primary hosp	2 359	19 024	12.4	11.7	10.6	7.0-15.1	1 768	16 980	10.4	10.9	9.0	6.2-12.9
Secondary hosp	796	6 286	12.7	10.8	8.4	4.6-12.0	603	5 621	10.7	10.5	9.2	4.4-16.0
Tertiary hosp	841	6 963	12.1	12.0	9.9	8.0-16.4	582	5 206	11.2	10.7	7.6	7.3-9.9
Incidence per 1 000 admissions												
Belgium	**3 996**	**1 736 439**	**2.30**	**3.04**	**1.81**	**1.06-3.10**	**2 833**	**1 505 415**	**1.88**	**2.26**	**1.53**	**0.91-2.63**
Flanders	1 510	1 031 737	1.46	1.66	1.13	0.62-1.73	1 163	941 811	1.23	1.44	0.98	0.60-1.65
Wallonia	1 891	462 576	4.09	4.14	3.23	2.16-5.53	1 360	398 935	3.41	3.19	2.40	1.62-4.27
Brussels	595	242 126	2.46	5.23	1.93	1.73-4.95	310	164 669	1.88	3.22	1.93	1.39-2.67
Primary hosp	2 359	1 085 735	2.17	3.18	1.69	1.08-3.12	1 725	983 706	1.75	2.28	1.43	0.81-2.45
Secondary hosp	796	379 256	2.10	2.34	1.77	0.75-2.84	526	325 409	1.62	1.88	1.53	0.75-2.68
Tertiary hosp	841	271 448	3.10	3.07	2.48	1.85-4.29	582	196 300	2.96	2.94	2.15	1.86-2.63
Incidence density per 1 000 patient days												
Belgium	**3 996**	**11 287 211**	**0.35**	**0.37**	**0.26**	**0.17-0.45**	**2 833**	**9 875 469**	**0.29**	**0.31**	**0.24**	**0.13-0.39**
Flanders	1 510	6 357 128	0.24	0.26	0.20	0.09-0.26	1 163	5 801 809	0.20	0.23	0.16	0.10-0.26
Wallonia	1 891	3 143 011	0.60	0.52	0.45	0.31-0.69	1 360	2 712 824	0.50	0.45	0.33	0.25-0.58
Brussels	595	1 787 072	0.33	0.37	0.29	0.23-0.44	310	1 360 836	0.23	0.24	0.21	0.14-0.38
Primary hosp	2 359	7 083 920	0.33	0.37	0.25	0.18-0.47	1 725	6 440 031	0.27	0.31	0.24	0.13-0.38
Secondary hosp	796	2 356 218	0.34	0.32	0.25	0.10-0.42	526	1 967 859	0.27	0.27	0.23	0.12-0.36
Tertiary hosp	841	1 847 073	0.46	0.45	0.35	0.30-0.57	582	1 467 579	0.40	0.40	0.33	0.21-0.42

Hosp = hospital; n = total number of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates, N = total number of *Staphylococcus aureus* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Figure 3. Evolution of the median incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) per 1 000 admissions by region (clinical samples only), Belgian acute care hospitals, 1994-2020

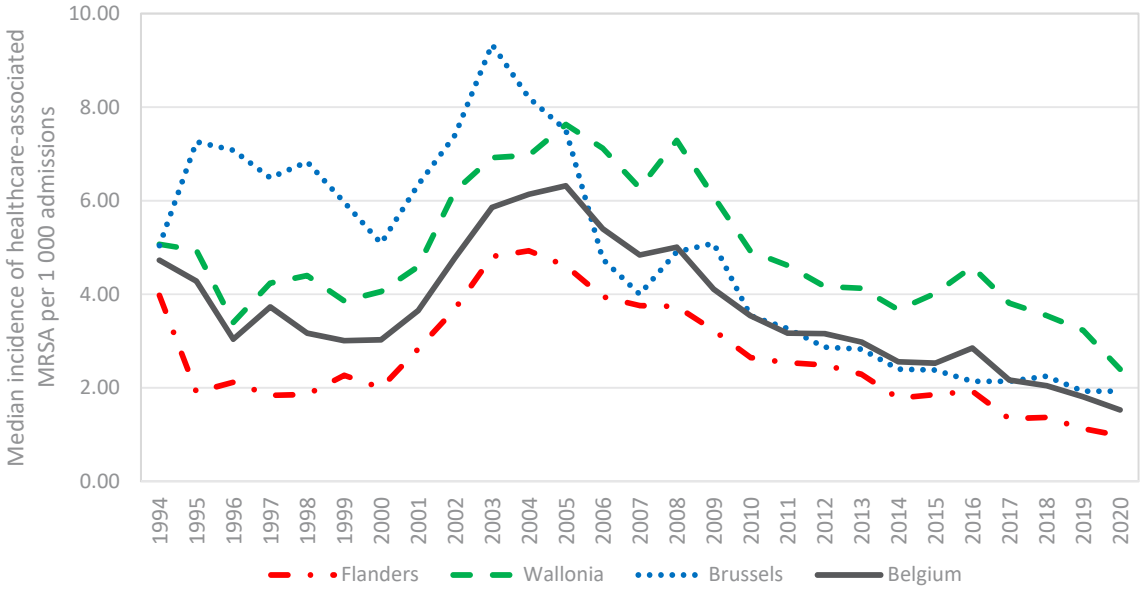
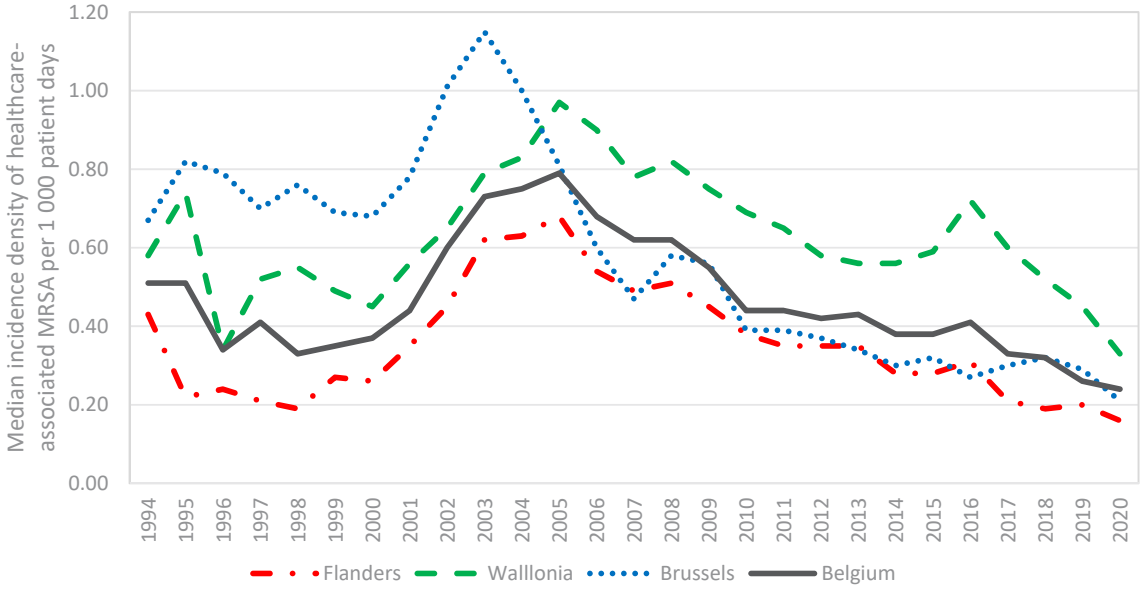


Figure 4. Evolution of the median incidence density of methicillin-resistant *Staphylococcus aureus* (MRSA) per 1 000 patient days by region (clinical samples only), Belgian acute care hospitals, 1994-2020

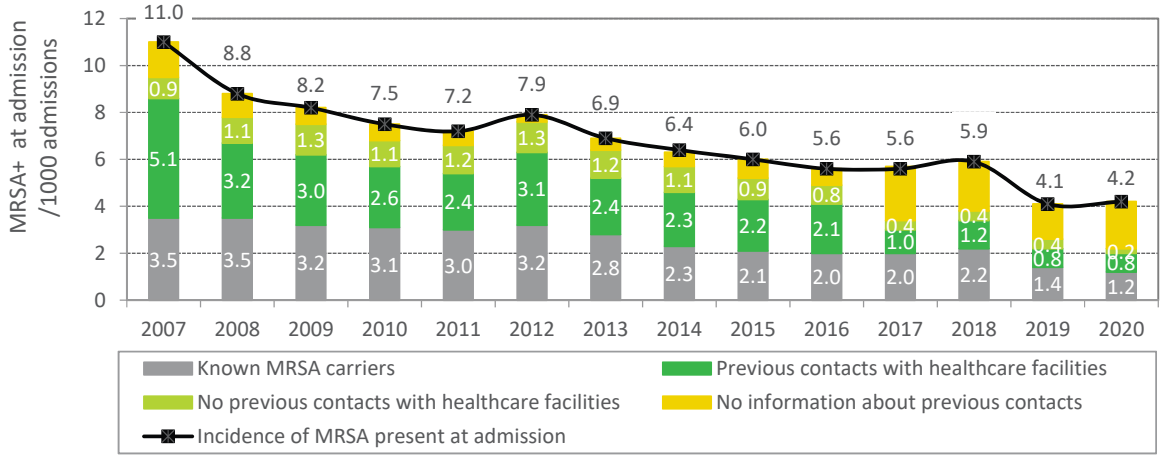


1.2 MRSA PRESENT AT ADMISSION

The incidence of patients who were MRSA positive on admission (optional data) could only be calculated for 29 and 39 acute care hospitals in 2019 and 2020, respectively. Both clinical samples and screening samples testing positive for MRSA within 48 hours after admission were taken into account.

The crude incidence of MRSA positive patients on admission was 4.1 cases per 1 000 admissions (n=2 024/495 536 admissions) in 2019 and 4.2 cases per 1 000 admissions (n=2 356/560 450 admissions) in 2020 (Figure 5).

Figure 5. Evolution of the crude incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) present at admission according to history of colonization and previous contact (past 12 months) with healthcare facilities, Belgian acute care hospitals, 2007-2020



In 2020, 29.4% of patients reported MRSA positive upon admission (n=693/2 356) were known to have been MRSA colonized/infected in the previous 12 months. Of the patients without a history of MRSA colonization/infection in the previous 12 months (n=1 663), 26.3% (n=438) were recently transferred to or had a recent stay in healthcare facility (e.g. acute care hospital, day care hospital, nursing home). For 7.5% of the patients (n=124), no contact with any of these facilities in the previous 12 months was reported, while for 66.2% (n=1 101) information about prior contact with healthcare facilities was unknown.

1.3 HEALTHCARE-ASSOCIATED MRSA

1.3.1 HEALTHCARE-ASSOCIATED MRSA IN CLINICAL SAMPLES

In 2019, 21.2% of all MRSA positive clinical samples (n=848/3 996) were collected more than 48 hours after admission in patients with no known MRSA carriership in the past 12 months, i.e. cases of healthcare-associated MRSA. In 2020, this percentage was similar (21.0%; n=621/2 953). The crude incidence of healthcare-associated MRSA was 0.49 cases per 1 000 admissions or 0.08 cases per 1 000 patient days in 2019 and 0.39 cases per 1 000 admissions or 0.06 cases per 1 000 patient days in 2020 (Table 5).

The evolution of these indicators (incidence and incidence density) is shown in Figure 6 and 7, respectively.

The overall median incidence of healthcare-associated MRSA decreased from 0.46 cases per 1 000 admissions in 2018 to 0.33 in 2020 (IRR=0.788, 95%CI: 0.740-0.840; p<0.001). Since 2004, the incidence shows a decreasing trend overall (IRR=0.882, 95%CI: 0.879-0.885; p<0.001) and in all three regions: IRR=0.876 (95%CI: 0.871-0.881; p<0.001) in Flanders, IRR=0.899 (95%CI: 0.894-0.905; p<0.001) in Wallonia and IRR=0.856 (95%CI: 0.847-0.865; p<0.001) in Brussels.

Table 5. Proportion, incidence and incidence density of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	Healthcare-associated MRSA (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Proportion healthcare-associated MRSA/MRSA (%)												
Belgium	**848**	**3 996**	**21.2**	**26.0**	**25.0**	**11.6-36.7**	**621**	**2 953**	**21.0**	**23.6**	**23.3**	**11.1-34.5**
Flanders	287	1 510	19.0	24.4	23.4	10.6-34.2	221	1 163	19.0	20.7	20.0	2.8-31.0
Wallonia	431	1 891	22.8	28.0	29.4	12.3-39.9	330	1 480	22.3	27.3	25.0	19.4-38.1
Brussels	130	595	21.8	26.6	25.0	14.0-40.0	70	310	22.6	25.3	23.3	12.5-37.0
Primary hosp	518	2 359	22.0	26.4	25.0	12.3-36.5	390	1 768	22.1	23.5	23.3	11.1-33.3
Secondary hosp	187	796	23.5	28.4	30.9	9.2-43.7	137	603	22.7	27.4	23.1	14.1-40.0
Tertiary hosp	143	841	17.0	15.8	14.1	9.6-22.6	94	582	16.2	15.0	15.3	8.5-22.6
Incidence per 1 000 admissions												
Belgium	**848**	**1 736 439**	**0.49**	**0.63**	**0.41**	**0.18-0.79**	**594**	**1 505 415**	**0.39**	**0.45**	**0.33**	**0.13-0.56**
Flanders	287	1 031 737	0.28	0.30	0.26	0.09-0.42	221	941 811	0.23	0.23	0.20	0.03-0.37
Wallonia	431	462 576	0.93	1.07	0.81	0.42-1.34	303	398 935	0.76	0.80	0.56	0.36-0.98
Brussels	130	242 126	0.54	0.68	0.52	0.33-0.91	70	164 669	0.43	0.47	0.39	0.12-0.63
Primary hosp	518	1 085 735	0.48	0.62	0.40	0.18-0.73	367	983 706	0.37	0.44	0.31	0.12-0.55
Secondary hosp	187	379 256	0.49	0.70	0.47	0.09-1.16	133	325 409	0.41	0.51	0.47	0.13-0.63
Tertiary hosp	143	271 448	0.53	0.51	0.44	0.26-0.61	94	196 300	0.48	0.44	0.38	0.20-0.44
Incidence density per 1 000 patient days												
Belgium	**848**	**11 287 211**	**0.08**	**0.08**	**0.06**	**0.03-0.11**	**594**	**9 875 469**	**0.06**	**0.07**	**0.05**	**0.02-0.08**
Flanders	287	6 357 128	0.05	0.05	0.04	0.02-0.07	221	5 801 809	0.04	0.04	0.03	0.01-0.05
Wallonia	431	3 143 011	0.14	0.12	0.10	0.07-0.17	303	2 712 824	0.11	0.11	0.09	0.06-0.14
Brussels	130	1 787 072	0.07	0.08	0.07	0.05-0.11	70	1 360 836	0.05	0.06	0.05	0.01-0.07
Primary hosp	518	7 083 920	0.07	0.08	0.06	0.03-0.10	367	6 440 031	0.06	0.06	0.05	0.02-0.08
Secondary hosp	187	2 356 218	0.08	0.09	0.07	0.02-0.15	133	1 967 859	0.07	0.08	0.05	0.02-0.13
Tertiary hosp	143	1 847 073	0.08	0.07	0.06	0.04-0.08	94	1 467 579	0.06	0.06	0.05	0.03-0.06

Hosp = hospital; n = total number of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) isolates, N = total number of MRSA isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Figure 6. Evolution of the median incidence of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) per 1 000 admissions by region (clinical samples only), Belgian acute care hospitals, 1994-2020

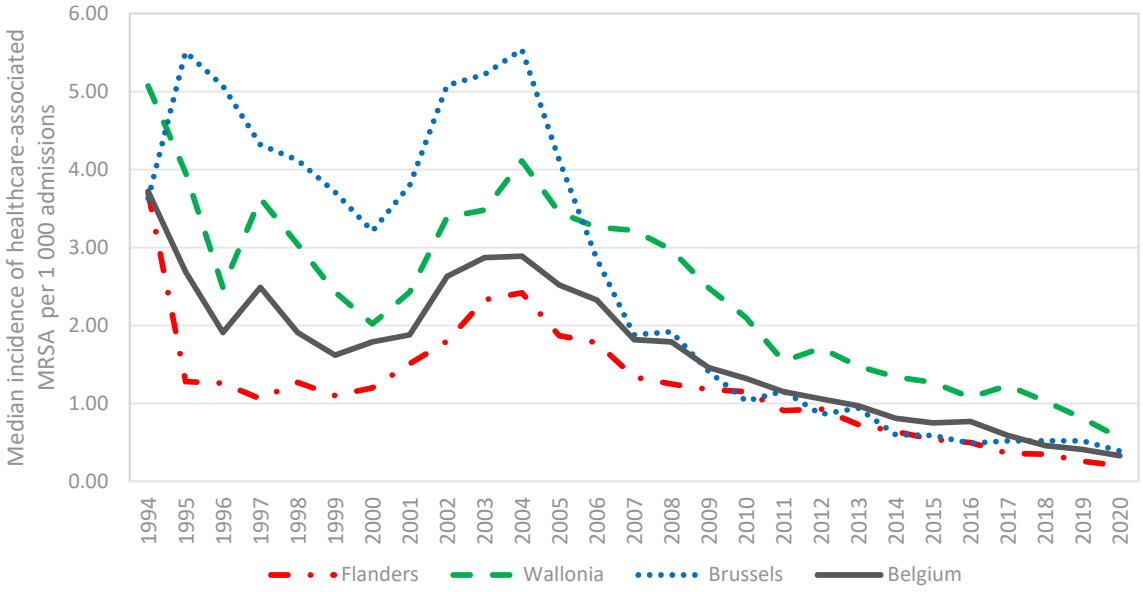


Figure 7. Evolution of the median incidence density of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) per 1 000 patient days by region (clinical samples only), Belgian acute care hospitals, 1994-2020

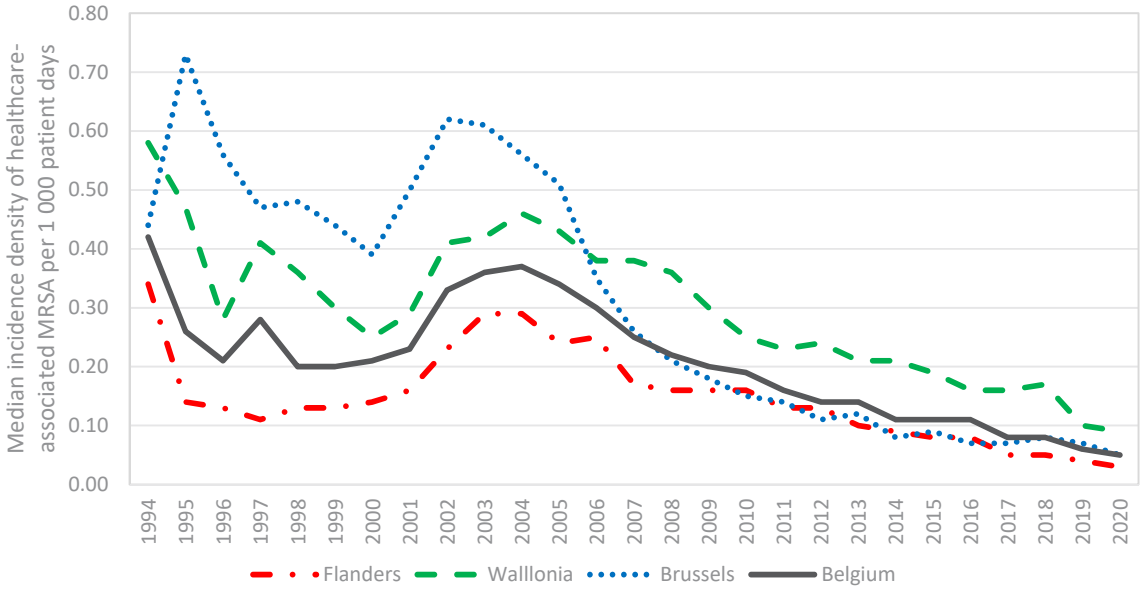
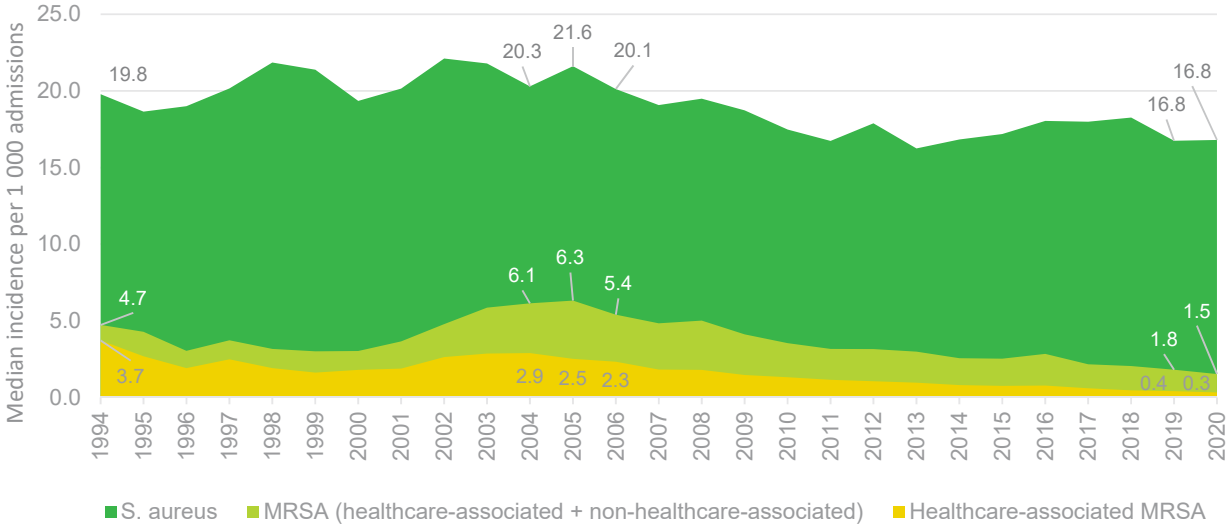


Figure 8 presents the overall evolution of the median incidence of *S. aureus*, MRSA and healthcare-associated MRSA. Due to the combined efforts of the infection prevention and control teams and a whole range of actions (among others recommendations for the prevention of MRSA transmission, more targeted screening policies and hand hygiene campaigns), the proportion of healthcare-associated MRSA on the total number of MRSA dropped from 78.8% in 1994 (start of the surveillance) to 39.8% in 2005 (peak in the MRSA incidence) and 43.1% in 2006 (year in which the surveillance became mandatory). Currently, this proportion is at its lowest: 22.4% in 2019 and 21.7% in 2020.

Figure 8. Evolution of the median incidence of *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA) and healthcare-associated MRSA per 1 000 admissions (clinical samples only), Belgian acute care hospitals, 1994-2020

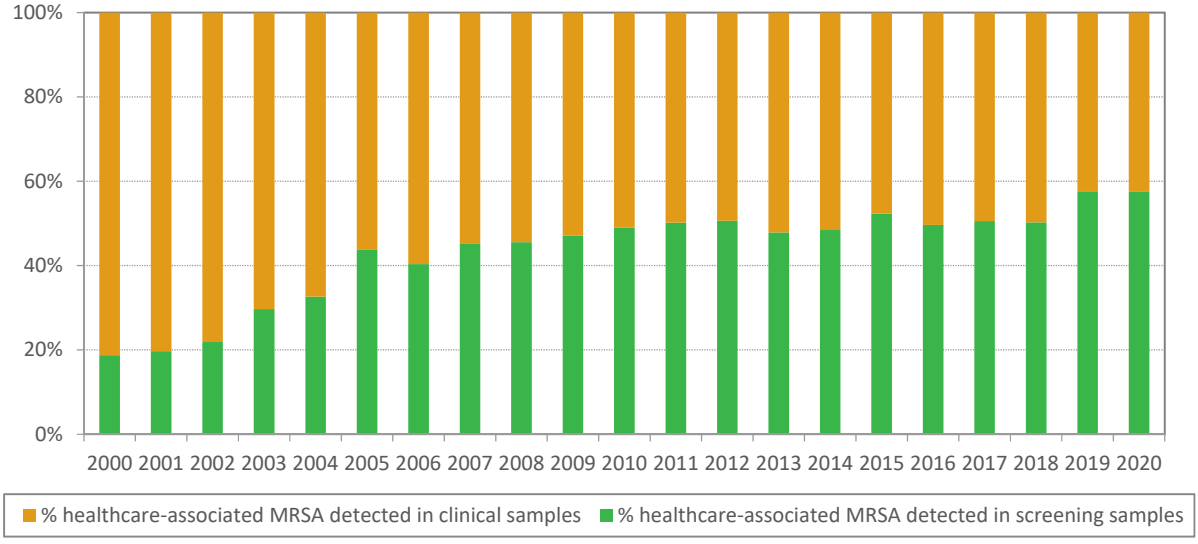


1.3.2 HEALTHCARE-ASSOCIATED MRSA IN SCREENING SAMPLES

In total, 1 147 and 753 screening samples were reported as MRSA positive more than 48 hours after admission in 2019 and 2020, respectively.

Whereas in recent years the number of healthcare-associated MRSA cases detected through screening varied around 50%, a slight increase was observed in 2019 (57.5%) and 2020 (57.6%) (Figure 9).

Figure 9. Evolution of the crude proportion of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) detected by clinical samples or by screening samples, Belgian acute care hospitals, 2000-2020



2. MRSA in chronic care hospitals

2.1 RESISTANCE IN *STAPHYLOCOCCUS AUREUS*

The crude proportion of MRSA on the total number of reported *S. aureus* was 14.3% (n=91/635) in 2019 and 16.2% (n=65/402) in 2020 (Table 6).

The overal evolution of the median MRSA resistance proportion and incidence density is shown in Figure 10. There is a non-significant trend in the resistance proportion of MRSA between 1998 and 2020 (-0.59% per year; p=0.138). In the same time span, the incidence density however significantly decreased (IRR=0.957, 95%CI: 0.943-0.970).

Figure 10. Evolution of the median resistance proportion and incidence density per 1 000 patient days of methicillin-resistant *Staphylococcus aureus* (MRSA; clinical samples only), Belgian chronic care hospitals, 1998-2020

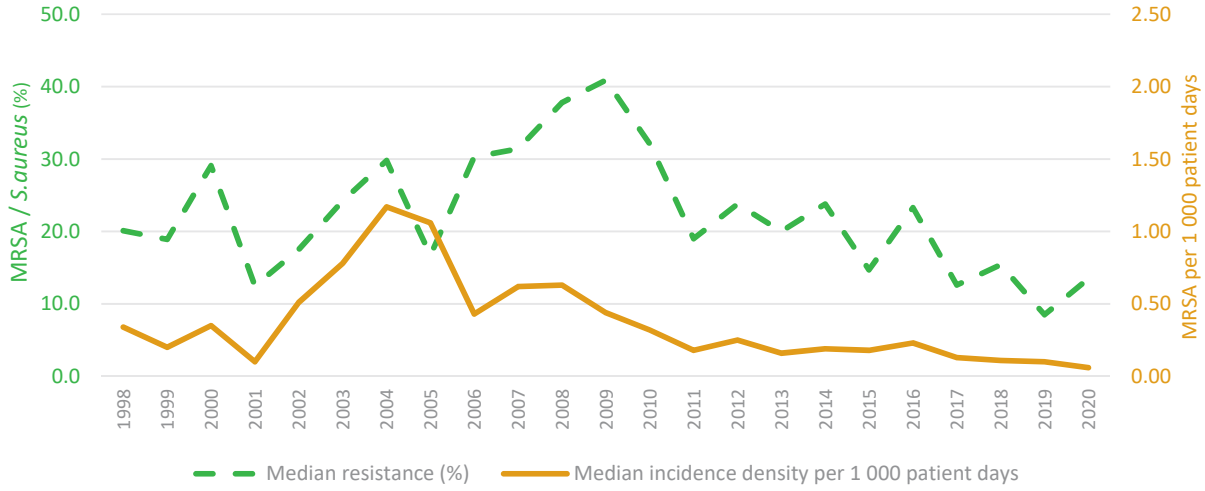


Table 6. Resistance proportion, incidence and incidence density of methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	MRSA (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**91**	**635**	**14.3**	**14.2**	**8.5**	**3.0-19.6**	**65**	**402**	**16.2**	**18.6**	**13.5**	**4.6-37.5**
Flanders	12	159	7.5	5.8	6.1	2.4-9.2	1	54	1.9	3.7	0.0	0.0-11.1
Wallonia	40	353	11.3	13.8	11.2	1.3-25.7	45	305	14.8	21.9	19.0	11.1-37.5
Brussels	39	123	31.7	32.3	32.3	7.9-56.7	19	43	44.2	44.2	44.2	44.2-44.2
Incidence per 1 000 admissions												
Belgium	**91**	**15 018**	**6.06**	**7.62**	**4.29**	**1.75-7.30**	**65**	**11 883**	**5.47**	**5.83**	**3.21**	**1.78-6.28**
Flanders	12	2 948	4.07	4.01	3.61	1.47-6.54	1	1 879	0.53	0.59	0.00	0.00-1.78
Wallonia	40	10 911	3.67	3.18	4.15	0.56-4.43	45	9 287	4.85	5.00	3.60	2.87-6.28
Brussels	39	1 159	33.65	28.18	28.18	17.24-39.13	19	717	26.50	26.50	26.50	26.50-26.50
Incidence density per 1 000 patient days												
Belgium	**91**	**556 617**	**0.16**	**0.17**	**0.10**	**0.03-0.19**	**65**	**397 365**	**0.16**	**0.15**	**0.06**	**0.04-0.25**
Flanders	12	152 334	0.08	0.06	0.06	0.02-0.11	1	87 765	0.01	0.02	0.00	0.00-0.05
Wallonia	40	332 136	0.12	0.12	0.10	0.01-0.23	45	276 411	0.16	0.15	0.13	0.06-0.25
Brussels	39	72 147	0.54	0.52	0.52	0.15-0.89	19	33 189	0.57	0.57	0.57	0.57-0.57

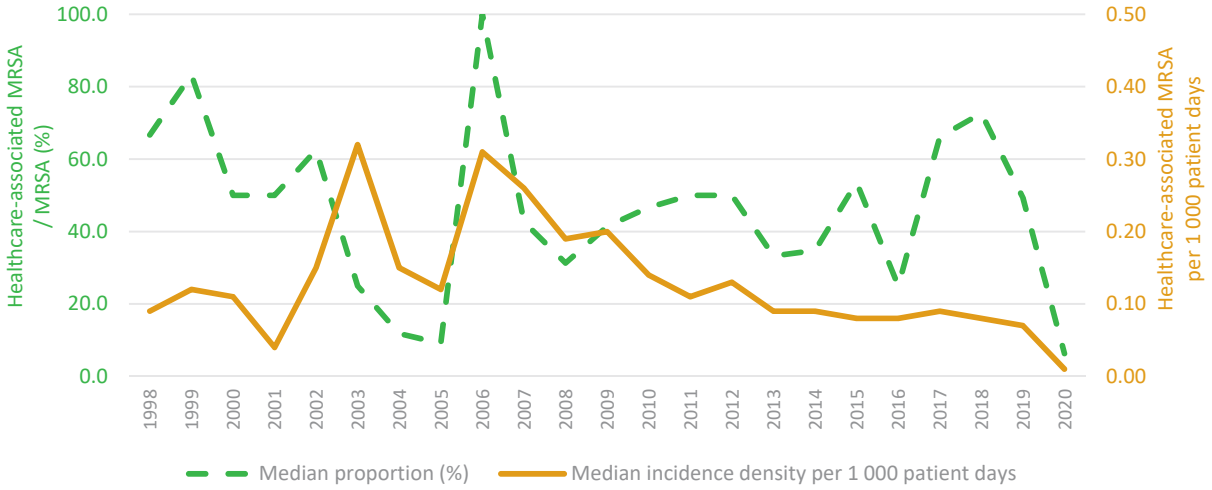
n = total number of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates, N = total number of *Staphylococcus aureus* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

2.2 HEALTHCARE-ASSOCIATED MRSA

Of all MRSA isolated from clinical samples, 53.8% (n=49/91) in 2019 and 23.1% (n=15/65) in 2020 were considered as healthcare-associated (Table 7). The crude incidence density of healthcare-associated MRSA was 0.09 cases per 1 000 patient days in 2019 and 0.04 cases per 1 000 patient days in 2020.

The overall evolution of these indicators (median proportion and incidence density) is presented in Figure 11. Since 2006, there is a significant decrease in the incidence density of healthcare-associated MRSA (IRR=0.896, 95%CI: 0.875-0.917; p<0.001).

Figure 11. Evolution of the median proportion and incidence density per 1 000 patient days of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA; clinical samples only), Belgian chronic care hospitals, 1998-2020



In addition, 51 and 13 cases of healthcare-associated MRSA were detected through screening in 2019 and 2020, respectively. Approximately half of all healthcare-associated MRSA (51.0% in 2019, 46.4% in 2020) were detected through screening (Figure 12).

Figure 12. Evolution of the crude proportion of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) detected by clinical samples or screening samples, Belgian chronic care hospitals, 2007-2020

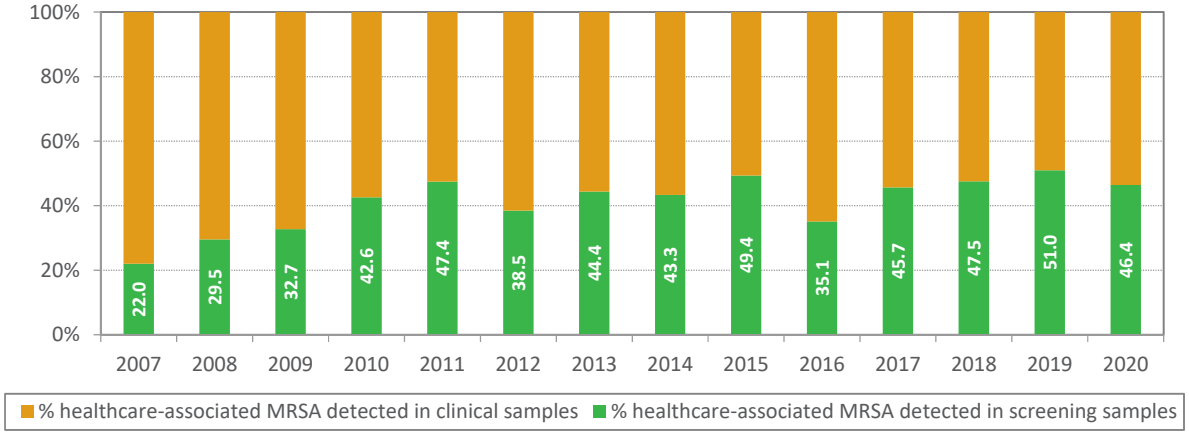


Table 7. Resistance proportion, incidence and incidence density of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Healthcare-associated MRSA (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Proportion healthcare-associated MRSA/MRSA (%)												
Belgium	**49**	**91**	**53.8**	**43.8**	**49.3**	**0.0-77.5**	**15**	**65**	**23.1**	**26.4**	**6.3**	**0.0-26.3**
Flanders	7	12	58.3	33.0	28.6	0.0-66.1	0	1	0.0	0.0	0.0	0.0-0.0
Wallonia	23	40	57.5	45.0	35.0	0.0-100	10	45	22.2	39.6	18.8	0.0-100
Brussels	19	39	48.7	62.1	62.1	44.1-80.0	5	19	26.3	26.3	26.3	26.3-26.3
Incidence per 1 000 admissions												
Belgium	**49**	**15 018**	**3.26**	**4.27**	**2.19**	**0.00-5.41**	**15**	**11 883**	**1.26**	**1.64**	**0.18**	**0.00-1.86**
Flanders	7	2 948	2.37	1.81	1.10	0.00-3.62	0	1 879	0.00	0.00	0.00	0.00-0.00
Wallonia	23	10 911	2.11	2.16	1.43	0.00-4.30	10	9 287	1.08	1.57	0.64	0.00-1.86
Brussels	19	1 159	16.39	15.53	15.53	13.79-17.26	5	717	6.97	6.97	6.97	6.97-6.97
Incidence density per 1 000 patient days												
Belgium	**49**	**556 617**	**0.09**	**0.09**	**0.07**	**0.00-0.12**	**15**	**397 365**	**0.04**	**0.04**	**0.01**	**0.00-0.06**
Flanders	7	152 334	0.05	0.03	0.03	0.00-0.07	0	87 765	0.00	0.00	0.00	0.00-0.00
Wallonia	23	332 136	0.07	0.07	0.06	0.00-0.13	10	276 411	0.04	0.04	0.04	0.00-0.06
Brussels	19	72 147	0.26	0.26	0.26	0.12-0.39	5	33 189	0.15	0.15	0.15	0.15-0.15

n = total number of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) isolates, N = total number of MRSA isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

PART 2. VANCOMYCIN-RESISTANT ENTEROCOCCI (VRE)

Although participation in the VRE surveillance was optional, 84.3% (n=86/102, i.e. one less than the mandatory MRSA surveillance) and 91.2% (n=93/102, i.e. three less than MRSA) of all Belgian acute care hospital administrative groups (mergers) participated with at least one hospital site in 2019 and 2020, respectively.

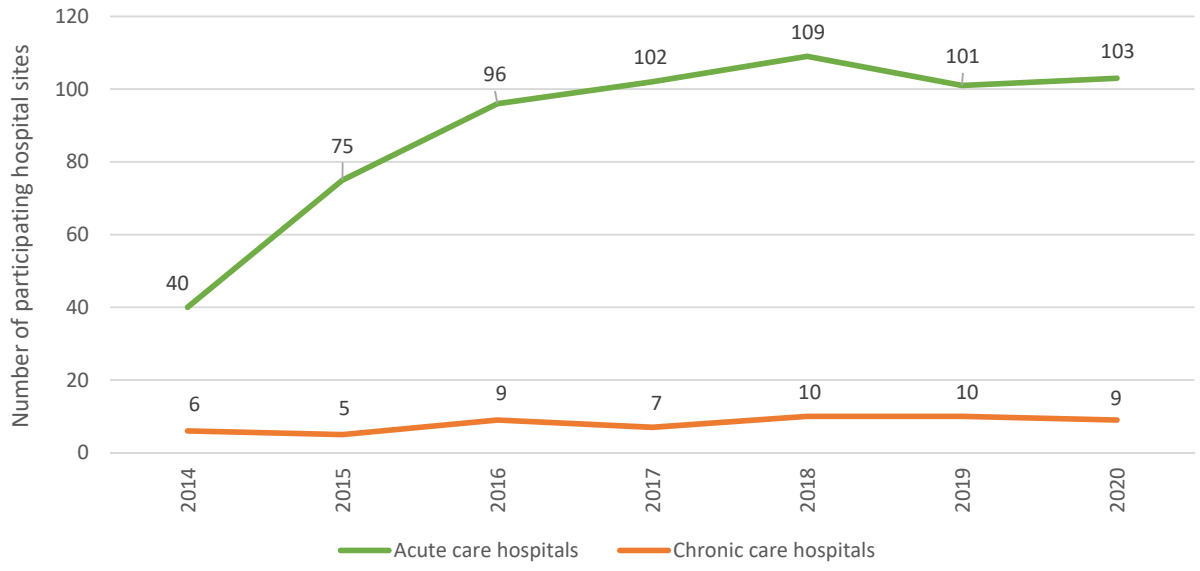
Table 8 presents the 2019 and 2020 participation in the VRE surveillance by hospital care type, region and level of specialty care within the hospital. All hospitals provided Type D data and were therefore included. Figure 13 shows the number of participating hospital sites since the beginning of the surveillance (2014).

Table 8. Participation in the surveillance of vancomycin-resistant enterococci by hospital care type, region and level of specialty care within the hospitals (for acute care hospitals only), Belgian acute and chronic care hospitals, 2019 and 2020

	2019				2020			
	Flanders	Wallonia	Brussels	Belgium	Flanders	Wallonia	Brussels	Belgium
N of acute care hospitals (%)	**50**	**36**	**15**	**101**	**52**	**38**	**13**	**103**
Primary hospitals	40	30	8	78	43	30	8	81
Secondary hospitals	7	5	4	16	6	7	3	16
Tertiary hospitals	3	1	3	7	3	1	2	6
N of chronic care hospitals (%)	**4**	**5**	**1**	**10**	**3**	**6**	**0**	**9**

N = number

Figure 13. Evolution of the participation in the surveillance of vancomycin-resistant enterococci based on the resistance proportion indicator, Belgian acute and chronic care hospital sites, 1994-2020



1. VRE in acute care hospitals

1.1 *ENTEROCOCCUS FAECIUM*

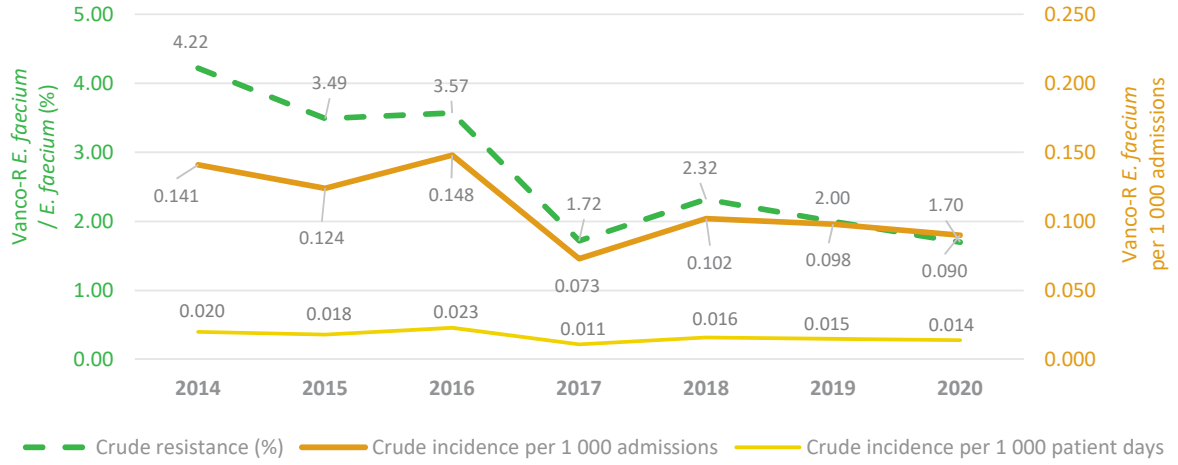
In 2019, 8 335 *E. faecium* (median: 56 isolates per hospital; IQR: 25-94) isolated from clinical samples (excluding faeces samples) were reported. These were 8 167 cases (median: 51 isolates per hospital; IQR: 29-99) in 2020.

Among these, 167 cases of vanco-R *E. faecium* were reported by 44 (43.6%) acute care hospitals (min-max: 1-22 isolates per hospital) in 2019. These were 139 cases reported by 32 (31.1%) acute care hospitals (min-max: 1-29 isolates) in 2020.

The crude resistance proportion and incidence of vanco-R *E. faecium* was 2.00% and 0.098 cases per 1 000 admissions in 2019. In 2020, these indicators were 1.70% and 0.090 cases per 1 000 admissions, respectively (Table 9).

No statistically significant trend can be observed in the resistance proportion (-0.13% per year; p=0.292) and incidence (IRR=0.981, 95%CI: 0.920-1.047; p=0.569) of vanco-R *E. faecium* (Figure 14).

Figure 14. Evolution of the crude resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of vancomycin resistance in Enterococcus faecium (clinical samples only), Belgian acute care hospitals, 2014-2020



Note: Prior to 2016, vancomycin resistance was separated under vancomycin resistance (defined as vanco-R and susceptible to teicoplanin or susceptibility unknown) and glycopeptide resistance (defined as vanco-R and teicoplanin resistant). Since 2017, vancomycin resistance is questioned independently from the susceptibility to teicoplanin.

1.2 *ENTEROCOCCUS FAECALIS*

A total of 24 384 *E. faecalis* (median: 163 isolates per hospital; IQR: 72-301) isolated from clinical samples (excluding faeces samples) were reported in 2019. These were 23 070 isolates (median: 155 per hospital; IQR: 72-301) in 2020.

In 2019, 12 cases of vanco-R *E. faecalis* were reported by 5 (7.9%) acute care hospitals (min-max: 1-5 isolates per hospital). Eighteen cases were reported by 12 (11.7%) acute care hospitals (min-max: 1-3 isolates) in 2020.

Table 9. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) vancomycin-resistant *Enterococcus faecium* (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	Vancomycin-resistant *Enterococcus faecium* (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**167**	**8 335**	**2.00**	**1.77**	**0.00**	**0.00-2.63**	**139**	**8 167**	**1.70**	**1.85**	**0.00**	**0.00-1.15**
Flanders	66	5 001	1.32	0.94	0.00	0.00-1.03	56	5 121	1.09	0.92	0.00	0.00-0.00
Wallonia	79	2 219	3.56	2.57	1.42	0.00-4.31	77	2 174	3.54	3.12	0.00	0.00-2.15
Brussels	22	1 115	1.97	2.59	0.00	0.00-3.85	6	872	0.69	1.88	0.00	0.00-1.39
Primary hosp	78	4 507	1.73	1.71	0.00	0.00-2.17	74	4 666	1.59	1.91	0.00	0.00-0.00
Secondary hosp	43	1 794	2.40	1.47	1.07	0.00-1.68	39	1 654	2.36	1.66	0.48	0.00-1.71
Tertiary hosp	46	2 034	2.26	3.00	2.98	0.71-5.73	26	1 847	1.41	1.59	1.22	0.53-2.16
Incidence per 1 000 admissions												
Belgium	**167**	**1 710 949**	**0.098**	**0.093**	**0.000**	**0.000-0.089**	**132**	**1 458 957**	**0.090**	**0.088**	**0.000**	**0.000-0.082**
Flanders	66	1 000 658	0.066	0.042	0.000	0.000-0.068	56	895 353	0.063	0.055	0.000	0.000-0.000
Wallonia	79	468 165	0.169	0.171	0.057	0.000-0.191	70	398 935	0.175	0.149	0.000	0.000-0.115
Brussels	22	242 126	0.091	0.080	0.000	0.000-0.152	6	164 669	0.036	0.051	0.000	0.000-0.059
Primary hosp	78	1 060 245	0.074	0.082	0.000	0.000-0.080	67	937 248	0.071	0.079	0.000	0.000-0.000
Secondary hosp	43	379 256	0.113	0.112	0.042	0.000-0.128	39	325 409	0.120	0.123	0.059	0.000-0.136
Tertiary hosp	46	271 448	0.169	0.175	0.152	0.055-0.328	26	196 300	0.132	0.123	0.142	0.045-0.170
Incidence density per 1 000 patient days												
Belgium	**167**	**11 129 680**	**0.015**	**0.012**	**0.000**	**0.000-0.014**	**132**	**9 592 710**	**0.014**	**0.013**	**0.000**	**0.000-0.012**
Flanders	66	6 166 239	0.011	0.006	0.000	0.000-0.010	56	5 519 050	0.010	0.008	0.000	0.000-0.000
Wallonia	79	3 176 369	0.025	0.019	0.008	0.000-0.027	70	2 712 824	0.026	0.021	0.000	0.000-0.017
Brussels	22	1 787 072	0.012	0.011	0.000	0.000-0.024	6	1 360 836	0.004	0.007	0.000	0.000-0.007
Primary hosp	78	6 926 389	0.011	0.009	0.000	0.000-0.013	67	6 157 272	0.011	0.012	0.000	0.000-0.000
Secondary hosp	43	2 356 218	0.018	0.016	0.007	0.000-0.018	39	1 967 859	0.020	0.016	0.007	0.000-0.020
Tertiary hosp	46	1 847 073	0.025	0.026	0.024	0.007-0.044	26	1 467 579	0.018	0.017	0.019	0.006-0.021

Hosp = hospital; n = total number of vancomycin-resistant *Enterococcus faecium* isolates, N = total number of *Enterococcus faecium* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

1.3 OUTBREAKS

An outbreak (i.e. at least one new secondary case within the same ward and within one month) with vanco-R enterococci was reported by 17.6% (n=16/91) of the participating hospitals in 2019. In 2020 (covid-19 year), merely 5.6% (n=5/89) of the participating hospitals reported at least one cluster. Table 10 presents the number of clusters reported and the number of patients involved between 2014 and 2020.

Table 10. Evolution of the number of outbreaks reported in the national surveillance of resistant, Belgian acute care hospitals, 2014-2020

	2014	2015	2016	2017	2018	2019	2020
N of hospitals reporting an outbreak (%)	3/40 (7.5)	7/75 (9.3)	7/95 (7.4)	13/98 (13.3)	13/96 (13.5)	16/91 (17.6)	5/89 (5.6)
N of hospitals with no answer or no type D data	0	0	1	4	13	10	14
N of clusters (min-max)	3 (1-1)	11 (1-4)	12 (1-3)	21 (1-6)	28 (1-13)	19 (1-3)*	7 (1-2)
N of patients involved	68	140	247	166	164	285	27
% patients colonised	*79.4*	*87.7*	*88.8*	*89.8*	*88.4*	*93.1*	*77.8*
% patients infected	*20.6*	*12.3*	*11.2*	*10.2*	*11.6*	*6.9*	*22.2*

*data missing for two hospitals

2. VRE in chronic care hospitals

In total, 131 *E. faecium* (median: 12 per hospital; IQR: 8-20) and 711 *E. faecalis* (median: 69 per hospital; IQR: 43-86) isolated from clinical samples (excluding faeces samples) were reported in 2019. These were 95 *E. faecium* (median: 11 per hospital; IQR: 4-12) and 296 *E. faecalis* (median: 27 per hospital; IQR: 25-50) in 2020.

There were no cases of vanco-R *E. faecium or E. faecalis* reported in both surveillance years. Furthermore, no outbreaks with vanco-R enterococci were reported by the participating chronic care hospitals between 2014 and 2020.

PART 3. RESISTANCE IN GRAM-NEGATIVE BACTERIA

Similar to the MRSA surveillance, 85.3% (n=87/102) and 94.1% (n=96/102) of all acute care hospital administrative groups (mergers) participated in the MRSA surveillance with at least one hospital site in 2019 and 2020, respectively. The number of participating hospital sites can be found in Table 11 by hospital care type, region and level of specialty care within the hospital.

Table 11. Participation in the surveillance of multiresistant gram-negative bacteria (MRGN) by hospital care type, region and level of specialty care within the hospital (for acute care hospitals only), Belgian acute and chronic care hospital sites, 2019 and 2020

	2019				2020			
	Flanders	Wallonia	Brussels	Belgium	Flanders	Wallonia	Brussels	Belgium
N of acute care hospitals (%)	**52**	**36**	**15**	**103**	**56**	**38**	**13**	**107**
Primary hospitals	42	30	8	80	47	30	8	85
Secondary hospitals	7	5	4	16	6	7	3	16
Tertiary hospitals	3	1	3	7	3	1	2	6
N of chronic care hospitals (%)	**4**	**6**	**2**	**12**	**3**	**6**	**1**	**10**

N = number

1. Resistant Gram-negative bacteria in acute care hospitals

1.1 RESISTANCE IN *ESCHERICHIA COLI*

In 2019, 9.9% (n=8 566/86 832) of all *E. coli* isolated from clinical samples were 3GC I/R. This crude resistance proportion decreased to 9.2% (n=8 025/87 152) in 2020. The crude incidence however increased from 4.95 in 2019 to 5.22 per 1 000 admissions in 2020 (Table 12a).

Between 2014 and 2020, a significant change in the resistance proportion (+0.25% per year; p=0.001) and incidence (IRR=1.018, 95%CI: 1.002-1.034; p=0.024) of 3GC I/R *E. coli* can be noted (Figure 15).

A total of 114 cases of meropenem I/R *E. coli* were reported by 53 (51.5%) acute care hospitals (min-max: 1-13 isolates) in 2019. In 2020, these were 87 meropenem I/R *E. coli* isolates reported by 46 (43.0%) hospitals (min-max: 1-8). The crude resistance proportion was 0.13% and 0.10% in 2019 and 2020, respectively. The crude incidence of meropenem I/R *E. coli* was 0.066 cases and 0.058 cases per 1 000 admission, respectively (Table 12b).

Between 2015 and 2020, a small but significant increase in the resistance proportion (+0.01% per year; p<0.001) and incidence (IRR=1.140, 95%CI: 1.069-1.215; p<0.001) of meropenem I/R *E. coli* can be observed.

Table 12a. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Escherichia coli* non-susceptible to third generation cephalosporins (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	Escherichia coli non-susceptible to third generation cephalosporins (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**8 566**	**86 832**	**9.9**	**10.0**	**10.1**	**8.0-12.2**	**8 025**	**87 152**	**9.2**	**9.1**	**9.1**	**7.5-10.7**
Flanders	5 106	53 282	9.6	9.3	9.7	7.2-11.4	4 762	54 413	8.8	8.2	8.4	6.3-9.6
Wallonia	2 268	23 173	9.8	10.1	10.1	8.2-11.6	2 216	23 523	9.4	9.8	9.4	8.4-10.7
Brussels	1 192	10 377	11.5	12.5	12.1	11.2-12.7	1 047	9 216	11.4	10.9	11.4	9.7-11.8
Primary hosp	5 419	58 559	9.3	9.8	10.0	7.8-11.8	5 173	57 778	9.0	8.9	9.1	7.5-10.7
Secondary hosp	1 419	13 407	10.6	10.7	11.4	9.1-12.9	1 319	14 160	9.3	9.3	8.9	8.0-10.5
Tertiary hosp	1 728	14 866	11.6	11.6	11.9	8.8-12.7	1 533	15 214	10.1	10.6	11.1	7.5-13.7
Incidence per 1 000 admissions												
Belgium	**8 566**	**1 729 326**	**4.95**	**5.95**	**4.86**	**3.36-6.81**	**7 859**	**1 505 415**	**5.22**	**5.52**	**5.32**	**3.33-7.14**
Flanders	5 106	1 031 737	4.95	5.05	4.71	3.39-6.51	4 762	941 811	5.06	5.16	5.25	3.04-6.61
Wallonia	2 268	462 576	4.90	7.40	4.96	3.11-7.28	2 050	398 935	5.14	5.84	5.27	3.40-7.78
Brussels	1 192	235 013	5.07	5.59	4.85	3.94-6.85	1 047	164 669	6.36	6.17	6.57	4.89-6.96
Primary hosp	5 419	1 078 622	5.02	6.24	5.02	3.34-6.89	5 096	983 706	5.18	5.52	5.31	3.70-7.04
Secondary hosp	1 419	379 256	3.74	4.32	3.92	3.34-4.82	1 230	325 409	3.78	4.58	4.68	2.52-6.87
Tertiary hosp	1 728	271 448	6.37	6.34	5.83	5.05-7.75	1 533	196 300	7.81	7.85	8.72	6.72-9.58
Incidence density per 1 000 patient days												
Belgium	**8 566**	**11 225 271**	**0.76**	**0.79**	**0.72**	**0.52-0.99**	**7 859**	**9 875 469**	**0.80**	**0.81**	**0.77**	**0.53-1.06**
Flanders	5 106	6 357 128	0.80	0.82	0.73	0.59-1.00	4 762	5 801 809	0.82	0.81	0.76	0.51-1.09
Wallonia	2 268	3 143 011	0.72	0.81	0.79	0.48-1.01	2 050	2 712 824	0.76	0.83	0.83	0.56-1.06
Brussels	1 192	1 725 132	0.69	0.65	0.66	0.39-0.83	1 047	1 360 836	0.77	0.70	0.77	0.53-0.95
Primary hosp	5 419	7 021 980	0.77	0.81	0.76	0.51-0.99	5 096	6 440 031	0.79	0.81	0.78	0.55-1.06
Secondary hosp	1 419	2 356 218	0.60	0.62	0.64	0.44-0.72	1 230	1 967 859	0.63	0.66	0.53	0.40-0.92
Tertiary hosp	1 728	1 847 073	0.94	0.97	0.91	0.66-1.09	1 533	1 467 579	1.04	1.08	1.11	0.95-1.24

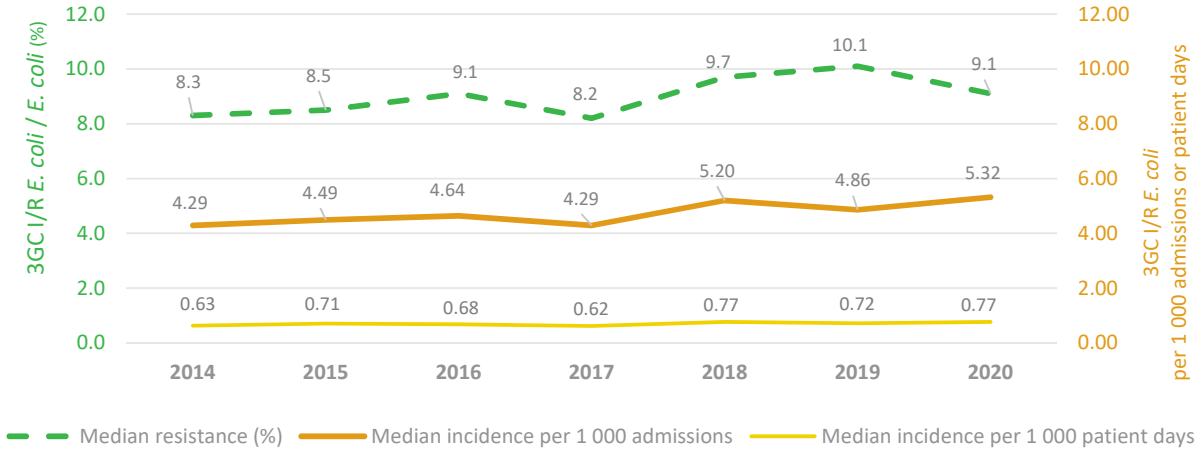
Hosp = hospital; n = total number of *Escherichia coli* non-susceptible (intermediate susceptibility or resistant) to 3rd generation cephalosporins isolates, N = total number of *Escherichia coli* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Table 12b. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Escherichia coli* non-susceptible to meropenem (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	Escherichia coli non-susceptible to meropenem (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**114**	**86 832**	**0.13**	**0.16**	**0.05**	**0.00-0.16**	**87**	**87 152**	**0.10**	**0.10**	**0.00**	**0.00-0.15**
Flanders	53	53 282	0.10	0.11	0.03	0.00-14	44	54 413	0.08	0.08	0.00	0.00-0.13
Wallonia	49	23 173	0.21	0.28	0.10	0.00-0.37	28	23 523	0.12	0.13	0.00	0.00-0.17
Brussels	12	10 377	0.12	0.09	0.00	0.00-0.13	15	9 216	0.16	0.12	0.06	0.00-0.18
Primary hosp	80	58 559	0.14	0.17	0.00	0.00-0.16	66	57 778	0.11	0.11	0.00	0.00-0.17
Secondary hosp	17	13 407	0.13	0.14	0.09	0.00-0.30	10	14 160	0.07	0.06	0.00	0.00-0.09
Tertiary hosp	17	14 866	0.11	0.13	0.08	0.05-0.13	11	15 214	0.07	0.09	0.09	0.00-0.18
Incidence per 1 000 admissions												
Belgium	**114**	**1 729 326**	**0.066**	**0.093**	**0.024**	**0.000-0.099**	**87**	**1 505 415**	**0.058**	**0.062**	**0.000**	**0.000-0.105**
Flanders	53	1 031 737	0.051	0.050	0.011	0.000-0.068	44	941 811	0.047	0.045	0.000	0.000-0.090
Wallonia	49	462 576	0.106	0.177	0.055	0.000-0.174	28	398 935	0.070	0.086	0.000	0.000-0.136
Brussels	12	235 013	0.051	0.041	0.000	0.000-0.073	15	164 669	0.091	0.070	0.039	0.000-0.135
Primary hosp	80	1 078 622	0.074	0.103	0.000	0.000-0.099	66	983 706	0.067	0.067	0.000	0.000-0.110
Secondary hosp	17	379 256	0.045	0.052	0.025	0.000-0.087	10	325 409	0.031	0.038	0.000	0.000-0.059
Tertiary hosp	17	271 448	0.063	0.072	0.033	0.025-0.073	11	196 300	0.056	0.061	0.055	0.000-0.121
Incidence density per 1 000 patient days												
Belgium	**114**	**11 225 271**	**0.010**	**0.013**	**0.003**	**0.000-0.015**	**87**	**9 875 469**	**0.009**	**0.009**	**0.000**	**0.000-0.016**
Flanders	53	6 357 128	0.008	0.008	0.002	0.000-0.013	44	5 801 809	0.008	0.007	0.000	0.000-0.014
Wallonia	49	3 143 011	0.016	0.024	0.009	0.000-0.025	28	2 712 824	0.010	0.013	0.000	0.000-0.017
Brussels	12	1 725 132	0.007	0.007	0.000	0.000-0.011	15	1 360 836	0.011	0.009	0.005	0.000-0.015
Primary hosp	80	7 021 980	0.011	0.014	0.000	0.000-0.015	66	6 440 031	0.010	0.010	0.000	0.000-0.017
Secondary hosp	17	2 356 218	0.007	0.009	0.004	0.000-0.014	10	1 967 859	0.005	0.005	0.000	0.000-0.007
Tertiary hosp	17	1 847 073	0.009	0.012	0.005	0.004-0.011	11	1 467 579	0.007	0.008	0.008	0.000-0.015

Hosp = hospital; n = total number of *Escherichia coli* non-susceptible (intermediate susceptibility or resistant) to meropenem isolates, N = total number of *Escherichia coli* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Figure 15. Evolution of the median resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Escherichia coli* non-susceptible to third generation cephalosporins (clinical samples only), Belgian acute care hospitals, 2014-2020



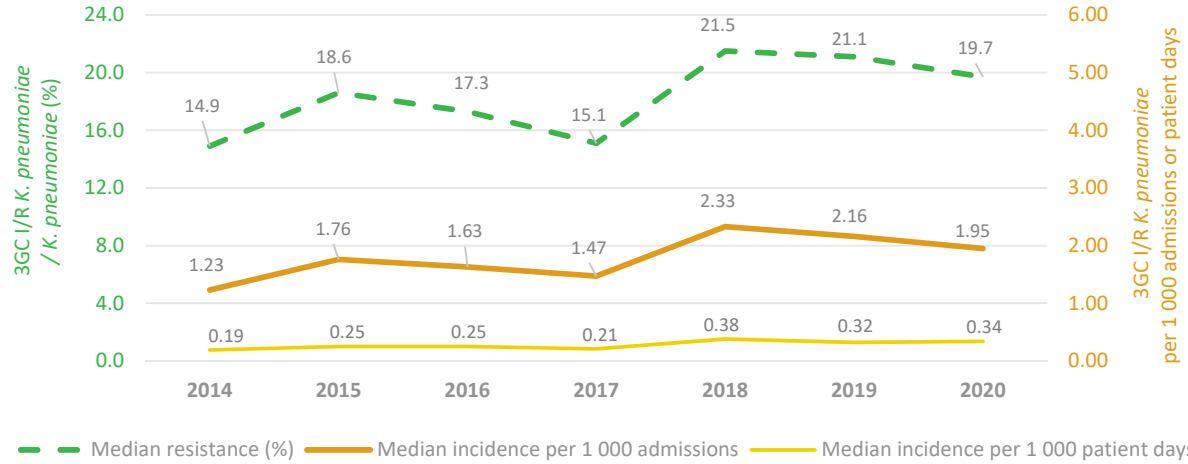
3GC = 3rd cephalosporins, I/R = intermediate susceptibility or resistant; note: prior to 2018 non-susceptibility to 4th generation cephalosporins was included

1.2 RESISTANCE IN *KLEBSIELLA PNEUMONIAE*

In 2019, the crude resistance proportion 3GC I/R *K. pneumoniae* was 22.7% (n=4 557/20 037), while the crude incidence was 2.64 per 1 000 admissions (clinical samples only). In 2020, these were 21.3% (n=4 128/19 338) and 2.67 cases per 1 000 admissions, respectively (Table 13a).

Between 2014 and 2020, the resistance proportion (+0.82% per year; p=0.002) and incidence (IRR=1.060, 95%CI: 1.040-1.080; p<0.001) of 3GC I/R *K. pneumoniae* significantly increased. Since 2018, a significant decrease in the resistance proportion (-1.62% per year; p<0.001) and a non-significant decline in incidence (IRR=0.961, 95%CI: 0.924-1.000; p=0.055) can however be observed (Figure 16).

Figure 16. Evolution of the median resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to third generation cephalosporins (clinical samples only), Belgian acute care hospitals, 2014-2020



3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant; note: prior to 2018 non-susceptibility to 4th generation cephalosporins was included

Table 13a. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to third generation cephalosporins (clinical samples only) by region and specialty care level within the hospital, Belgian acute care hospitals, 2019 and 2020

	Klebsiella pneumoniae non-susceptible to third generation cephalosporins (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**4 557**	**20 037**	**22.7**	**23.4**	**21.1**	**13.9-30.1**	**4 128**	**19 338**	**21.3**	**21.2**	**19.7**	**11.6-29.1**
Flanders	1 967	10 682	18.4	18.5	15.3	11.2-19.0	1 790	10 685	16.8	15.8	12.9	9.2-19.4
Wallonia	1 834	6 431	28.5	28.6	27.3	22.4-39.0	1 716	6 209	27.6	27.5	29.1	20.5-33.8
Brussels	756	2 924	25.9	28.1	29.5	21.7-33.0	622	2 444	25.5	25.9	27.0	22.1-30.5
Primary hosp	2 712	12 353	22.0	22.3	19.0	12.9-29.0	2 571	12 088	21.3	21.1	19.7	11.0-29.1
Secondary hosp	857	3 399	25.2	28.7	23.9	16.3-35.0	821	3 720	22.1	21.5	20.5	15.8-29.1
Tertiary hosp	988	4 285	23.1	24.1	22.5	18.4-30.7	736	3 530	20.8	21.4	19.6	16.7-23.5
Incidence per 1 000 admissions												
Belgium	**4 557**	**1 729 326**	**2.64**	**3.66**	**2.16**	**1.16-3.80**	**4 017**	**1 505 415**	**2.67**	**3.04**	**1.95**	**1.07-4.18**
Flanders	1 967	1 031 737	1.91	1.90	1.37	1.00-2.17	1 790	941 811	1.90	1.84	1.33	0.92-2.02
Wallonia	1 834	462 576	3.96	6.22	3.19	2.15-7.63	1 605	398 935	4.02	4.68	4.19	2.03-6.58
Brussels	756	235 013	3.22	3.61	3.12	2.16-4.75	622	164 669	3.78	3.62	3.34	2.71-4.50
Primary hosp	2 712	1 078 622	2.51	3.82	2.00	1.04-3.87	2 502	983 706	2.54	2.99	1.83	1.03-4.31
Secondary hosp	857	379 256	2.26	2.76	2.16	1.43-3.46	779	325 409	2.39	2.97	2.21	1.55-3.34
Tertiary hosp	988	271 448	3.64	3.79	3.19	2.77-5.75	736	196 300	3.75	3.92	3.31	3.08-4.90
Incidence density per 1 000 patient days												
Belgium	**4 557**	**11 225 271**	**0.41**	**0.44**	**0.32**	**0.19-0.52**	**4 017**	**9 875 469**	**0.41**	**0.43**	**0.34**	**0.16-0.57**
Flanders	1 967	6 357 128	0.31	0.29	0.21	0.16-0.32	1 790	5 801 809	0.31	0.29	0.20	0.14-0.35
Wallonia	1 834	3 143 011	0.58	0.65	0.53	0.35-0.83	1 605	2 712 824	0.59	0.64	0.60	0.36-0.91
Brussels	756	1 725 132	0.44	0.41	0.42	0.26-0.46	622	1 360 836	0.46	0.42	0.50	0.33-0.53
Primary hosp	2 712	7 021 980	0.39	0.43	0.30	0.19-0.53	2 502	6 440 031	0.39	0.42	0.31	0.16-0.60
Secondary hosp	857	2 356 218	0.36	0.40	0.34	0.20-0.48	779	1 967 859	0.40	0.42	0.42	0.25-0.50
Tertiary hosp	988	1 847 073	0.53	0.58	0.44	0.42-0.84	736	1 467 579	0.50	0.55	0.43	0.38-0.53

Hosp = hospital; n = total number of *Klebsiella pneumoniae* non-susceptible (intermediate susceptibility or resistant) to 3rd generation cephalosporins isolates, N = total number of *Klebsiella pneumoniae* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Table 13b. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to meropenem (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

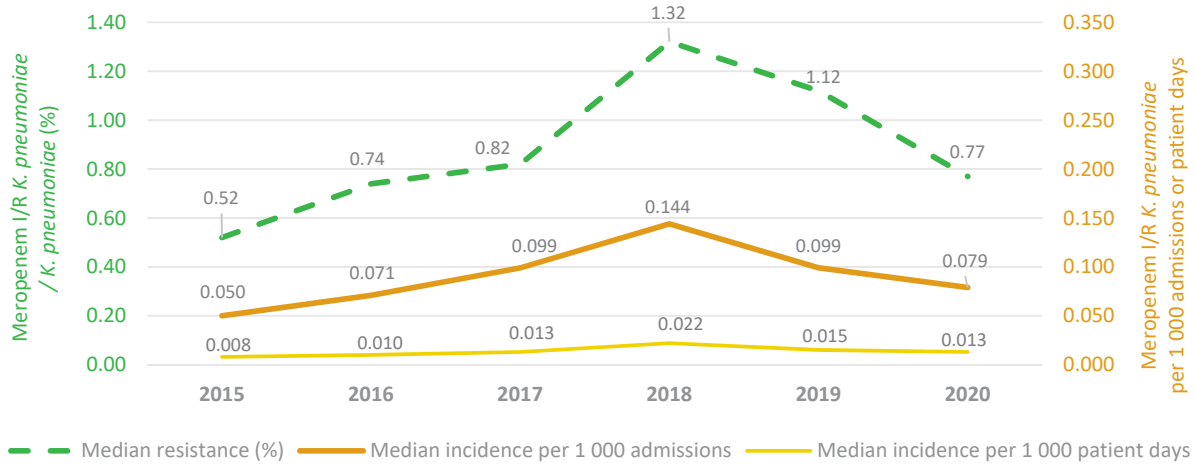
	Klebsiella pneumoniae non-susceptible to meropenem (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**424**	**20 037**	**2.12**	**2.05**	**1.12**	**0.00-2.35**	**342**	**19 338**	**1.77**	**1.52**	**0.77**	**0.00-2.04**
Flanders	107	10 682	1.00	0.93	0.19	0.00-1.48	108	10 685	1.01	0.80	0.00	0.00-1.11
Wallonia	225	6 431	3.50	3.33	1.52	0.00-4.17	177	6 209	2.85	2.51	1.67	0.66-4.17
Brussels	92	2 924	3.15	2.83	1.42	1.13-4.00	57	2 444	2.33	1.70	1.72	0.00-2.63
Primary hosp	215	12 353	1.74	1.90	1.11	0.00-2.25	197	12 088	1.63	1.36	0.53	0.00-1.72
Secondary hosp	93	3 399	2.74	2.33	0.00	0.00-1.90	71	3 720	1.91	2.08	2.04	0.30-3.24
Tertiary hosp	116	4 285	2.71	3.09	2.26	1.38-4.61	74	3 530	2.10	2.19	1.43	1.04-3.65
Incidence per 1 000 admissions												
Belgium	**424**	**1 729 326**	**0.245**	**0.344**	**0.099**	**0.000-0.325**	**336**	**1 505 415**	**0.223**	**0.255**	**0.079**	**0.000-0.301**
Flanders	107	1 031 737	0.104	0.104	0.019	0.000-0.149	108	941 811	0.115	0.096	0.000	0.000-0.120
Wallonia	225	462 576	0.486	0.683	0.231	0.000-0.672	171	398 935	0.429	0.493	0.219	0.028-0.776
Brussels	92	235 013	0.391	0.365	0.173	0.134-0.432	57	164 669	0.346	0.279	0.265	0.000-0.415
Primary hosp	215	1 078 622	0.199	0.327	0.094	0.000-0.303	194	983 706	0.197	0.235	0.051	0.000-0.247
Secondary hosp	93	379 256	0.245	0.367	0.000	0.000-0.238	68	325 409	0.209	0.296	0.204	0.025-0.441
Tertiary hosp	116	271 448	0.427	0.485	0.381	0.199-0.758	74	196 300	0.377	0.428	0.260	0.170-0.764
Incidence density per 1 000 patient days												
Belgium	**424**	**11 225 271**	**0.038**	**0.045**	**0.015**	**0.000-0.041**	**336**	**9 875 469**	**0.034**	**0.036**	**0.013**	**0.000-0.045**
Flanders	107	6 357 128	0.017	0.016	0.003	0.000-0.022	108	5 801 809	0.019	0.016	0.000	0.000-0.019
Wallonia	225	3 143 011	0.072	0.087	0.036	0.000-0.089	171	2 712 824	0.063	0.067	0.037	0.005-0.091
Brussels	92	1 725 132	0.053	0.043	0.026	0.015-0.041	57	1 360 836	0.042	0.034	0.033	0.000-0.051
Primary hosp	215	7 021 980	0.031	0.038	0.015	0.000-0.041	194	6 440 031	0.030	0.033	0.008	0.000-0.032
Secondary hosp	93	2 356 218	0.039	0.063	0.000	0.000-0.029	68	1 967 859	0.035	0.045	0.039	0.006-0.063
Tertiary hosp	116	1 847 073	0.063	0.075	0.050	0.028-0.140	74	1 467 579	0.050	0.057	0.034	0.021-0.112

Hosp = hospital; n = total number of *Klebsiella pneumoniae* non-susceptible (intermediate susceptibility or resistant) to meropenem isolates, N = total number of *Klebsiella pneumoniae* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Cases of meropenem I/R *K. pneumoniae* were reported by 62.1% (n=64/103; min-max: 1-60 isolates) and 59.8% (n=64/107; min-max: 1-30 isolates) of the acute care hospitals in 2019 and 2020, respectively. The crude resistance proportion and incidence were 2.12% or 0.245 cases per 1 000 admissions in 2019 and 1.77% or 0.223 cases per 1 000 admissions in 2020, respectively (Table 13b).

Between 2015 and 2020, a non-significant increase in the resistance proportion (+0.07% per year; p=0.295) and incidence (IRR=1.025, 95%CI: 0.977-1.075; p=0.311) of meropenem I/R *K. pneumoniae* can be observed. Since 2018, there is however a significant decrease in the resistance proportion (-0.35% per year; p=0.010) and a non-significant decline in the incidence (IRR=0.919, 95%CI: 0.820-1.029; p=0.143) (Figure 17).

Figure 17. Evolution of the median resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to meropenem (clinical samples only), Belgian acute care hospitals, 2014-2020



I/R = intermediate susceptibility or resistant

1.3 RESISTANCE IN *ACINETOBACTER BAUMANNII*

A minority of acute care hospitals reported at least one meropenem I/R *A. baumannii*: 28.2% (n=29/103; min-max: 1-9 isolates) in 2019 and 23.4% (n=25/107; min-max: 1-15 isolates) in 2020 (clinical samples only). The crude resistance proportion and incidence of meropenem I/R *A. baumannii* in clinical samples was 6.75% (n=56/830) and 0.032 cases per 1 000 admissions in 2019. In 2020, these were slightly higher: 7.28% (n=59/810) and 0.034 cases per 1 000 admissions, respectively (Table 14).

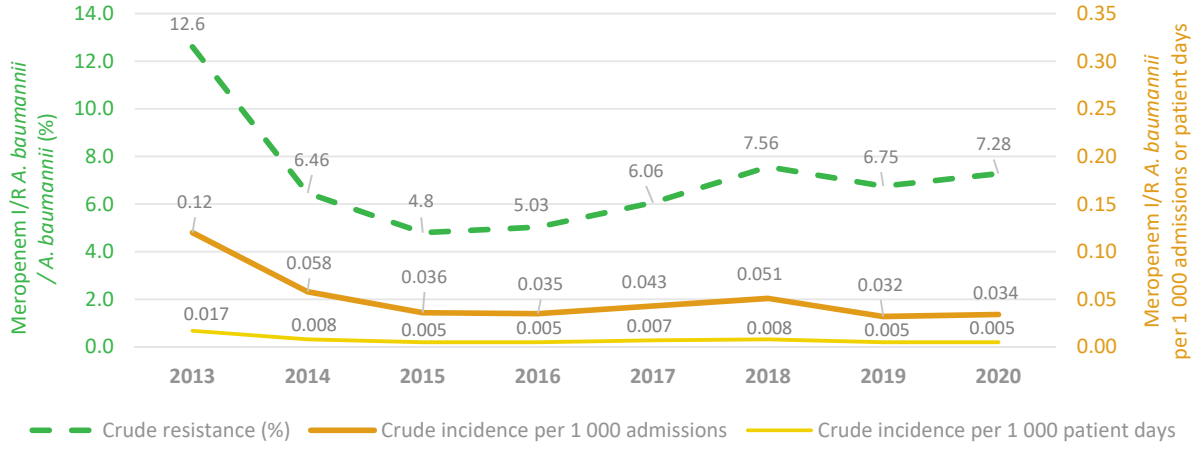
Figure 18 presents the evolution of the crude (median all zero values) resistance proportion and incidence of meropenem I/R *A. baumannii*. Since 2013, no significant change in the evolution of the resistance proportion (-0.18% per year; p=0.545) can be observed. The incidence however significantly decreased between 2013 and 2020 (IRR=0.912, 95%CI: 0.860-0.966; p=0.002).

Table 14. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Acinetobacter baumannii* non-susceptible to meropenem (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	Acinetobacter baumannii non-susceptible to meropenem (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**56**	**830**	**6.75**	**6.61**	**0.00**	**0.00-4.88**	**59**	**810**	**7.28**	**5.67**	**0.00**	**0.00-0.00**
Flanders	19	476	3.99	3.03	0.00	0.00-0.00	18	448	4.02	3.43	0.00	0.00-0.00
Wallonia	13	234	5.56	4.01	0.00	0.00-0.00	21	240	8.75	6.69	0.00	0.00-0.00
Brussels	24	120	20.00	25.23	15.91	0.00-33.33	20	122	16.39	12.33	0.00	0.00-10.00
Primary hosp	16	412	3.88	4.88	0.00	0.00-0.00	18	381	4.72	4.56	0.00	0.00-0.00
Secondary hosp	12	177	6.78	12.66	4.92	0.00-22.50	14	174	8.05	8.47	0.00	0.00-6.52
Tertiary hosp	28	241	11.62	12.46	10.00	4.88-15.91	27	255	10.59	13.86	5.82	2.82-28.30
Incidence per 1 000 admissions												
Belgium	**56**	**1 729 326**	**0.032**	**0.033**	**0.000**	**0.000-0.029**	**51**	**1 505 415**	**0.034**	**0.031**	**0.000**	**0.000-0.000**
Flanders	19	1 031 737	0.018	0.014	0.000	0.000-0.000	18	941 811	0.019	0.020	0.000	0.000-0.000
Wallonia	13	462 576	0.028	0.037	0.000	0.000-0.000	13	398 935	0.033	0.029	0.000	0.000-0.000
Brussels	24	235 013	0.102	0.088	0.047	0.000-0.166	20	164 669	0.121	0.084	0.000	0.000-0.063
Primary hosp	16	1 078 622	0.015	0.023	0.000	0.000-0.000	17	983 706	0.017	0.023	0.000	0.000-0.000
Secondary hosp	12	379 256	0.032	0.047	0.025	0.000-0.061	7	325 409	0.022	0.020	0.000	0.000-0.031
Tertiary hosp	28	271 448	0.103	0.116	0.071	0.000-0.178	27	196 300	0.138	0.176	0.055	0.039-0.201
Incidence density per 1 000 patient days												
Belgium	**56**	**11 225 271**	**0.005**	**0.004**	**0.000**	**0.000-0.005**	**51**	**9 875 469**	**0.005**	**0.004**	**0.000**	**0.000-0.000**
Flanders	19	6 357 128	0.003	0.002	0.000	0.000-0.000	18	5 801 809	0.003	0.003	0.000	0.000-0.000
Wallonia	13	3 143 011	0.004	0.003	0.000	0.000-0.000	13	2 712 824	0.005	0.004	0.000	0.000-0.000
Brussels	24	1 725 132	0.014	0.012	0.006	0.000-0.024	20	1 360 836	0.015	0.010	0.000	0.000-0.006
Primary hosp	16	7 021 980	0.002	0.002	0.000	0.000-0.000	17	6 440 031	0.003	0.003	0.000	0.000-0.000
Secondary hosp	12	2 356 218	0.005	0.007	0.004	0.000-0.007	7	1 967 859	0.004	0.002	0.000	0.000-0.005
Tertiary hosp	28	1 847 073	0.015	0.018	0.009	0.006-0.028	27	1 467 579	0.018	0.022	0.007	0.000-0.034

Hosp = hospital; n = total number of *Acinetobacter baumannii* non-susceptible (intermediate susceptibility or resistant) to meropenem isolates, N = total number of *Acinetobacter baumannii* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Figure 18. Evolution of the crude resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Acinetobacter baumannii* non-susceptible to meropenem (clinical samples only), Belgian acute care hospitals, 2013-2020



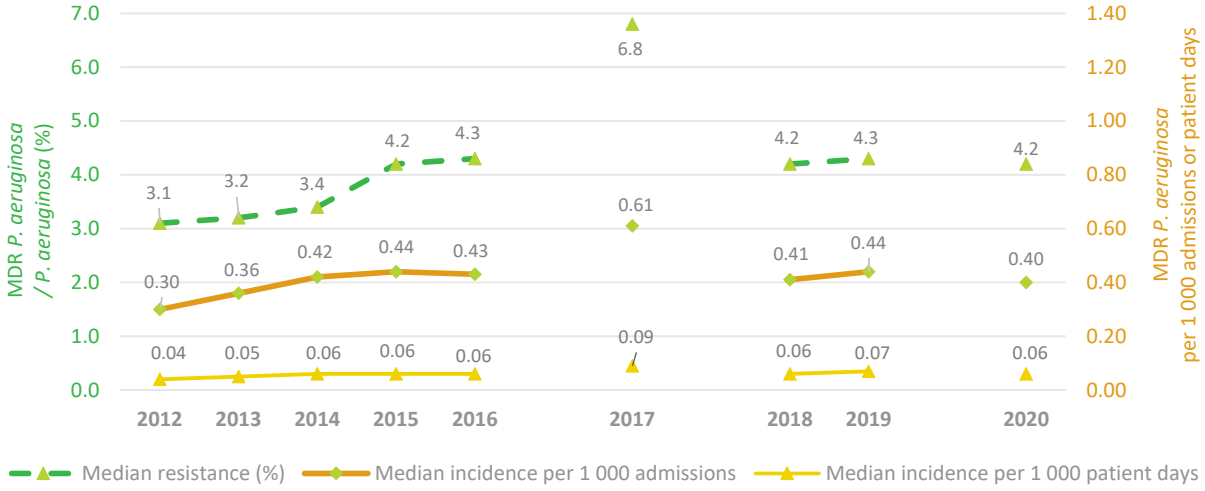
I/R = intermediate susceptibility or resistant

1.4 RESISTANCE IN *PSEUDOMONAS AERUGINOSA*

The crude resistance proportion of multidrug-resistant (MDR) *P. aeruginosa* isolated from clinical samples was 6.7% in both 2019 (n=1 270/18 990) and 2020 (n=1 212/18 109). The crude incidence varied from 0.73 in 2019 to 0.77 cases per 1 000 admissions in 2020 (Table 15).

Definition changes in 2017, 2018 and 2020 (see methods) make it difficult to interpret the evolution of MDR *P. aeruginosa.* Since 2018, there is a stabilization in the resistance proportion (-0.08% per year; p=0.753) and incidence (IRR=0.941, 95%CI: 0.868-1.020; p=0.140) (Figure 19).

Figure 19. Evolution of the median resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only), Belgian acute care hospitals, 2012-2020



Note: Between 2016 and 2017, the definition of MDR P. aeruginosa changed from reduced susceptibility (I or R) to at least one antibiotic in four out of the five following antibiotic classes to reduced susceptibility to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin, levofloxacin), aminoglycosides (gentamicin, tobramycin, amikacin), carbapenems (meropenem, imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime, cefepime) and anti-pseudomonas penicillins (piperacillin/tazobactam). In 2018, anti-pseudomonas penicillins (piperacillin/tazobactam) were dropped from the definition. Since 2020, only resistance (R) is considered.

Table 15. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2019 and 2020

	multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**1 270**	**18 990**	**6.7**	**5.2**	**4.3**	**2.5-7.1**	**1 212**	**18 109**	**6.7**	**5.4**	**4.2**	**1.5-8.3**
Flanders	708	10 438	6.8	4.4	3.3	1.9-5.6	583	10 240	5.7	3.7	2.6	0.0-5.2
Wallonia	321	5 393	6.0	5.4	4.4	2.9-6.8	367	5 593	6.6	6.4	5.7	2.9-8.7
Brussels	241	3 159	7.6	7.2	7.1	4.2-8.4	262	2 276	11.5	9.7	10.5	7.1-13.0
Primary hosp	456	10 770	4.2	4.4	3.9	2.2-6.1	489	10 765	4.5	4.5	3.4	1.0-7.2
Secondary hosp	261	3 628	7.2	6.8	6.3	3.5-8.3	242	3 581	6.8	7.5	5.6	2.8-12.4
Tertiary hosp	553	4 592	12.0	10.5	9.6	3.9-14.2	481	3 763	12.8	12.6	13.8	8.5-15.6
Incidence per 1 000 admissions												
Belgium	**1 270**	**1 729 326**	**0.73**	**0.78**	**0.44**	**0.20-0.81**	**1 159**	**1 505 415**	**0.77**	**0.73**	**0.40**	**0.13-0.93**
Flanders	708	1 031 737	0.69	0.47	0.28	0.16-0.52	583	941 811	0.62	0.45	0.21	0.00-0.47
Wallonia	321	462 576	0.69	1.09	0.53	0.21-1.13	314	398 935	0.79	0.89	0.64	0.37-1.18
Brussels	241	235 013	1.03	1.08	0.99	0.61-1.56	262	164 669	1.59	1.49	1.41	0.79-1.89
Primary hosp	456	1 078 622	0.42	0.67	0.34	0.19-0.59	443	983 706	0.45	0.54	0.36	0.10-0.73
Secondary hosp	261	379 256	0.69	0.87	0.76	0.31-1.30	235	325 409	0.72	1.12	0.48	0.13-2.13
Tertiary hosp	553	271 448	2.04	1.80	1.27	0.69-2.40	481	196 300	2.45	2.43	2.43	1.75-3.30
Incidence density per 1 000 patient days												
Belgium	**1 270**	**11 225 271**	**0.11**	**0.09**	**0.07**	**0.03-0.11**	**1 159**	**9 875 469**	**0.12**	**0.10**	**0.06**	**0.02-0.12**
Flanders	708	6 357 128	0.11	0.07	0.04	0.03-0.08	583	5 801 809	0.10	0.06	0.03	0.0-0.07
Wallonia	321	3 143 011	0.10	0.10	0.08	0.03-0.15	314	2 712 824	0.12	0.12	0.09	0.05-0.19
Brussels	241	1 725 132	0.14	0.13	0.10	0.05-0.15	262	1 360 836	0.19	0.17	0.12	0.08-0.28
Primary hosp	456	7 021 980	0.06	0.07	0.05	0.03-0.09	443	6 440 031	0.07	0.07	0.05	0.01-0.10
Secondary hosp	261	2 356 218	0.11	0.11	0.10	0.06-0.14	235	1 967 859	0.12	0.13	0.09	0.04-0.21
Tertiary hosp	553	1 847 073	0.30	0.27	0.21	0.10-0.38	481	1 467 579	0.33	0.34	0.31	0.23-0.44

Hosp = hospital; n = total number of multidrug-resistant (MDR) *Pseudomonas aeruginosa* isolates, N = total number of *Pseudomonas aeruginosa* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

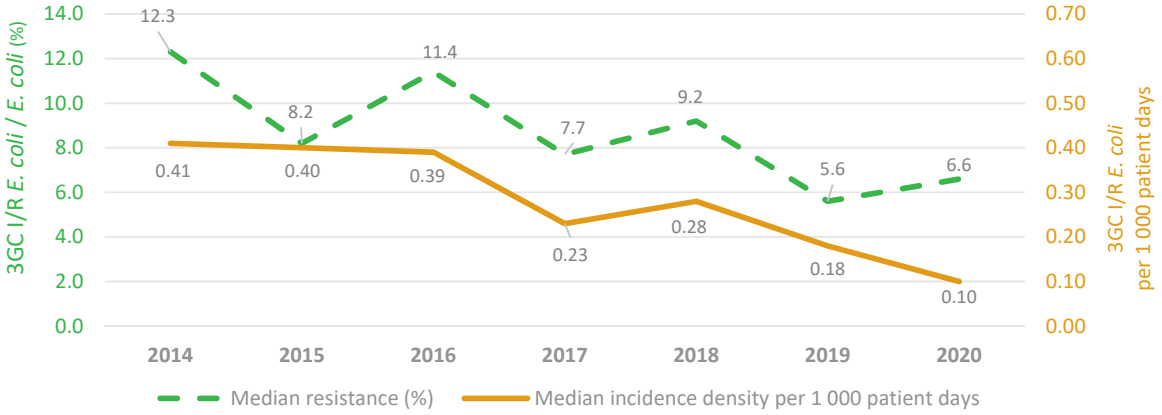
2. Resistant Gram-negative bacteria in chronic care hospitals

2.1 RESISTANCE IN *ESCHERICHIA COLI*

In 2019, the crude resistance proportion was 8.4% (n=152/1 800) for 3GC I/R *E. coli* and 0.39% (n=7/1 800) for meropenem I/R *E. coli* (clinical samples only). The crude incidence density was 0.27 per 1 000 patient days for 3GC I/R *E. coli* and 0.013 per 1 000 patient days for meropenem I/R *E. coli*. The crude resistance proportion (11.1%; n=130/1 171) and incidence density (0.33 per 1 000 patient days) of 3GC I/R *E. coli* were slightly higher in 2020. In that same year, no cases of meropenem I/R *E. coli* were reported (Table 16a and 16b).

While a non-significant decline in the resistance proportion (-0.41% per year; p=0.442) of 3GC I/R *E. coli* can be observed, a significant decrease in incidence density (IRR=0.880, 95%CI: 0.811-0.955; p=0.002) can be seen between 2014 and 2020 (Figure 20).

Figure 20. Evolution of the median resistance proportion and incidence density (per 1 000 patient days) of *Escherichia coli* non-susceptible to third generation cephalosporins (clinical samples only), Belgian chronic care, 2014-2020



3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant

Table 16a. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Escherichia coli* non-susceptible to third generation cephalosporins (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Escherichia coli non-susceptible to third generation cephalosporins (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**152**	**1 800**	**8.4**	**7.2**	**5.6**	**2.1-10.9**	**130**	**1 171**	**11.1**	**8.9**	**6.6**	**0.0-13.9**
Flanders	33	450	7.3	6.1	5.3	1.8-10.4	24	270	8.9	6.3	3.2	0.0-15.6
Wallonia	74	1 077	6.9	5.5	3.0	2.3-7.8	93	770	12.1	10.1	5.6	0.0-13.9
Brussels	45	273	16.5	14.6	14.6	9.8-19.4	13	131	9.9	9.9	9.9	9.9-9.9
Incidence per 1 000 admissions												
Belgium	**152**	**15 018**	**10.12**	**11.81**	**9.09**	**2.56-14.89**	**130**	**11 883**	**10.94**	**8.96**	**5.69**	**0.00-18.13**
Flanders	33	2 948	11.19	9.67	10.90	5.16-14.18	24	1 879	12.77	11.69	16.57	0.00-18.49
Wallonia	74	10 911	6.78	5.48	4.03	0.56-9.62	93	9 287	10.01	6.06	1.43	0.00-9.13
Brussels	45	1 159	38.83	35.08	35.08	27.59-42.58	13	717	18.13	18.13	18.13	18.13-18.13
Incidence density per 1 000 patient days												
Belgium	**152**	**556 617**	**0.27**	**0.27**	**0.18**	**0.06-0.33**	**130**	**397 365**	**0.33**	**0.33**	**0.10**	**0.00-0.46**
Flanders	33	152 334	0.22	0.17	0.16	0.06-0.29	24	87 765	0.27	0.20	0.14	0.00-0.46
Wallonia	74	332 136	0.22	0.23	0.11	0.01-0.33	93	276 411	0.34	0.38	0.04	0.00-0.63
Brussels	45	72 147	0.62	0.60	0.60	0.23-0.97	13	33 189	0.39	0.39	0.39	0.39-0.39

Hosp = hospital; n = total number of *Escherichia coli* non-susceptible (intermediate susceptibility or resistant) to 3rd generation cephalosporins isolates, N = total number of *Escherichia coli* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Table 16b. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Escherichia coli* non-susceptible to meropenem (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Escherichia coli non-susceptible to meropenem (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**7**	**1 800**	**0.39**	**0.54**	**0.00**	**0.00-1.19**	**0**	**1 171**	**0.00**	**0.00**	**0.00**	**0.00-0.00**
Flanders	4	450	0.89	0.70	0.67	0.00-1.40	0	270	0.00	0.00	0.00	0.00-0.00
Wallonia	1	1 077	0.09	0.44	0.00	0.00-0.00	0	770	0.00	0.00	0.00	0.00-0.00
Brussels	2	273	0.73	0.52	0.52	0.00-1.05	0	131	0.00	0.00	0.00	0.00-0.00
Incidence per 1 000 admissions												
Belgium	**7**	**15 018**	**0.466**	**0.571**	**0.000**	**0.000-1.016**	**0**	**11 883**	**0.000**	**0.000**	**0.000**	**0.000-0.000**
Flanders	4	2 948	1.357	0.998	0.736	0.000-1.996	0	1 879	0.000	0.000	0.000	0.000-0.000
Wallonia	1	10 911	0.092	0.093	0.000	0.000-0.000	0	9 287	0.000	0.000	0.000	0.000-0.000
Brussels	2	1 159	1.726	1.151	1.151	0.000-2.301	0	717	0.000	0.000	0.000	0.000-0.000
Incidence density per 1 000 patient days												
Belgium	**7**	**556 617**	**0.013**	**0.012**	**0.000**	**0.000-0.026**	**0**	**397 365**	**0.000**	**0.000**	**0.000**	**0.000-0.000**
Flanders	4	152 334	0.026	0.019	0.019	0.000-0.039	0	87 765	0.000	0.000	0.000	0.000-0.000
Wallonia	1	332 136	0.003	0.002	0.000	0.000-0.000	0	276 411	0.000	0.000	0.000	0.000-0.000
Brussels	2	72 147	0.028	0.026	0.026	0.000-0.053	0	33 189	0.000	0.000	0.000	0.000-0.000

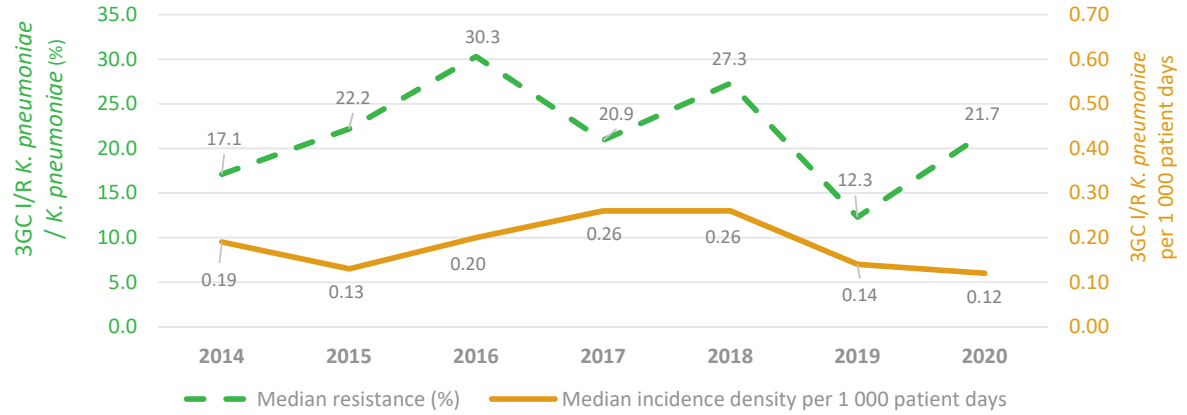
Hosp = hospital; n = total number of *Escherichia coli* non-susceptible (intermediate susceptibility or resistant) to meropenem isolates, N = total number of *Escherichia coli* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

2.2 RESISTANCE IN *KLEBSIELLA PNEUMONIAE*

While the crude resistance proportion of 3GC I/R *K. pneumoniae* isolated from clinical samples increased between 2019 (23.1%; n=139/601) and 2020 (27.2%; n=96/353) in the participating chronic care hospitals, the incidence density slightly decreased from 0.25 to 0.24 cases per 1 000 patient days in the same time span (Table 17a).

The resistance proportion of 3GC I/R *K. pneumoniae* showed a non-signficant trend between 2014 and 2020 (-0.52% per year; p=0.609). The incidence density showed a significant decline between 2018 and 2020 (IRR=0.783, 95%CI: 0.649-0.945; p=0.011), but non-significantly changed between 2014 and 2020 (IRR=0.954, 95%CI: 0.871-1.045; p=0.313) (Figure 21).

Figure 21. Evolution of the median resistance proportion and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to third generation cephalosporins (clinical samples only), Belgian chronic care, 2014-2020



3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant

The crude resistance proportion and incidence density of meropenem I/R *K. pneumoniae* was 2.50% and 0.027 cases per 1 000 patient days in 2019. In 2020, these were 3.12% and 0.028 cases per 1 000 patient days, respectively (Table 17b)

The incidence density of meropenem I/R *K. pneumoniae* remained stable between 2015 and 2020 (IRR=1.016, 95%CI: 0.820-1.259; p=0.887) (Figure 22).

Table 17a. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to third generation cephalosporins (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Klebsiella pneumoniae non-susceptible to third generation cephalosporins (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**139**	**601**	**23.1**	**16.9**	**12.3**	**2.1-28.9**	**96**	**353**	**27.2**	**21.4**	**21.7**	**1.7-34.9**
Flanders	21	135	15.6	9.7	8.8	0.0-19.3	19	88	21.6	15.4	11.4	0.0-34.9
Wallonia	88	362	24.3	17.7	6.2	4.2-32.2	65	228	28.5	22.5	18.6	1.7-37.5
Brussels	30	104	28.8	28.9	28.9	28.8-29.0	12	37	32.4	32.4	32.4	32.4-32.4
Incidence per 1 000 admissions												
Belgium	**139**	**15 018**	**9.26**	**9.10**	**4.89**	**0.28-16.36**	**96**	**11 883**	**8.08**	**8.01**	**4.99**	**0.62-15.78**
Flanders	21	2 948	7.12	5.17	4.05	0.00-10.35	19	1 879	10.11	11.77	13.20	0.00-22.10
Wallonia	88	10 911	8.07	5.55	2.88	0.56-6.89	65	9 287	7.00	4.68	2.41	0.62-6.85
Brussels	30	1 159	25.88	27.60	27.60	24.17-31.03	12	717	16.74	16.74	16.74	16.74-16.74
Incidence density per 1 000 patient days												
Belgium	**139**	**556 617**	**0.25**	**0.24**	**0.14**	**0.01-0.37**	**96**	**397 365**	**0.24**	**0.25**	**0.12**	**0.02-0.36**
Flanders	21	152 334	0.14	0.10	0.10	0.00-0.20	19	87 765	0.22	0.17	0.19	0.00-0.33
Wallonia	88	332 136	0.26	0.28	0.06	0.01-0.48	65	276 411	0.24	0.27	0.04	0.02-0.47
Brussels	30	72 147	0.42	0.41	0.41	0.26-0.55	12	33 189	0.36	0.36	0.36	0.36-0.36

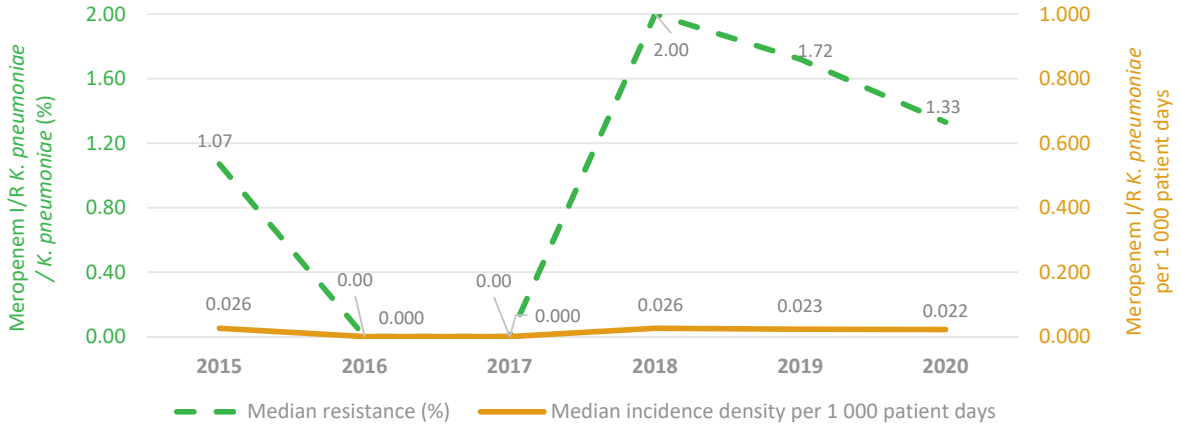
Hosp = hospital; n = total number of *Klebsiella pneumoniae* non-susceptible (intermediate susceptibility or resistant) to 3rd generation cephalosporins isolates, N = total number of *Klebsiella pneumoniae* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Table 17b. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to meropenem (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Klebsiella pneumoniae non-susceptible to meropenem (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**15**	**601**	**2.50**	**2.97**	**1.72**	**0.00-4.63**	**11**	**353**	**3.12**	**3.15**	**1.33**	**0.00-5.71**
Flanders	1	135	0.74	0.44	0.00	0.00-0.88	5	88	5.68	6.79	5.71	4.65-10.00
Wallonia	7	362	1.93	3.43	1.73	0.00-2.82	6	228	2.63	1.86	0.00	0.00-2.67
Brussels	7	104	6.73	6.65	6.65	6.45-6.85	0	37	0.00	0.00	0.00	0.00-0.00
Incidence per 1 000 admissions												
Belgium	**15**	**15 018**	**0.999**	**1.523**	**0.659**	**0.000-1.592**	**11**	**11 883**	**0.926**	**1.713**	**0.359**	**0.000-1.779**
Flanders	1	2 948	0.339	0.315	0.000	0.000-0.630	5	1 879	2.661	4.863	1.779	1.761-11.050
Wallonia	7	10 911	0.642	0.727	0.659	0.000-1.120	6	9 287	0.646	0.424	0.000	0.000-0.717
Brussels	7	1 159	6.040	6.325	6.325	5.754-6.897	0	717	0.000	0.000	0.000	0.000-0.000
Incidence density per 1 000 patient days												
Belgium	**15**	**556 617**	**0.027**	**0.027**	**0.023**	**0.000-0.029**	**11**	**397 365**	**0.028**	**0.036**	**0.022**	**0.000-0.047**
Flanders	1	152 334	0.007	0.005	0.000	0.000-0.010	5	87 765	0.057	0.062	0.047	0.044-0.094
Wallonia	7	332 136	0.021	0.018	0.025	0.000-0.029	6	276 411	0.022	0.029	0.000	0.000-0.047
Brussels	7	72 147	0.097	0.095	0.095	0.059-0.132	0	33 189	0.000	0.000	0.000	0.000-0.000

Hosp = hospital; n = total number of *Klebsiella pneumoniae* non-susceptible (intermediate susceptibility or resistant) to meropenem isolates, N = total number of *Klebsiella pneumoniae* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

Figure 22. Evolution of the median resistance proportion and incidence density (per 1 000 patient days) of *Klebsiella pneumoniae* non-susceptible to meropenem (clinical samples only), Belgian chronic care, 2015-2020



I/R = intermediate susceptibility or resistant

2.3 RESISTANCE IN *ACINETOBACTER BAUMANNII*

None of the participating chronic care hospitals in Flanders and Brussels reported a meropenem I/R *A. baumannii* in 2019 and 2020. In both years, one Walloon hospital reported two and one isolates from clinical samples, respectively. The crude resistance proportion was 11.76% (n=2/17) in 2019 and 10.00% (n=1/10) in 2020. The crude incidence density was 0.004 and 0.003 cases of meropenem I/R *A. baumannii* per 1 000 patient days, respectively (Table 18).

Table 18. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of *Acinetobacter baumannii* non-susceptible to meropenem (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Acinetobacter baumannii non-susceptible to meropenem (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**2**	**17**	**11.76**	**10.00**	**0.00**	**0.00-0.00**	**1**	**10**	**10.00**	**3.33**	**0.00**	**0.00-0.00**
Flanders	0	3	0.00	0.00	0.00	0.00-0.00	0	3	0.00	0.00	0.00	0.00-0.00
Wallonia	2	7	28.57	20.00	0.00	0.00-20.00	1	6	16.67	5.56	0.00	0.00-0.00
Brussels	0	7	0.00	0.00	0.00	0.00-0.00	0	1	0.00	0.00	0.00	0.00-0.00
Incidence per 1 000 admissions												
Belgium	**2**	**15 018**	**0.133**	**0.000**	**0.000**	**0.000-0.000**	**1**	**11 883**	**0.084**	**0.062**	**0.000**	**0.000-0.000**
Flanders	0	2 948	0.000	0.000	0.000	0.000-0.000	0	1 879	0.000	0.000	0.000	0.000-0.000
Wallonia	2	10 911	0.183	0.221	0.000	0.000-0.362	1	9 287	0.108	0.104	0.000	0.000-0.000
Brussels	0	1 159	0.000	0.000	0.000	0.000-0.000	0	717	0.000	0.000	0.000	0.000-0.000
Incidence density per 1 000 patient days												
Belgium	**2**	**556 617**	**0.004**	**0.003**	**0.000**	**0.000-0.000**	**1**	**397 365**	**0.003**	**0.002**	**0.000**	**0.000-0.000**
Flanders	0	152 334	0.000	0.000	0.000	0.000-0.000	0	87 765	0.000	0.000	0.000	0.000-0.000
Wallonia	2	332 136	0.006	0.006	0.000	0.000-0.013	1	276 411	0.004	0.003	0.000	0.000-0.000
Brussels	0	72 147	0.000	0.000	0.000	0.000-0.000	0	33 189	0.000	0.000	0.000	0.000-0.000

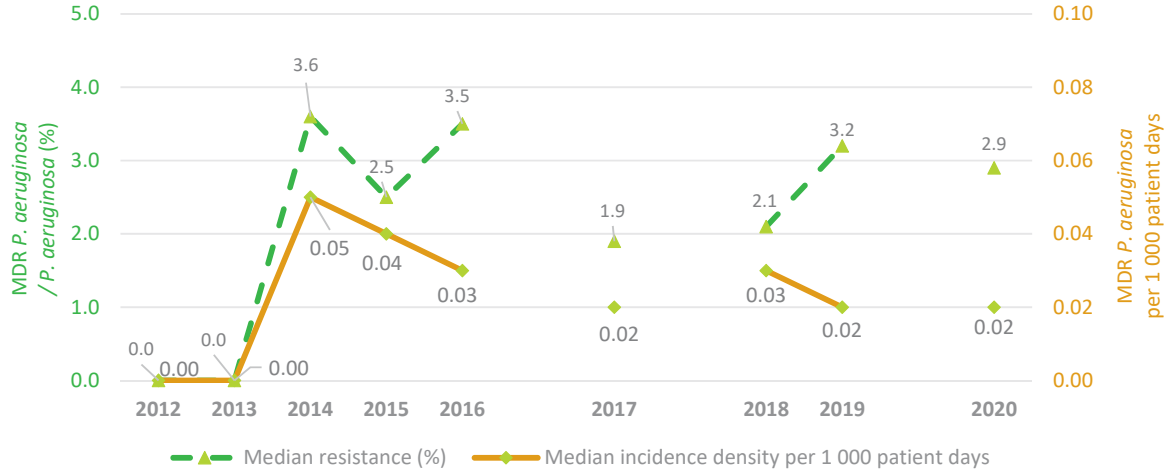
Hosp = hospital; n = total number of *Acinetobacter baumannii* non-susceptible (intermediate susceptibility or resistant) to meropenem isolates, N = total number of *Acinetobacter baumannii* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

2.4 RESISTANCE IN *PSEUDOMONAS AERUGINOSA*

In 2019, 4.4% of all reported *P. aeruginosa* (n=21/472) matched the definition of multidrug-resistance (clinical samples only). These cases were reported by seven hospitals (58.3%; min-max: 1-7 isolates). The crude incidence density accounted 0.04 cases per 1 000 patient days. The crude resistance proportion and incidence density of MDR *P. aeruginosa* were 6.6% (n=20/305) and 0.05 cases per 1 000 patient days in 2020, respectively. These cases were reported by six hospitals (60.0%; min-max: 1-8 isolates) (Table 19).

Figure 23 presents the evolution of the median resistance proportion and incidence density of MDR *P. aeruginosa*.

Figure 23. Evolution of the median resistance proportion and incidence density (per 1 000 patient days) of multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only), Belgian chronic care hospitals, 2012-2020



Note: Between 2016 and 2017, the definition of MDR P. aeruginosa changed from reduced susceptibility (I or R) to at least one antibiotic in four out of the five following antibiotic classes to reduced susceptibility to at least three of the following antibiotic classes: fluoroquinolones (ciprofloxacin, levofloxacin), aminoglycosides (gentamicin, tobramycin, amikacin), carbapenems (meropenem, imipenem), 3rd and/or 4th generation cephalosporins (ceftazidime, cefepime) and anti-pseudomonas penicillins (piperacillin/tazobactam). In 2018, anti-pseudomonas penicillins (piperacillin/tazobactam) were dropped from the definition. Since 2020, only resistance (R) is considered

Table 19. Resistance proportion, incidence (per 1 000 admissions) and incidence density (per 1 000 patient days) of multidrug-resistant *Pseudomonas aeruginosa* (clinical samples only) by region, Belgian chronic care hospitals, 2019 and 2020

	Multidrug-resistant *Pseudomonas aeruginosa* (clinical samples only)											
	2019						2020					
	n	N	Crude	Mean	Median	P25 - P75	n	N	Crude	Mean	Median	P25 - P75
Resistance proportion (%)												
Belgium	**21**	**472**	**4.4**	**4.7**	**3.2**	**0.0-8.8**	**20**	**305**	**6.6**	**4.7**	**2.9**	**0.0-9.1**
Flanders	12	136	8.8	10.0	9.3	6.3-13.8	4	72	5.6	5.5	7.3	0.0-9.1
Wallonia	6	255	2.4	1.4	0.0	0.0-2.9	16	211	7.6	5.2	2.9	0.0-10.2
Brussels	3	81	3.7	4.3	4.3	0.0-8.6	0	22	0.0	0.0	0.0	0.0-0.0
Incidence per 1 000 admissions												
Belgium	**21**	**15 018**	**1.40**	**2.90**	**0.55**	**0.00-6.05**	**20**	**11 883**	**1.68**	**1.27**	**0.46**	**0.00-2.64**
Flanders	12	2 948	4.07	5.41	6.05	2.15-8.68	4	1 879	2.13	1.47	1.78	0.00-2.64
Wallonia	6	10 911	0.55	0.46	0.00	0.00-0.36	16	9 287	1.72	1.38	0.46	0.00-3.65
Brussels	3	1 159	2.59	5.17	5.17	0.00-10.34	0	717	0.00	0.00	0.00	0.00-0.00
Incidence density per 1 000 patient days												
Belgium	**21**	**556 617**	**0.04**	**0.04**	**0.02**	**0.00-0.08**	**20**	**397 365**	**0.05**	**0.05**	**0.02**	**0.00-0.07**
Flanders	12	152 334	0.08	0.08	0.08	0.05-0.12	4	87 765	0.05	0.04	0.05	0.00-0.07
Wallonia	6	332 136	0.02	0.02	0.00	0.00-0.03	16	276 411	0.06	0.07	0.02	0.00-0.12
Brussels	3	72 147	0.04	0.04	0.04	0.00-0.09	0	33 189	0.00	0.00	0.00	0.00-0.00

Hosp = hospital; n = total number of multidrug-resistant *Pseudomonas aeruginosa* isolates, N = total number of *Pseudomonas aeruginosa* isolates for the calculation of the resistance proportion, total number of admissions for the incidence or total number of patient days for the incidence density calculations, crude = n/N

DISCUSSION

This report presents the results of three national surveillance programs on antimicrobial resistance, i.e. the surveillance of (1) MRSA, (2) VRE and (3) MRGN. The data used in this report were collected retrospectively (in the following year) and aggregated at hospital level. Data originating from acute and chronic care hospitals were presented separately. Acute care hospitals with a length of stay of ≥ 16 days were classified as chronic care hospitals.

To our knowledge, our AMR surveillance is one of the few programs that does not merely focus on invasive samples (e.g. cerebrospinal fluid and blood samples), but includes both invasive and non-invasive sample types (e.g. urine samples). Although data for both clinical samples and screening samples were collected in the MRSA and VRE surveillance, only data for clinical samples were used in this report (unless otherwise stipulated). This was done to limit the inter-hospital variability due to the heterogeneity in local screening practices.

Due to the COVID-19 pandemic, BAPCOC declared there was no legal obligation for hospitals to participate in the national surveillances in 2020 and 2021. For this reason and because of delayed data delivery, this report combined the 2019 and 2020 data. When interpreting the results, it is important to keep in mind that the 2019 findings reflect the pre-pandemic period, while the 2020 data can be impacted by altered hospital activities owing to the crisis.
Caution is also needed when interpreting the numbers and figures presented in this report for the latter as there were only 12 and 10 participating chronic care hospitals in 2019 and 2020, respectively.

Although there was no legal obligation, 85.3% and 94.1% of all mergers (n=102) succeeded (with or without a considerable delay) in transmitting MRSA and MRGN data for 2019 and 2020, respectively. Moreover, the participation rate for the VRE surveillance was above 84% in the relevant years.

Since 2004, a significantly decreasing trend in the resistance proportion and incidence of MRSA can be observed. The decrease in incidence was however not statistically significant between 2018 and 2020. Due to the combined efforts of the infection prevention and control teams and a whole range of actions, the proportion of healthcare-associated MRSA on the total number of MRSA is currently at its lowest.

Less than 50% of the participating hospitals reported cases of vanco-R *E. faecium*. No significant trend (2014-2020) can be observed in the resistance proportion and incidence of vanco-R *E. faecium*.

Between 2014 and 2020, the resistance proportion and incidence of 3GC I/R *E. coli and K. pneumoniae* significantly increased. Since 2018, a significant decrease in the resistance proportion and a non-significant decline in the incidence of 3GC I/R *K. pneumoniae* can however be observed. This decrease is also seen in the resistance (significant) and incidence (non-significant) of meropenem I/R *K. pneumoniae.*

Since 2013, no significant change in the evolution of the resistance proportion of meropenem I/R *A. baumannii* can be observed. The incidence however significantly decreased in the same time span.

Definition changes in 2017, 2018 and 2020 make it difficult to interpret the evolution of MDR *P. aeruginosa.* Since 2018, there seems to be a stabilization in the resistance proportion and incidence.

Due to the method of data collection (aggregated at the hospital level), it is impossible to estimate whether the changes we observe in the 2020 data are the result of natural evolution or are caused by the COVID-19 crisis

and the associated altered hospital and primary care activities. Also in the literature, there is no clear evidence yet of how the COVID-19 pandemic and the response to it impacted antimicrobial resistance. More research is required in this area, but it is reasonable to believe that the answer will be multifactorial. There were significant changes in population-level behaviour (e.g. social distancing) and healthcare provision (reduced healthcare seeking and less referrals, less antimicrobial consumption in primary care). Also within the hospitals many changes occurred such as enhanced infection prevention and control programs with renforcement of hand hygiene and use of personal protective equipment, change in patient mix and cancellations of elective and non-urgent surgeries.[3,4]

The effect of COVID-19 is seen in the national surveillance of bloodstream infections (BSI). The 2020 surveillance results show an increase in the incidence of hospital-associated (HA) and central line-associated BSIs and an increase in the proportion of HA-BSI secondary to pulmonary infection and among critical ill patients. No change in the antimicrobial resistance profile of selected causal microorganismes was however observed. Between 2013 and 2020, a significant decrease in the crude resistance proportion (from 20.9 to 8.9%) of MRSA isolated from hospital-associated BSI is seen. In the same time periode, changes in the proportion of 3GC-R (from 14.0% to 15.0%) and carbapenem-R (from 0.3% to 0.7%) *E. coli* and 3GC-R (from 25.8% to 29.1%) and carbapenem-R (from 2.4% to 4.8%) *K. pneumoniae* were non-significant.[5]

The evolution of acquired AMR is also monitored by the Belgian subpart of the European Antimicrobial Resistance Surveillance Network (EARS-Net), called EARS-BE. This surveillance program retrospectively collects data from clinical hospital and private laboratories. EARS-BE differs from EARS-Net in the additional collection of data on antimicrobial susceptibility test (AST) results of isolates found in urine samples in addition to invasive samples (i.e. blood and cerebrospinal fluid).
Similarly to the national AMR surveillance results, EARS-BE found a decreasing trend in the mean resistance proportion of MRSA (6.8% in 2020). The surveillance also reported no clear trends in the proportion of 3GC-R *E. coli* (9.8% in 2020), 3GC-R *K. pneumoniae* (20.5% in 2020) and carbapenem-R *K. pneumoniae* (1.4% in 2020) in the last 4-5 years.[6]

In 2019 and 2020, a limited number of hospitals participated in a pilot study and tested a harmonized AMR/EARS-BE protocol. For the AMR surveillance, this will imply abandoning an aggregated data collection and going for the collection of detailed laboratory data at isolate/antimicrobial susceptibility testing level. This type of data collection will result in more detailed and standardized data as data validation will be possible and interpretation discrepancies will be minimized. By combining the two surveillances, Sciensano hopes to reduce the workload for laboratories (collecting data only once) and increase the number of participants in the EARS-BE project.[7] Data analyses are pending and results will be included in the next report.

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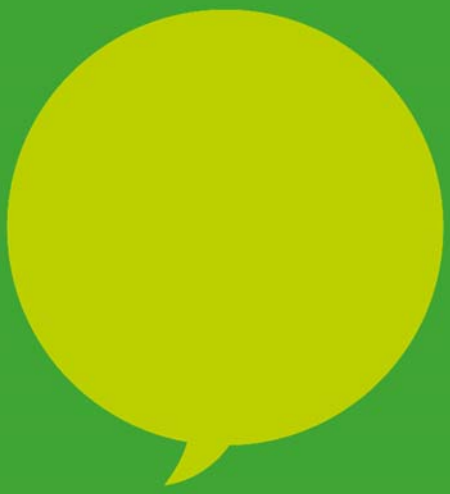

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