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HEALTHCARE-ASSOCIATED INFECTIONS AND ANTIMICROBIAL RESISTANCE

SURVEILLANCE OF ANTIMICROBIAL RESISTANT BACTERIA IN BELGIAN HOSPITALS

Report 2018

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WHO WE ARE

SCIENSANO can count on more than 700 staff members who commit themselves, day after day, to achieving our motto: Healthy all life long. As our name suggests, science and health are central to our mission. Sciensano's strength and uniqueness lie within the holistic and multidisciplinary approach to health. More particularly we focus on the close and indissoluble interconnection between human and animal health and their environment (the "One health" concept). By combining different research perspectives within this framework, Sciensano contributes in a unique way to everybody's health.

For this, Sciensano builds on the more than 100 years of scientific expertise of the former Veterinary and Agrochemical Research Centre (CODA-CERVA) and the ex-Scientific Institute of Public Health (WIV-ISP).

Sciensano

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EXECUTIVE SUMMARY

Introduction

The service “Healthcare-associated infections and antimicrobial resistance” of Sciensano organizes, collects and analyzes surveillance data on antimicrobial resistance (AMR) retrieved from Belgian hospitals. The Royal Decree of 8 January 2015 stipulates that Belgian acute care hospitals mandatorily have to participate in the surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) and multiresistant Gram-negative bacteria (MRGN). The surveillance of vancomycin-resistant enterococci (VRE) is one of the four additional programs from which hospitals must choose one for participation.

The objective of the three epidemiological AMR surveillances (i.e. MRSA, MRGN and VRE) is to follow up the national evolution of the resistance proportion and incidence of multidrug resistant organisms (MDRO) in Belgian hospitals.

The current report aims to present the 2018 results of the three surveillance programs and to describe AMR trends in Belgian acute and/or chronic care hospitals.

Methods

The surveillance results were collected retrospectively (year 2018) by the microbiological laboratories only or in collaboration with the infection control teams of the participating hospitals and aggregated at hospital level.

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:

- Methicillin or oxacillin resistance in *Staphylococcus aureus (S. aureus)*
- Non-susceptibility* to 3rd generation cephalosporins (3GC I/R) and/or to meropenem (meropenem I/R) in *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*)
- Non-susceptibility* to meropenem in *Acinetobacter baumannii* (*A. baumannii*)
- Multidrug-resistant (MDR) *Pseudomonas aeruginosa* (*P. aeruginosa*), i.e. non-susceptibility 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)
- Vancomycin resistance in *Enterococcus faecalis* (*E. faecalis*) and in *Enterococcus faecium* (*E. faecium*)

** 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 potentially nosocomial character of acquisition was only assessed for MRSA. Nosocomial 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 and an incidence (number of cases per 1 000 hospital admissions) and/or incidence density (cases per 1 000 patient days) were calculated. Data were analysed in STATA 14.1

(StataCorp LP, College Station, Texas, USA) and presented by region and by 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 2018. All but four hospital administrative groups (mergers; n=97/101) participated in the MRSA and MRGN surveillance with at least one hospital site. Despite the optional character of the VRE surveillance, 92.1% of all mergers (n=93/101) participated with at least one hospital site.

Table 1. Resistance proportion and incidence per 1 000 admissions of the bacteria included in the surveillance of antimicrobial resistance, Belgian acute care hospitals, 2018

			Resistance proportion (%)		Incidence per 1 000 admissions	
		N hosp	Crude	Median	Crude	Median
Staphylococcus aureus	Methicillin R	112	14.2	11.2	2.67	2.05
Nosocomial *Staphylococcus aureus*	Methicillin R	112	24.7	28.7	0.66	0.46
Enterococcus faecium	Vancomycin R	109	2.3	0.0	0.02	0.00
Enterococcus faecalis	Vancomycin R	109	0.1	0.0	0.01	0.00
Escherichia coli	3GC I/R	112	10.1	9.7	5.25	5.20
	Meropenem I/R	113	0.1	0.0	0.06	0.00
Klebsiella pneumoniae	3GC I/R	112	24.1	21.5	2.81	2.33
	Meropenem I/R	113	2.2	1.3	0.25	0.14
Acinetobacter baumannii	Meropenem I/R	113	7.6	0.0	0.05	0.00
Pseudomonas aeruginosa	MDR	113	7.2	4.2	0.80	0.41

N hosp = number of hospitals (mergers or single hospital sites), R = resistant, I/R = intermediate susceptibility or resistant, 3GC = 3rd generation cephalosporins, MDR = reduced susceptibility (I or 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 or cefepime)

Since 2004, a significantly decreasing trend in the median resistance proportion of MRSA and in the median incidence of nosocomial MRSA can be observed. The decrease in both parameters was however not statistically significant between 2017 and 2018.

In the participating acute care hospitals, the median resistance proportion and incidence was 9.7% and 5.20 cases per 1 000 admissions for 3GC I/R *E. coli* in 2018. Both indicators significantly increased between 2017 and 2018. The median resistance proportion and incidence of meropenem I/R *E. coli* however did not change over time (all zero values).

Since 2015, there is a significant increase in the median resistance proportion (but not in the median incidence) of meropenem I/R *K. pneumoniae*. In 2018, the median resistance proportion and incidence of meropenem I/R *K. pneumoniae* was 1.32% and 0.144 cases per 1 000 admissions.

No significant change in the evolution of the crude resistance proportion of meropenem I/R *A. baumannii* was observed between 2013 and 2018 in acute care hospitals (median = 0.0%). The incidence of meropenem I/R *A. baumannii* significantly decreased between 2013 and 2015, but remained stable since then.

Definition changes in 2017 and 2018 make it difficult to interpret the evolution of MDR *P. aeruginosa.* In a cohort of acute care hospitals that participated at least three years in the surveillance, the median resistance proportion decreased from 6.9% in 2017 to 4.3% in 2018, a resistance level in line with 2016.

Table 2 shows the resistance proportion and incidence density per 1 000 patient days of the bacteria under surveillance (clinical samples only) in Belgian chronic care hospitals in 2018. These numbers should however be interpreted with caution as the number of participating chronic care hospitals was low.

Table 2. Resistance proportion and incidence density per 1 000 patient days of the bacteria included in the surveillance of antimicrobial resistance, Belgian chronic care hospitals, 2018

			Resistance proportion (%)		Incidence per 1 000 patient days	
		N hosp	Crude	Median	Crude	Median
Staphylococcus aureus	Methicillin R	12	16.1	13.2	0.17	0.10
Nosocomial *Staphylococcus aureus*	Methicillin R	12	52.6	78.0	0.09	0.07
Enterococcus faecium	Vancomycin R	9	1.0	0.0	0.00	0.00
Enterococcus faecalis	Vancomycin R	9	0.0	0.0	0.00	0.00
Escherichia coli	3GC I/R	12	9.6	9.0	0.35	0.29
	Meropenem I/R	12	0.2	0.0	0.01	0.00
Klebsiella pneumoniae	3GC I/R	12	35.2	27.4	2.33	1.96
	Meropenem I/R	12	0.4	0.2	0.02	0.02
Acinetobacter baumannii	Meropenem I/R	12	37.5	0.0	0.01	0.00
Pseudomonas aeruginosa	MDR	12	5.4	2.0	0.05	0.02

N hosp = number of hospitals (mergers or single hospital sites), R = resistant, I/R = intermediate susceptibility or resistant, 3GC = 3rd generation cephalosporins, MDR = reduced susceptibility (I or 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 or cefepime)

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. These national programs aim to monitor trends in the proportion and incidence (density) of the antimicrobial resistant bacteria under surveillance over time and thus to provide national data.

The data used in this report were collected retrospectively (2018 data to be reported by the end of March 2019) and were aggregated at hospital level. Hence, no information on at-risk patients, high-risk wards or origin (i.e. community onset, healthcare associated or hospital-acquired; except for MRSA) was available.

To our knowledge, our Belgian 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). Screening samples were excluded to avoid potential misleading results due to the heterogeneity in screening practices between the different hospitals.

In contrast to the previous years, the currrent report presents the results of acute care hospitals also by level of specialty care provided within the hospital. Only in the MRGN surveillance differences by specialty care type were found.

Mechanisms of resistance including extended spectrum beta-lactamase (ESBL) and carbapenemase production (CPE) in *E. coli* and *K. pneumoniae* were no longer included in the 2018 data collection for MRGN because laboratories may not look for them locally or if they do, they often use very heterogeneous methodologies. In replacement, the national reference centre (NRC) for antibiotic resistant gram-negative bacilli launched in 2019 (from May to October) a national prospective surveillance to determine the occurrence and distribution of carbapenem resistant *E. coli* and *K. pneumoniae* and/or colistin resistant *E. coli* (ColREC) clones and/or transferrable resistance/genetic elements and to identify epidemiological risk factors for infection or colonisation with CRE and/or ColREC. Results are soon awaited.

Sciensano is currently working on harmonizing the data collection for the national AMR surveillances and the Belgian subpart of the European Antimicrobial Resistance Surveillance (EARS-BE). For the AMR surveillance, this will imply abandoning an aggregated data collection and going for the collection of detailed laboratory data at isolate/AST test result 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 avoided.

SAMENVATTING

Inleiding

De dienst "Zorginfecties en antibioticaresistentie" van Sciensano organiseert, verzamelt en analyseert surveillancegegevens over antimicrobiële resistentie (AMR) van Belgische ziekenhuizen. Het Koninklijk Besluit van 8 januari 2015 bepaalt dat Belgische acute ziekenhuizen verplicht moeten deelnemen aan de surveillance van meticilline resistente *Staphylococcus aureus* (MRSA) en multiresistente gram-negatieve bacteriën (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 doel van de drie epidemiologische AMR surveillances (d.i. MRSA, MRGN en VRE) is het opvolgen van de evolutie van het resistentiepercentage en de incidentie van multidrug-resistente organismen (MDRO) in Belgische ziekenhuizen.

Het huidige rapport beoogt de gegevens van 2018 met betrekking tot de drie surveillanceprogramma's voor te stellen en trends in AMR in Belgische acute en/of chronische ziekenhuizen te beschrijven.

Methodologie

De surveillancegegevens werden retrospectief verzameld (jaar 2018) door de laboratoria voor microbiologie alleen of in samenwerking met de ziekenhuishygiëneteams en geaggregeerd op ziekenhuisniveau.

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

Volgende micro-organismen en resistenties werden onderzocht:

- Meticilline of oxacilline resistentie in *Staphylococcus aureus (S. aureus)*
- *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.i. verminderde gevoeligheid (intermediair of resistent) 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)
- Vancomycine resistentie in *Enterococcus faecalis* (*E. faecalis*) en in *Enterococcus faecium* (*E. faecium*)

** 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) verschaften, werden in de analyses opgenomen. In dit rapport werden echter 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 nosocomiaal karakter van verwerking werd enkel voor MRSA beoordeeld. Nosocomiale MRSA werd gedefinieerd als kolonisatie of infectie met MRSA die in het ziekenhuis geacht 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 werd de resistentieproportie en incidentie (aantal gevallen per 1 000 ziekenhuisopnames) en/of incidentiedensiteit (aantal gevallen per 1 000 hospitalisatiedagen) berekend. Gegevens werden geanalyseerd in STATA 14.1 (StataCorp LP, College Station, Texas, VS) en voorgesteld per regio en per specialisatietype van het ziekenhuis. Verschillen werden als significant beschouwd indien $p<0.05$.

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 stalen) in Belgische acute ziekenhuizen in 2018 weer. Alle behalve vier ziekenhuisbestuursgroepen (fusies; n=97/101) namen met minstens één ziekenhuissite aan de MRSA en MRGN surveillance deel. Ondanks het optioneel karakter van de VRE surveillance nam 92,1% van alle fusieziekenhuizen (n=93/101) met minstens één ziekenhuissite deel.

Tabel 1. Resistentieproportie en incidentie per 1 000 opnames van de bacteriën opgenomen in de surveillance van antimicrobiële resistentie, Belgische acute ziekenhuizen, 2018

			Resistentieproportie (%)		Incidentie per 1 000 opnames	
		N ZH'en	Crude	Mediaan	Crude	Mediaan
Staphylococcus aureus	Meticilline R	112	14,2	11,2	2,67	2,05
Nosocomiale *Staphylococcus aureus*	Meticilline R	112	24,7	28,7	0,66	0,46
Enterococcus faecium	Vancomycine R	109	2,3	0,0	0,02	0,00
Enterococcus faecalis	Vancomycine R	109	0,1	0,0	0,01	0,00
Escherichia coli	3GC I/R	112	10,1	9,7	5,25	5,20
	Meropenem I/R	113	0,1	0,0	0,06	0,00
Klebsiella pneumoniae	3GC I/R	112	24,1	21,5	2,81	2,33
	Meropenem I/R	113	2,2	1,3	0,25	0,14
Acinetobacter baumannii	Meropenem I/R	113	7,6	0,0	0,05	0,00
Pseudomonas aeruginosa	MDR	113	7,2	4,2	0,80	0,41

N ZH'en = aantal ziekenhuizen (fusies of één ziekenhuis sites), R = resistent, I/R = intermediaire gevoeligheid of resistentie, 3GC = 3de generatie cefalosporines, MDR = verminderde gevoeligheid (I of R) 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)

Sinds 2004 wordt een significante afname van de mediane MRSA resistentieproportie en incidentie van nosocomiale MRSA waargenomen. De daling van beide parameters was echter niet statistisch significant tussen 2017 en 2018.

In 2018 bedroeg de mediane resistentieproportie en incidentie van 3GC I/R *E. coli* respectievelijk 9,7 % en 5,20 gevallen per 1000 opnames in de acute ziekenhuizen. Beide indicatoren namen significant toe tussen 2017 en 2018 . De mediane resistentieproportie en incidentie van meropenem I/R *E. coli* veranderde echter niet doorheen de tijd (telkens nul als waard).

Sinds 2015 is er een significante toename van de mediane resistentieproportie (maar niet van de mediane incidentie) van meropenem I/R *K. pneumoniae*. In 2018 waren de mediane resistentieproportie en incidentie van meropenem I/R *K. pneumoniae* respectievelijk 1,32% en 0.144 gevallen per 1 000 opnames.

Er werd geen significante verandering in de evolutie van de ruwe resistentieproportie van meropenem I/R *A. baumannii* waargenomen tussen 2013 en 2018 in acute ziekenhuizen (mediaan=0,0%). De incidentie van meropenem I/R *A. baumannii* daalde tussen 2013 en 2015 significant, maar bleef sindsdien stabiel.

Definitiewijzigingen in 2017 en 2018 maken het moeilijk om de evolutie van MDR *P. aeruginosa* te interpreteren. In een cohort van acute ziekenhuizen die minstens drie jaar aan de surveillance deelnamen, daalde de mediane resistentieproportie van 6,9% in 2017 tot 4,3% in 2018, hetzelfde resistentieniveau als in 2016.

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 2018. Deze cijfers moeten echter met enige voorzichtigheid geïnterpreteerd worden aangezien het aantal deelnemende chronische ziekenhuizen beperkt was.

Tabel 2. Resistentieproportie en incidentiedensiteit per 1 000 hospitalisatiedagen van de bacteriën opgenomen in de surveillance van antimicrobiële resistentie, Belgische chronische ziekenhuizen, 2018

			Resistentieproportie (%)		Incidentiedensiteit per 1 000 hospitalisatiedagen	
		N ZH'en	Crude	Mediaan	Crude	Mediaan
Staphylococcus aureus	Methicilline R	12	16.1	13.2	0.17	0.10
Nosocomiale *Staphylococcus aureus*	Methicilline R	12	52.6	78.0	0.09	0.07
Enterococcus faecium	Vancomycine R	9	1.0	0.0	0.00	0.00
Enterococcus faecalis	Vancomycine R	9	0.0	0.0	0.00	0.00
Escherichia coli	3GC I/R	12	9.6	9.0	0.35	0.29
	Meropenem I/R	12	0.2	0.0	0.01	0.00
Klebsiella pneumoniae	3GC I/R	12	35.2	27.4	2.33	1.96
	Meropenem I/R	12	0.4	0.2	0.02	0.02
Acinetobacter baumannii	Meropenem I/R	12	37.5	0.0	0.01	0.00
Pseudomonas aeruginosa	MDR	12	5.4	2.0	0.05	0.02

N ZH'en = aantal ziekenhuizen (fusies of één ziekenhuis sites), R = resistent, I/R = intermediaire gevoeligheid of resistentie, 3GC = 3de generatie cefalosporines, MDR = verminderde gevoeligheid (I of R) 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 de drie nationale surveillanceprogramma's over antimicrobiële resistentie, namelijk de surveillance van (1) MRSA, (2) VRE en (3) MRGN. Deze nationale programma's hebben als doel trends in de resistentieproportie en incidentie(densiteit) van (multi)resistente bacteriën in de tijd op te volgen en zo nationale gegevens te verstrekken.

De in dit rapport gebruikte gegevens werden retrospectief verzameld (d.i. de 2018 gegevens dienden voor eind maart 2019 gerapporteerd te worden) en geaggregeerd op ziekenhuisniveau. Hierdoor was er geen informatie over risicopatiënten, risicovolle afdelingen of herkomst (d.w.z. community-onset, zorggerelateerd of ziekenhuisverworven; met uitzondering van MRSA) beschikbaar.

Voor zover wij weten is onze Belgische AMR surveillance één van de weinige programma's die zich niet alleen richt op invasieve stalen (vb. cerebrospinaal vocht en bloed), maar ook alle niet-invasieve staaltypes (vb. urine) includeert. Screeningsstalen werden uitgesloten om mogelijke misleidende resultaten, door de heterogeniteit in screeningpraktijken tussen de verschillende ziekenhuizen, te voorkomen.

In tegenstelling tot de voorgaande jaren geeft het huidige rapport de resultaten van acute ziekenhuizen ook per type van specialistische zorg die binnen het ziekenhuis wordt verleend, weer. Alleen in de MRGN surveillance werden echter verschillen per type specialistische zorg gevonden.

Resistentiemechanismen waaronder de productie van extended spectrum beta-lactamasen (ESBL) en carbapenemasen (CPE) in *E. coli* en *K. pneumoniae* werden niet langer opgenomen in de MRGN gegevensverzameling van 2018, omdat laboratoria er mogelijk niet lokaal naar zoeken of, als ze het wel doen, ze gebruik maken van vaak zeer heterogene methoden. Ter vervanging organiseerde het nationale referentiecentrum (NRC) voor antibioticaresistente gram-negatieve bacillen van mei tot en met oktober 2019 een nationale prospectieve surveillance teneinde het voorkomen en de distributie van carbapenem resistente *E. coli* en *K. pneumoniae* (CRE) en/of van colistine resistante *E. coli* (ColREC) klonen en/of van overdraagbare weerstand/genetische elementen te bepalen en om epidemiologische risicofactoren voor infectie of kolonisatie met CRE en/of ColREC te identificeren. De resultaten worden binnenkort verwacht.

Sciensano werkt momenteel aan de harmonisering van de gegevensverzameling voor de nationale AMR surveillances en voor de Belgische luik van de Europese surveillance van antimicrobiële resistentie (EARS-BE). Voor de AMR surveillance betekent dit dat een geaggregeerde gegevensverzameling wordt verlaten en er wordt gekozen voor het verzamelen van gedetailleerde laboratoriumgegevens op het niveau van het isolaat/de gevoeligheidstest. Dit type van gegevensverzameling zal resulteren in meer gedetailleerde en gestandaardiseerde gegevens die datavalidatie mogelijk maken en interpretatieverschillen vermijden.

RÉSUMÉ

Introduction

Le service « Infections liées aux soins et antibiorésistance » de Sciensano collecte et analyse les données de surveillance de la résistance aux agents antimicrobiens (BMR) recueillies dans les hôpitaux belges. 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.

L'objectif des trois surveillances épidémiologiques BMR (MRSA, MRGN et VRE) est de suivre l'évolution nationale de la proportion de résistance et de l'incidence des organismes multirésistants (MDRO) dans les hôpitaux belges.

Le présent rapport vise à présenter les résultats 2018 des trois programmes de surveillance et à décrire les tendances de la résistance BMR dans les hôpitaux de soins aigus et/ou chroniques belges.

Méthodes

Les données de surveillance ont été collectées rétrospectivement (année 2018) par les laboratoires de microbiologie seuls ou avec la collaboration des équipes d'hygiène hospitalière et ont été agrégées au niveau hospitalier.

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

Les micro-organismes et résistances suivants ont été étudiés:

- *Staphylococcus aureus (S. aureus)* résistant à la méticilline ou à l'oxacilline
- *Escherichia coli* (*E. coli*) et *Klebsiella pneumoniae* (*K. pneumoniae*) non-sensible* aux céphalosporines de 3ème génération (3GC I/R) et/ou au méropéneme (méropénème I/R)
- *Acinetobacter baumannii* (*A. baumannii*) non-sensible* au méropéneme (méropénème I/R)
- *Pseudomonas aeruginosa* (*P. aeruginosa*) multirésistant (MDR), c.-à-d. une sensibilité réduite (intermédiare ou résistance) vis-à-vis d'au moins trois classes d'antibiotiques parmi les suivantes: fluoroquinolones (ciprofloxacine ou lévofloxacine), aminoglycosides (gentamicine, tobramycine ou amikacine), carbapénèmes (imipénème ou méropénème), céphalosporines de 3ème ou 4ème génération (ceftazidime ou cefepime)
- *Enterococcus faecalis* (*E. faecalis*) et *Enterococcus faecium* (*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 données provenant d'échantillons cliniques (sauf indication contraire). Tous les types d'échantillons (p.ex. sang, urine) ont été inclus à l'exception des selles considérées comme échantillons de dépistage et qui ont donc été exclues.

Le caractère potentiellement nosocomial de l'acquisition n'a été évalué que pour le MRSA. Un MRSA nosocomial 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 présent 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 et l'incidence (nombre de cas pour 1 000 hospitalisations) et/ou la densité d'incidence (nombre de cas pour 1 000 jours-patients) ont été calculées. Les données ont été analysées dans STATA 14.1 (StataCorp LP, College Station, Texas, États-Unis) et présentées par région et par niveau de soins spécialisés au sein de l'hôpital. Les différences étaient considérées comme significatives si la valeur p <0,05.

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 2018. Tous les groupes administratifs hospitaliers à l'exception de quatre hôpitaux (fusions; n=97/101) ont participé à la surveillance des MRSA et des MRGN avec au moins un site hospitalier. Malgré le caractère facultatif de la surveillance des VRE, 79,4% de tous les hôpitaux fusionnés (n=93/101) ont participé avec au moins un site hospitalier.

Tableau 1. La proportion de résistance et l'incidence par 1 000 admissions des bactéries incluses dans la surveillance de la résistance aux antimicrobiens, hôpitaux de soins aigus belges, 2018

			Proportion de résistance (%)		Incidence par 1 000 admissions	
		N hôpitaux	Brute	Médiane	Brute	Médiane
Staphylococcus aureus	Méticilline R	112	14,2	11,2	2,67	2,05
Staphylococcus aureus nosocomial	Méticilline R	112	24,7	28,7	0,66	0,46
Enterococcus faecium	Vancomycine R	109	2,3	0,0	0,02	0,00
Enterococcus faecalis	Vancomycine R	109	0,1	0,0	0,01	0,00
Escherichia coli	3GC I/R	112	10,1	9,7	5,25	5,20
	Méropénème I/R	113	0,1	0,0	0,06	0,00
Klebsiella pneumoniae	3GC I/R	112	24,1	21,5	2,81	2,33
	Méropénème I/R	113	2,2	1,3	0,25	0,14
Acinetobacter baumannii	Méropénème I/R	113	7,6	0,0	0,05	0,00
Pseudomonas aeruginosa	MDR	113	7,2	4,2	0,80	0,41

N Hôpitaux = nombre d'hôpitaux (fusions ou sites hospitaliers simples), 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)

Depuis 2004, une diminution significative est observée dans la proportion de résistance de MRSA et dans l'incidence médiane de MRSA nosocomial. Cependant, la diminution de ces deux paramètres n'était pas statistiquement significative entre 2017 et 2018.

Dans les hôpitaux de soins aigus, la proportion et l'incidence médiane d'*E. coli* 3GC I/R était de 9,7 % et 5,20 cas par 1 000 admissions en 2018. Ces deux indicateurs ont augmenté de manière significative entre 2017 et 2018. La proportion de résistance et l'incidence médiane d'*E. coli* méropénème I/R n'ont cependant pas changé au fil du temps (médiane: toutes des valeurs nulles).

Depuis 2015, la proportion médiane (mais pas de l'incidence médiane) de *K. pneumoniae* méropénème I/R augmente de façon significative. En 2018, la proportion de résistance et l' incidence médiane *K. pneumoniae* méropénème I/R était 1,32% et 0,144 cas par 1 000 admissions.

Aucun changement significatif n'a été observé dans l'évolution de la proportion de résistance brute d'*A. baumannii* méropénème I/R entre 2013 et 2018 dans les hôpitaux de soins aigus (médiane=0,0%). L'incidence d'*A. baumannii* méropénème I/R a diminué significativement entre 2013 et 2015, mais est restée stable depuis lors.

Les changements de définition en 2017 et 2018 rendent difficile l'interprétation de l'évolution de *P. aeruginosa* MDR. Dans une cohorte d'hôpitaux de soins aigus ayant participé à la surveillance au moins trois ans, la proportion de résistance médiane est passée de 6,9% en 2017 à 4,3% en 2018, le même niveau de résistance qu'en 2016.

Le tableau 2 montre la proportion de résistance et la densité d'incidence par 1 000 jours-patients des bactéries sous surveillance (échantillons cliniques uniquement) dans les hôpitaux de soins chroniques belges en 2018. Ces chiffres doivent cependant être interprétés avec prudence étant donné le taux faible de participation.

Tableau 2. La proportion de résistance et la densité d'incidence par 1 000 jours-patients de bactéries incluses dans la surveillance de la résistance aux antimicrobiens, hôpitaux de soins chroniques belges, 2018

			Proportion de résistance (%)		Incidence par 1 000 jours-patient	
		N hôpitaux	Brute	Médiane	N hôpitaux	Brute
Staphylococcus aureus	Méticilline R	12	16,1	13,2	0,17	0,10
Staphylococcus aureus nosocomial	Méticilline R	12	52,6	78,0	0,09	0,07
Enterococcus faecium	Vancomycine R	9	1,0	0,0	0,00	0,00
Enterococcus faecalis	Vancomycine R	9	0,0	0,0	0,00	0,00
Escherichia coli	3GC I/R	12	9,6	9,0	0,35	0,29
	Méropénème I/R	12	0,2	0,0	0,01	0,00
Klebsiella pneumoniae	3GC I/R	12	35,2	27,4	2,33	1,96
	Méropénème I/R	12	0,4	0,2	0,02	0,02
Acinetobacter baumannii	Méropénème I/R	12	37,5	0,0	0,01	0,00
Pseudomonas aeruginosa	MDR	12	5,4	2,0	0,05	0,02

N Hôpitaux = nombre d'hôpitaux (fusions ou sites hospitaliers simples), 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 de trois programmes nationaux de surveillance BMR, à savoir la surveillance de (1) MRSA, (2) VRE et (3) MRGN. Ces programmes ont pour objectif de suivre l'évolution de la proportion et de l'incidence (de densité) des bactéries résistantes aux agents antimicrobiens au cours du temps et de fournir ainsi des données nationales.

Les données analysées dans ce rapport ont été collectées rétrospectivement (données 2018 à déclarer fin mars 2019) et agrégées au niveau hospitalier. Par conséquent, elles ne fournissent aucun éclairage sur les profils/types de patients, sur les services à haut risque, ni sur l'origine d'acquisition (c.-à-d. en communauté, vs liées aux soins dans un hôpital aigu ou dans un autre type d'établissement de soins); à l'exception des MRSA

À notre connaissance, notre surveillance BMR belge est l'un des rares programmes qui ne se concentre pas uniquement sur les échantillons invasifs (p.ex. les échantillons de liquide céphalo-rachidien et de sang), mais

comprend à la fois les types d'échantillons invasifs et non invasifs (p.ex. les urines). Les échantillons de dépistage (portage asymptomatique de colonisation) ont été exclus afin de limiter des artefacts dans les taux de résistances renconrtrés liés à des situation épidemiologicales parfois très différentes localement et variables au cours du temps (p.ex : présence d' épidemies) et donc des différences parfois très importantes dans l'intensité du dépistage dans les différents hôpitaux.

Contrairement aux années précédentes, le rapport actuel présente les résultats des hôpitaux de soins aigus également par type de soins spécialisés dispensés au sein de l'hôpital. Seules des différences par type de soins spécialisés ont été trouvées pour la surveillance MRGN.
Les mécanismes de résistance, y compris la bêta-lactamase à spectre étendu (BLSE) et la production de carbapénémases (CPE) chez *E. coli* et *K. pneumoniae,* n'étaient plus inclus dans la collecte de données 2018 pour MRGN parce que les laboratoires peuvent ne pas chercher localement ou s'ils le font, ils utilisent souvent des méthodologies très hétérogènes. En remplacement, le centre national de référence (NRC) pour les bacilles à Gram négatifs résistants aux antibiotiques a initié en 2019 (de mai à octobre) une surveillance prospective nationale visant à confirmer la présence et la proportion relative des différents mécanismes de résistance aux carbapénémes (chez *E. coli* et *K. pneumoniae*) et de résistance à la colistine (chez *E. coli*; ColREC). Cette étude a également pour objectif de caractériser par typage moléculaire les clones bactériens multi-résistants à risque ainsi que les éléments/supports génétiques de résistance transférables rencontrés et enfin de tenter d'identifier des facteurs épidémiologiques de risque associés à la colonisation et à l'infection par CRE et/ou ColREC. Les résultats sont attendus prochainement.

Sciensano travaille actuellement à l'harmonisation des données recueillies par la surveillance nationale BMR et par la partie belge de la surveillance européenne de la résistance aux antimicrobiens (EARS-BE). Pour la surveillance BMR, cela impliquera l'abandon d'une collecte de données agrégées et le recours à la collecte de données de laboratoire détaillées au niveau des résultats des tests d'isolat/tests de sensibilité microbienne. Ce type de collecte de données devrait permettre l'obtention de données plus détaillées et mieux standardisées car la validation des données sera possible et les divergences d'interprétation seront évitées.

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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 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 hospital 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 is mandatory since 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 nosocomial 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 has been made compulsory since 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 2018 results of the three surveillance programs (MRSA, MRGN and VRE) and to describe trends in antimicrobial resistance in Belgian acute and/or chronic care hospitals.

METHODOLOGY

The surveillance results were collected and reported by the microbiology laboratories and/or infection control teams of the participating hospitals to the service "Healthcare-associated infections and antimicrobial resistance" of Sciensano. The data were collected retrospectively (year 2018) and 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-susceptibility to 3rd generation cephalosporins (3GC I/R):
  reduced susceptibility (I) or resistance (R) to 3rd generation (cefotaxime ceftriaxone, ceftazidime) according to EUCAST* or CLSI criteria.

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

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

  3) Multidrug-resistant (MDR) *Pseudomonas aeruginosa* (*P. aeruginosa*):
  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)

  Note: compared to previous years, non-susceptibility to anti-Pseudomonas penicillins (piperacillin +/- tazobactam) is no longer included in the definition.

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

* Note: using the EUCAST criterium for the "I" category before 2019 [1]

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 any of the three 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 nosocomial character of acquisition was only explored for MRSA. 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 for MRSA collected more than 48h after admission) or known in the patient's history (past 12 months).

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 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.

Results are presented overall (all participating hospitals), by hospital type (acute care or chronic care), 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 within the hospital	Definition ECDC [2]	Definition FPS [3]
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

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 1000

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 = P75 - P25)

Because the median is less affected by outliers (e.g. hospitals that experienced 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.
In order to compare resistance proportions and incidences across regions Kruskal-Wallis tests were performed. Differences were considered significant if $p<0.05$.

Historical data are used to present the evolution of a resistance proportion or an incidence. 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).

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 2018, all but four acute care hospital administrative groups (mergers; n=97/101) participated in the MRSA surveillance with at least one hospital site. In total, 113 acute care hospital mergers or sites and 12 chronic care hospitals/sites provided data. One acute care hospital was excluded from further analyses because they did not provide Type D data.

In total, 111 acute care hospitals (99.1%; 44 676 beds) provided annual data. One acute care hospital participated in only one semester. All 12 chronic care hospitals (1 880 beds) provided annual data. Table 3 presents the participation in the MRSA surveillance by hospital care type, region, hospital size and level of specialty care within the hospital.

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 hospitals, 2018

	Flanders	Wallonia	Brussels	Belgium
N of acute care hospitals (%)	**56 (50.0)**	**42 (37.5)**	**14 (12.5)**	**112**
Primary hospitals	48 (85.7)	33 (78.6)	6 (42.9)	87 (77.7)
Secondary hospitals	5 (8.9)	8 (19.1)	4 (28.6)	17 (15.2)
Tertiary hospitals	3 (5.4)	1 (2.4)	3 (21.4)	7 (6.3)
Specialised hospitals			1 (7.1)	1 (0.9)
N of chronic care hospitals (%)	**5 (41.7)**	**5 (41.7)**	**2 (16.7)**	**12**

N = number

1. MRSA in acute care hospitals

1.1 RESISTANCE IN *STAPHYLOCOCCUS AUREUS*

The crude proportion of MRSA on the total number of *S. aureus* isolates (clinical samples only) was 14.2% (n=4 785/33 627). Significant differences in median proportion were found between Wallonia and Brussels (p=0.012) and between Wallonia and Flanders (p<0.001) (Table 4).

The crude incidence of MRSA was 2.67 cases per 1 000 admissions or 0.41 cases per 1 000 patient days. The median incidence and incidence density of MRSA was significantly higher in Wallonia compared to Flanders (both p<0.001) and Brussels (p=0.037 and p=0.003, respectively), The median incidence density was also significantly lower in Flanders compared to Brussels (p=0.04) (Table 4).

No statistically significant differences in the resistance proportion or incidence (density) of MRSA were found by level of specialty care provided by the hospitals (Table 4).

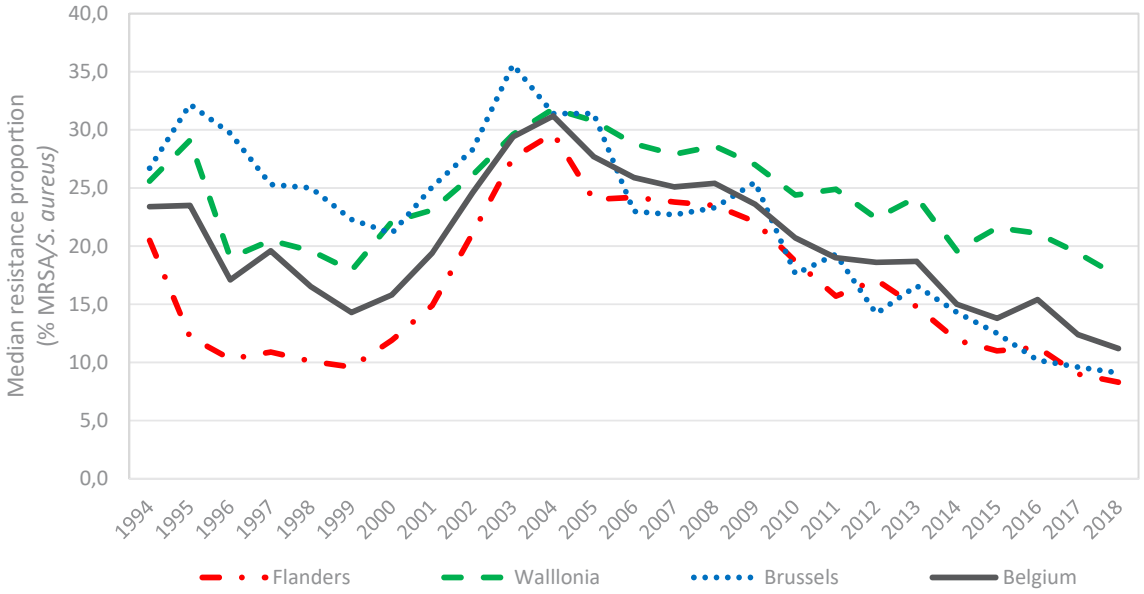
Between 2017 and 2018 the median resistance proportion decreased non significantly overall (from 12.4 to 11.2%) and in all three regions: from 9.0 to 8.3% in Flanders, from 19.4 to 17.4% in Wallonia and from 9.5 to 9.1% in Brussels. Since 2004, the resistance proportion is significantly decreasing in Belgium (-1.19% per year; p<0.001) and in all three regions: -1.38% per year in Flanders (p<0.001), -0.89% per year in Wallonia (p<0.001) and -1.41% per year in Brussels (p<0.001) (Figure 1).

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, 2018

	MRSA (clinical samples only)				
	N of hospitals	Crude	Mean	Median	P25 - P75
Resistance proportion (%)					
Belgium	**112**	**14.2**	**14.4**	**11.2**	**7.1 – 17.9**
Flanders	56	10.3	10.5	8.4	6.3 – 12.9
Wallonia	42	21.3	20.6	17.4	11.6 – 25.2
Brussels	14	11.0	11.6	8.9	8.0 – 11.2
Primary hospitals	87	13.7	14.4	11.2	7.1 – 18.5
Secondary hospitals	17	17.6	15.8	11.6	8.0 – 17.4
Tertiary hospitals	7	12.4	11.9	11.2	8.1 – 12.8
Incidence per 1 000 admissions					
Belgium	**112**	**2.67**	**2.87**	**2.05**	**1.10 – 3.60**
Flanders	56	1.77	1.78	1.37	0.81 – 2.17
Wallonia	42	4.39	4.43	3.55	2.28 – 5.27
Brussels	14	2.29	2.55	2.25	1.63 – 3.19
Primary hospitals	87	2.44	2.80	1.85	1.05 – 3.54
Secondary hospitals	17	3.33	3.31	2.91	1.10 – 4.21
Tertiary hospitals	7	2.86	2.81	2.60	1.48 – 3.72
Incidence density per 1 000 patient days					
Belgium	**112**	**0.41**	**0.41**	**0.32**	**0.17 – 0.52**
Flanders	56	0.28	0.27	0.19	0.14 – 0.34
Wallonia	42	0.69	0.63	0.52	0.32 – 0.84
Brussels	14	0.32	0.32	0.32	0.20 – 0.37
Primary hospitals	87	0.37	0.40	0.31	0.17 – 0.52
Secondary hospitals	17	0.52	0.49	0.34	0.18 – 0.63
Tertiary hospitals	7	0.43	0.44	0.37	0.19 – 0.67

N = number; the results of one hospital site providing specialised care are not shown

Figure 1. 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 with at least 5 years of participation in the surveillance, 1994-2018

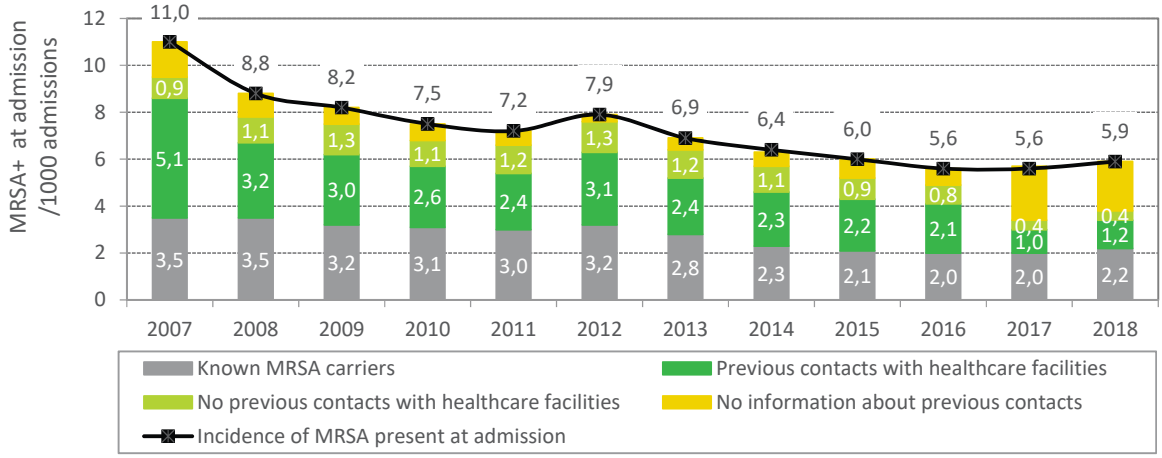


1.2 MRSA PRESENT AT ADMISSION

The incidence of patients who were MRSA positive on admission could only be calculated for 42 acute care hospitals (optional data). Both clinical samples and screening samples testing positive for MRSA within 48 hours after admission were taken into account.

In total, 4 174 patients were reported to be MRSA positive upon admission to these hospitals. The crude and median incidence of MRSA positive patients on admission was 5.9 cases per 1 000 admissions (n=4 174/705 037 admissions) and 5.8 cases per 1 000 admissions (IQR: 3.1-7.7), respectively (Figure 2).

Figure 2. 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, 2007-2018



Less than half of the patients reported MRSA positive upon admission (36.9%; n=1 542) 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 (63.1%; n=2 632), 32.1% were recently transferred to or had a recent stay in healthcare facility (e.g. acute care hospital, day care hospital, nursing home). For 11.8% of the patients (n=310) no contact with any of these facilities in the previous 12 months was reported, while for 56.2% of the patients (n=1 478) information about prior contact with healthcare facilities was unknown.

1.3 NOSOCOMIAL MRSA

Of all clinical samples reported MRSA positive (n=4 785), 24.7% (n= 1 180) were collected more than 48 hours after admission, i.e. nosocomial or hospital-acquired MRSA. This proportion did not significantly differ by region or by level of specialty care of the hospital (Table 5). In addition, 1 193 screening samples were reported as MRSA positive more than 48 hours after admission.

Table 5. Proportion, incidence and incidence density of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2018

	Nosocomial MRSA (clinical samples only)				
	N of hospitals	Crude	Mean	Median	P25 - P75
Proportion nosocomial MRSA/MRSA (%)					
Belgium	**112**	**24.7**	**31.8**	**28.7**	**16.4 – 46.0**
Flanders	56	22.0	30.5	26.0	14.7 – 45.3
Wallonia	42	25.8	31.7	30.2	18.9 – 44.4
Brussels	14	28.1	37.0	32.0	16.5 – 50.0
Primary hospitals	87	25.6	31.6	28.8	16.7 – 44.4
Secondary hospitals	17	22.0	34.3	31.1	14.9 – 52.5
Tertiary hospitals	7	24.7	25.3	16.3	13.0 – 31.8
Incidence per 1 000 admissions					
Belgium	**112**	**0.66**	**0.76**	**0.46**	**0.27 – 1.15**
Flanders	56	0.39	0.45	0.35	0.20 – 0.58
Wallonia	42	1.13	1.12	1.03	0.63 – 1.47
Brussels	14	0.64	0.90	0.52	0.41 – 1.16
Primary hospitals	87	0.62	0.72	0.44	0.26 – 1.15
Secondary hospitals	17	0.73	0.98	0.71	0.26 – 1.79
Tertiary hospitals	7	0.71	0.66	0.41	0.34 – 0.89
Incidence density per 1 000 patient days					
Belgium	**112**	**0.10**	**0.11**	**0.08**	**0.04 – 0.17**
Flanders	56	0.06	0.07	0.05	0.03 – 0.09
Wallonia	42	0.18	0.17	0.17	0.09 – 0.23
Brussels	14	0.09	0.11	0.08	0.05 – 0.13
Primary hospitals	87	0.10	0.11	0.07	0.04 – 0.17
Secondary hospitals	17	0.11	0.13	0.11	0.07 – 0.22
Tertiary hospitals	7	0.11	0.10	0.07	0.05 – 0.12

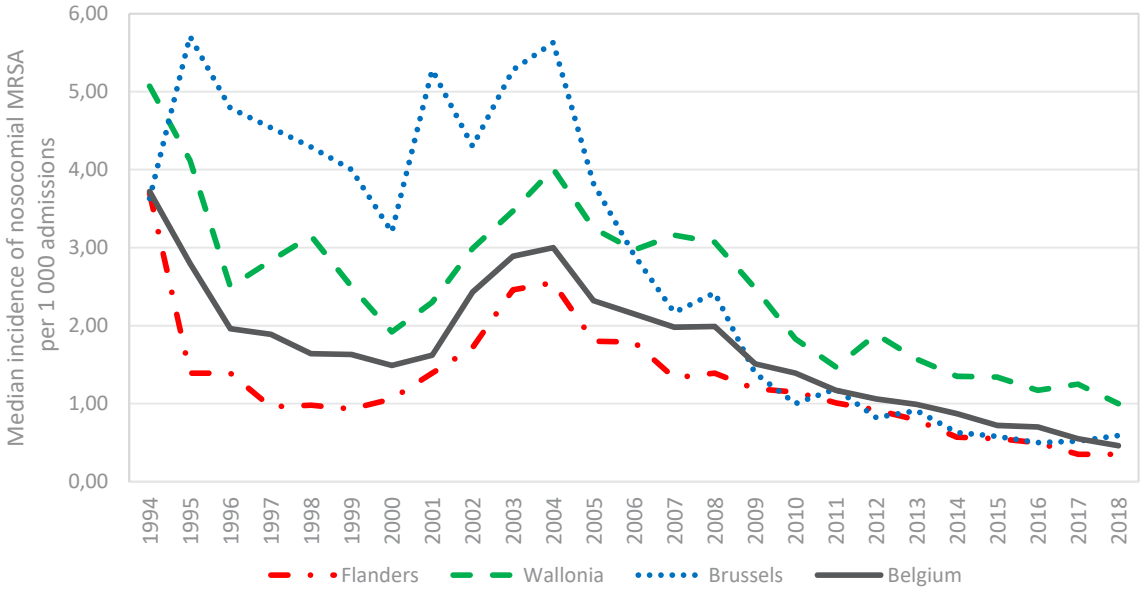
N = number; the results of one hospital site providing specialised care are not shown

The crude incidence of nosocomial MRSA (clinical samples only) was 0.66 cases per 1 000 admissions or 0.10 cases per 1 000 patient days. The median incidence and incidence density of nosocomial MRSA was significantly higher in Wallonia compared to Flanders (both p≤0.001) and Brussels (p=0.010 and p=0.017, respectively) (Table 5).

Between 2017 and 2018, the median incidence of nosocomial MRSA per 1 000 admissions decreased overall (from 0.55 to 0.46 cases per 1 000 admissions, p=0.77) and in Wallonia (from 1.25 to 1.00, p=0.16), but increased in Brussels (from 0.52 to 0.59 cases, p=0.36) and remained stable in Flanders (0.35 cases, p=0.89) when looking in a cohort of hospitals that participated at least five time in the surveillance (Figure 3).

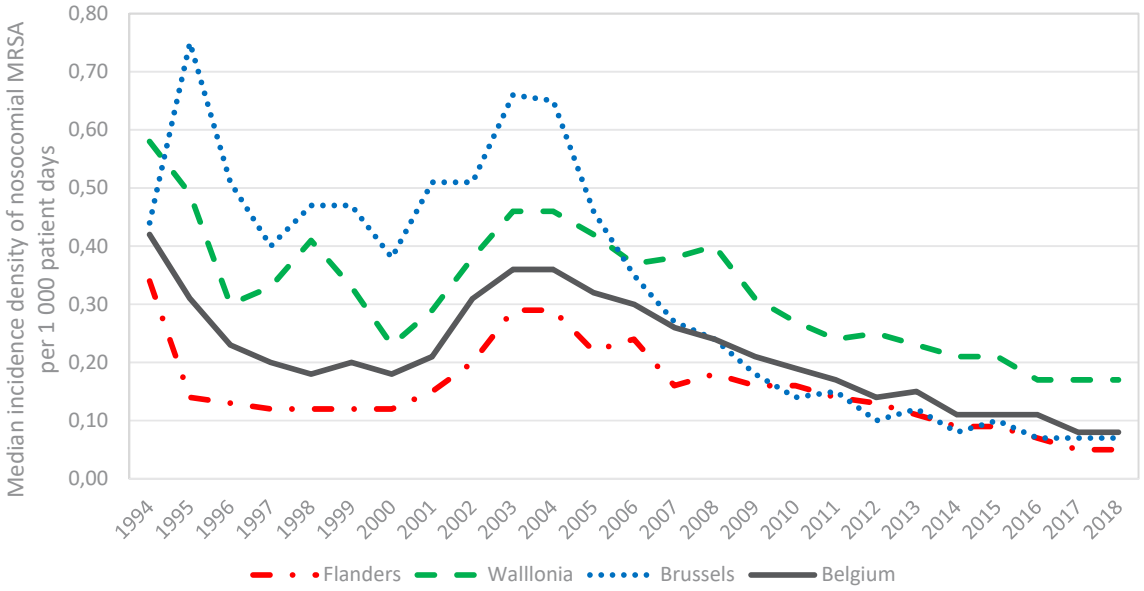
The median incidence of nosocomial MRSA significantly decreased between 2004 and 2018 in Belgium (IRR: 0.89, 95%CI: 0.88-0.89, p<0.001) and in all three regions: IRR=0.88 (95%CI: 0.87-0.89, p<0.001) in Flanders, IRR=0.91 (95%CI: 0.90-0.92), p<0.001) in Wallonia and IRR=0.88 (95%CI: 0.84-0.86, p<0.001) in Brussels.

Figure 3. Evolution of the median incidence of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) per 1000 admissions by region (clinical samples only), Belgian acute care hospitals with at least 5 years of participation in the surveillance, 1994-2018



The median incidence density of nosocomial MRSA remained exactly the same in 2018 as in 2017. Between 2004 and 2018 there was a significant decrease (IRR: 0.90, 95%CI: 0.90-0.91, p<0.001) overall and in all three regions (all p<0.001) (Figure 4).

Figure 4. Evolution of the median incidence density of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) per 1 000 patient days by region (clinical samples only), Belgian acute care hospitals with at least 5 years of participation in the surveillance, 1994-2018



1.4 MRSA SCREENING

Screening on admission most commonly depended on where the patient stayed prior to admission (e.g. another hospital or a nursing home; 86.6%) and to which ward the patient was admitted (e.g. intensive care units; 80.4%). MRSA screening during hospital stay was routinely performed in case of an outbreak (91.1%) or in specific wards (90.2%) (Table 6).

Of all patients hospitalised during the surveillance year, 18.0% (n=226 018/1 254 399) were screened on admission (median: 12.7%; IQR: 7.0-24.6).

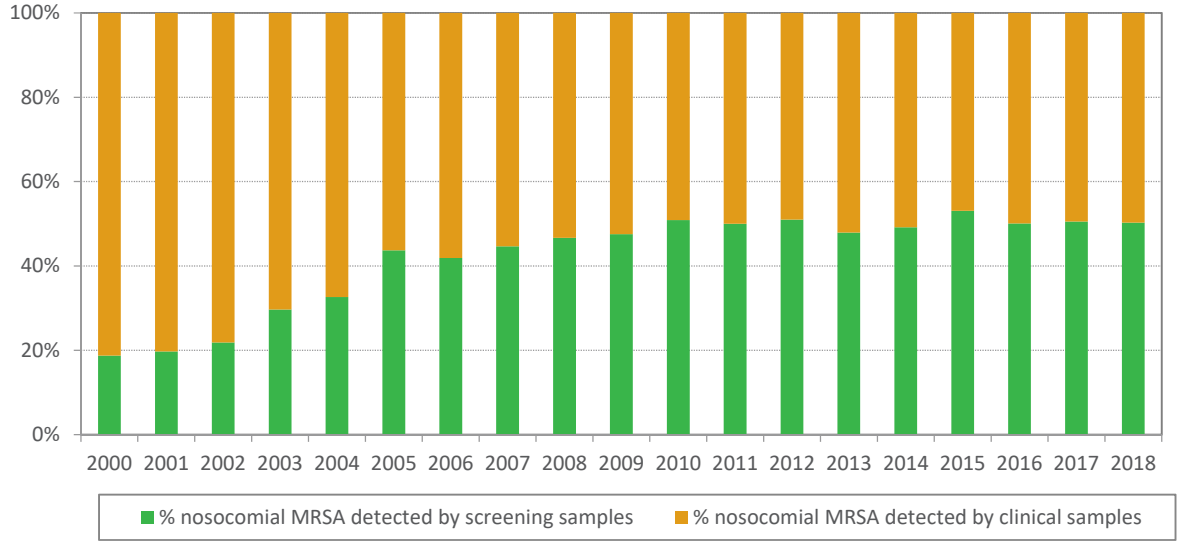
Half of all nosocomial MRSA cases (50.3%) were detected through screening. This proportion remained stable in the past years (Figure 5).

Table 6. Screening for methicillin-resistant *Staphylococcus aureus* (MRSA) on admission and during the hospital stay: hospital practices by region and level of specialty care within the hospital, Belgian acute care hospitals, 2018

% hospitals with these indications	Flanders n=56	Wallonia n=42	Brussels n=14	Primary n=87	Secondary n=17	Tertiary n=7	Belgium n=112
Screening on admission							
Systematic: all patients, all wards	8.9	9.5	7.1	8.1	11.8	14.3	**8.9**
In case of an outbreak in the referral centre	53.6	54.8	64.3	57.5	52.9	28.6	**55.4**
Ward specific screening	71.4	85.7	100.0	77.0	88.2	100.0	**80.4**
Depending on where the patient stayed prior to admission	94.6	71.4	100.0	85.1	88.2	100.0	**86.6**
Depending on the patient's risk	78.6	66.7	92.9	72.4	88.2	85.7	**75.9**
No screening on admission	0.0	0.0	0.0	0.0	0.0	0.0	**0.0**
Screening during the hospital stay							
In case of an outbreak	89.3	90.5	100.0	93.1	82.4	85.7	**91.1**
Routinely in specific wards	87.5	90.5	100.0	89.7	88.2	100.0	**90.2**
Depending on the patient's risk	76.8	59.5	78.6	69.0	76.5	71.4	**70.5**
No screening during hospital stay	0.0	0.0	0.0	0.0	0.0	0.0	**0.0**

The results of one hospital site providing specialised care are not shown

Figure 5. Evolution of the crude proportion of nosocomial-methicillin resistant *Staphylococcus aureus* (MRSA) detected by clinical samples or by screening samples, Belgian acute care hospitals, 2000-2018



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 16.1% (n=97/604) in the 12 participating chronic hospital sites. No significant differences in resistance proportion, incidence and incidence density were found by region (Table 7).

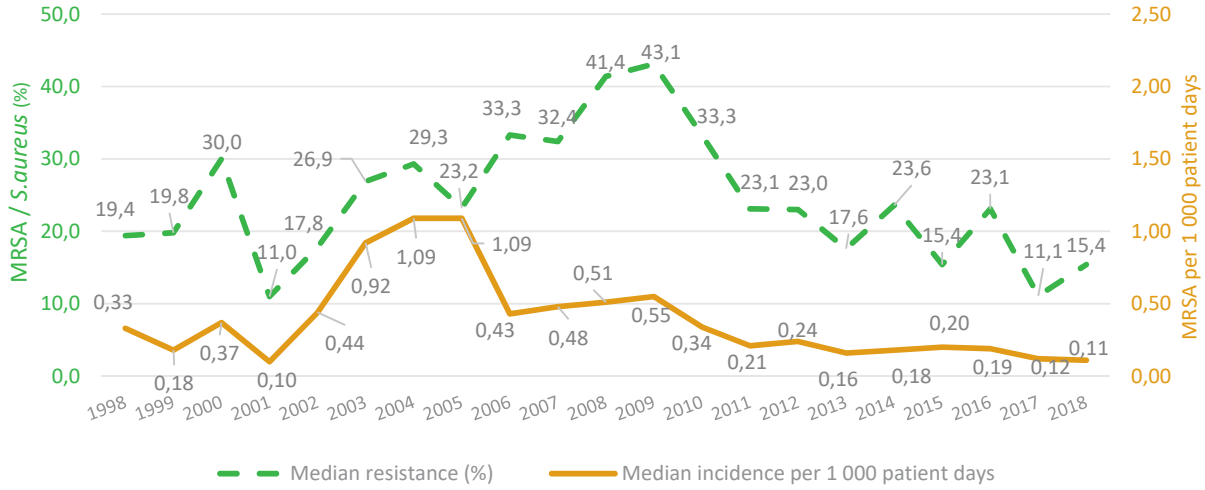
Table 7. Resistance proportion, incidence and incidence density of methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region, Belgian chronic care hospitals, 2018

	MRSA (clinical samples only)				
	N of hospitals	Crude	Mean	Median	P25 - P75
Resistance proportion (%)					
Belgium	**12**	**16.1**	**19.0**	**13.2**	**5.4 – 22.4**
Flanders	5	11.0	11.8	11.1	6.7 – 15.4
Wallonia	5	22.9	32.0	22.6	21.5 – 33.3
Brussels	2	5.2	4.7	4.7	1.8 – 7.5
Incidence per 1 000 admissions					
Belgium	**12**	**5.98**	**6.02**	**4.62**	**3.26 – 8.19**
Flanders	5	4.09	4.00	4.22	3.40 – 4.46
Wallonia	5	6.66	6.65	6.13	5.34 – 10.25
Brussels	2	5.85	9.51	9.51	1.16 – 17.86
Incidence density per 1 000 patient days					
Belgium	**12**	**0.17**	**0.17**	**0.10**	**0.05 – 0.17**
Flanders	5	0.09	0.08	0.09	0.07 – 0.09
Wallonia	5	0.24	0.30	0.16	0.14 – 0.35
Brussels	2	0.10	0.10	0.10	0.03 – 0.18

N = number

The overall median MRSA resistance proportion in a cohort of chronic care hospitals with at least 5 participations increased from 11.1% in 2017 to 15.4% (p=0.32). The incidence density remained stable (p=0.32) (Figure 6).

Figure 6. Methicillin-resistant *Staphylococcus aureus* (MRSA): median resistance proportion and incidence density in a cohort of chronic care hospitals with at least 5 years of participation in the surveillance (clinical samples only), 1998-2018



2.2 MRSA PRESENT AT ADMISSION

Three hospitals provided complete data on the presence of MRSA at admission (optional part). Of the 61 patients who were MRSA positive on admission, 6 (9.8%) had a history of MRSA colonization or infection in the past 12 months.
Because of the limited number of data available, the incidence of patients who were MRSA positive on admission was not calculated.

2.3 NOSOCOMIAL MRSA

The participating chronic care hospitals (n=11) reported 49 clinical samples and 44 screening samples to be MRSA positive more than 48 hours after admission.

Of all MRSA isolated from clinical samples, 52.6% (n=51/97) could be considered as nosocomial (hospital acquired). The median proportion of nosocomial MRSA on the total number of MRSA was significantly lower in Flanders compared to Brussels (p=0.02) (Table 8).

The crude incidence of nosocomial MRSA was 3.14 cases per 1 000 admissions (n=75/15 674) or 0.09 cases per 1 000 patient days (n=75/569 865). The median incidence density was significantly lower in Flanders compared to Wallonia (p=0.047) (Table 8).

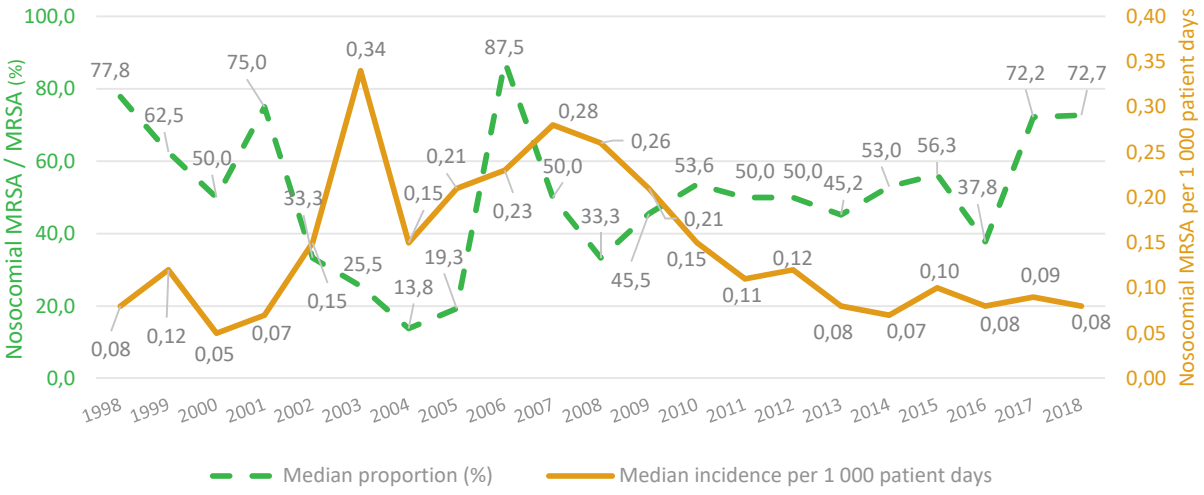
In a cohort of chronic care hospitals with at least 5 participations, the overall median proportion of nosocomial MRSA on the total number of MRSA reported fluctuated greatly throughout the years. The median incidence density did not change significantly (IRR: 1.00, 95%CI: 0.95-1.04) since 2010 (Figure 7).

Table 8. **Proportion, incidence and incidence density of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) (clinical samples only) by region, Belgian chronic care hospitals, 2018**

	Nosocomial MRSA (clinical samples only)				
	N of hospitals	Crude	Mean	Median	P25 - P75
Proportion nosocomial MRSA/MRSA (%)					
Belgium	**12**	**52.6**	**61.1**	**78.0**	**32.8 – 95.5**
Flanders	5	50.0	43.3	33.3	0.0 – 83.3
Wallonia	5	50.0	66.5	72.7	36.8 – 90.9
Brussels	2	85.7	91.7	91.7	83.3 – 100.0
Incidence per 1 000 admissions					
Belgium	**12**	**3.14**	**3.74**	**2.82**	**1.10 – 4.82**
Flanders	5	2.05	1.96	1.49	0.00 – 3.52
Wallonia	5	3.33	3.80	3.38	2.26 – 4.86
Brussels	2	5.01	8.02	8.02	1.16 – 14.88
Incidence density per 1 000 patient days					
Belgium	**12**	**0.09**	**0.09**	**0.07**	**0.03 – 0.14**
Flanders	5	0.04	0.04	0.04	0.00 – 0.07
Wallonia	5	0.12	0.13	0.13	0.10 – 0.15
Brussels	2	0.08	0.09	0.09	0.03 – 0.15

N = number

Figure 7. **Nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA): median proportion of nosocomial MRSA on the total number of MRSA reported and median incidence density in a cohort of chronic care hospitals with at least 5 years of participation in the surveillance (clinical samples only), 1998-2018**



2.4 MRSA SCREENING

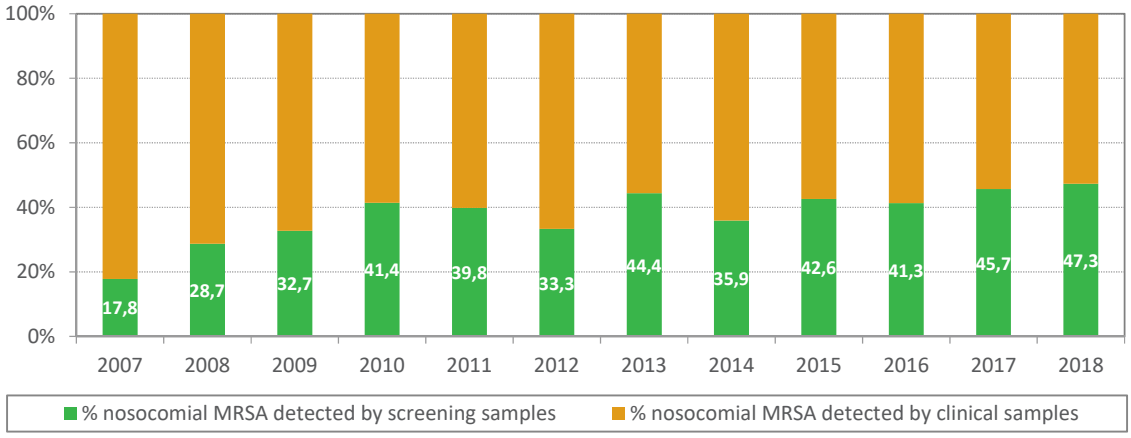
In 2018, all participating chronic care hospitals had a practice for MRSA screening on admission and during the hospital stay. Compared to 2017, the biggest increase was seen for hospitals screening on admission in case of an outbreak in the referral centre (from 8.3% to 58.3%, i.e. +6 hospitals) (Table 9). In total, 18.6% of all patients admitted to these chronic hospitals (n=2 776/14 800) were screened for MRSA on admission.

Table 9. Screening for methicillin-resistant *Staphylococcus aureus* (MRSA) on admission and during the hospital stay: hospital practices by region, Belgian chronic care hospitals, 2018

	Flanders n=5	Wallonia n=5	Brussels n=2	Belgium n=12
Screening on admission (% hospitals with these indications)				
Systematic: all patients, all wards	20.0	20.0	100.0	**33.3**
In case of an outbreak in the referral centre	60.0	60.0	50.0	**58.3**
Ward specific screening	40.0	40.0	100.0	**50.0**
Depending on where the patient stayed prior to admission	60.0	40.0	100.0	**58.3**
Depending on the patient's risk	40.0	40.0	100.0	**50.0**
No screening on admission	0.0	0.0	0.0	**0.0**
Screening during the hospital stay (% hospitals with theses indications)				
In case of an outbreak	100.0	60.0	100.0	**83.3**
Routinely in specific wards	60.0	40.0	0.0	**41.7**
Depending on the patient's risk	100.0	40.0	50.0	**66.7**
No screening during the hospital stay	0.0	0.0	0.0	**0.0**

Less than half of all nosocomial MRSA (47.3%) were detected through screening (Figure 8).

Figure 8. Evolution of the crude proportion of nosocomial methicillin resistant *Staphylococcus aureus* (MRSA) detected by clinical samples or by screening samples, Belgian chronic care hospitals, 2007-2018



PART 2. VANCOMYCIN-RESISTANT ENTEROCOCCI (VRE)

Although participation in the VRE surveillance was optional, 92.1% of all Belgian acute care hospital administrative groups (mergers; n=93/101) participated with at least one hospital site. In total, 109 acute care hospital sites and 9 chronic care hospitals provided Type D data. Because of the small numbers data from acute and chronic care hospitals were combined (Table 10).

Table 10. 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, 2018

	Flanders	Wallonia	Brussels	Belgium
N of acute care hospitals (%)	**53 (48.6)**	**42 (38.5)**	**14 (12.8)**	**109**
Primary hospitals	44 (83.0)	33 (78.6)	6 (42.9)	83 (76.2)
Secondary hospitals	6 (11.3)	8 (19.1)	4 (28.6)	18 (16.5)
Tertiary hospitals	3 (5.7)	1 (2.4)	3 (21.4)	7 (6.4)
Specialised hospitals	-	-	1 (7.1)	1 (0.9)
N of chronic care hospitals (%)	**4 (44.4)**	**4 (44.4)**	**1 (11.1)**	**9**

N = number

1. VRE in acute care hospitals

In total, 8 102 *Enterococcus faecium* (median: 49 per hospital; IQR: 26-81) and 25 241 *Enterococcus faecalis* (median: 143 per hospital; IQR: 63.5-323) isolated from clinical samples (excluding faeces samples) were reported.

The crude resistance proportion and incidence of vancomycin resistance (vanco-R) in *E. faecalis* was 0.08% and 0.010 cases per 1 000 admissions, respectively.

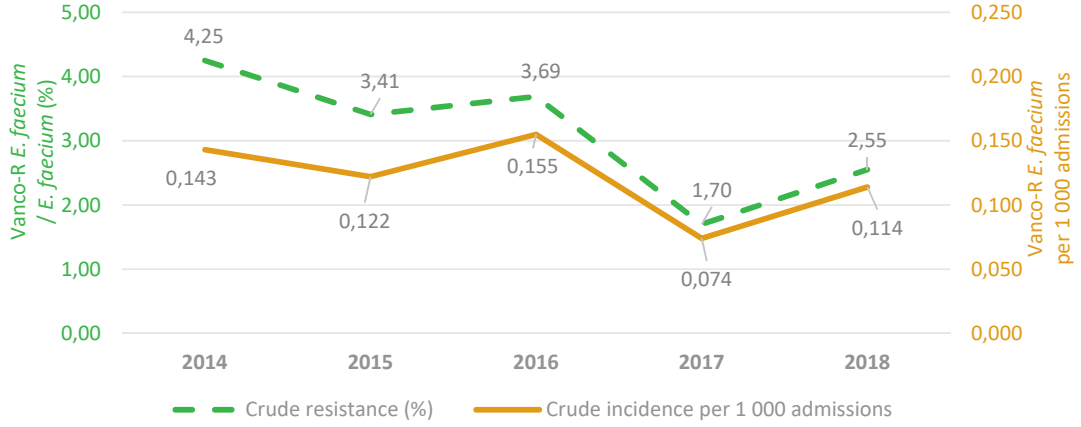
In total, 188 cases of vanco-R *E. faecium* were reported by 47 (43.1%) acute care hospitals (min-max: 1-24). The crude resistance proportion and incidence of vanco-R *E. faecium* was 2.32% and 0.102 cases per 1 000 admissions, respectively. Both indicators were significantly lower in Flanders compared to Wallonia (p=0.009 and p=0.014, respectively) and Brussels (p=0.034 and p=0.034, respectively) (Table 11).
In a cohort of acute care hospitals that participated at least three time in the surveillance, no statistically significant trend could be observed in the crude resistance proportion and incidence of vanco-R *E. faecium* (Figure 9).

Table 11. Resistance proportion and incidence of vancomycin-resistant *Enterococcus faecium* (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2018

	Vancomycin resistance				
	N hospitals	Crude	Mean	Median	P25-P75
Resistance (%)					
Belgium	**109**	**2.32**	**3.03**	**0.00**	**0.00 – 3.17**
Flanders	53	1.38	1.41	0.00	0.00 – 1.27
Wallonia	42	4.68	5.33	1.32	0.00 – 7.30
Brussels	14	2.35	2.28	1.57	0.00 – 4.13
Primary hospitals	83	2.21	3.02	0.00	0.00 – 2.33
Secondary hospitals	18	2.84	2.82	1.99	0.00 – 4.13
Tertiary hospitals	7	2.05	2.97	2.11	0.62 – 4.60
Incidence					
Belgium (per 1 000 pd)	**109**	**0.016**	**0.016**	**0.000**	**0.000 – 0.027**
Belgium (per 1 000 adm)	**109**	**0.102**	**0.111**	**0.000**	**0.000 – 0.161**
Flanders (per 1 000 adm)	53	0.065	0.061	0.000	0.000 – 0.053
Wallonia (per 1 000 adm)	42	0.162	0.166	0.048	0.000 – 0.285
Brussels (per 1 000 adm)	14	0.116	0.135	0.054	0.000 – 0.226
Primary (per 1 000 adm)	83	0.082	0.098	0.000	0.000 – 0.095
Secondary (per 1 000 adm)	18	0.118	0.146	0.063	0.000 – 0.231
Tertiary (per 1 000 adm)	7	0.156	0.163	0.132	0.056 – 0.301

N = number, pd = patient days, adm = admissions; the results of one hospital site providing specialised care are not shown

Figure 9. Vancomycin resistance in *Enterococcus faecium*: crude resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance (clinical samples only), 2014-2018



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.

An outbreak (i.e. at least one new secondary case within the same ward and within one month) with vancomycin-resistant enterococci was reported by 11.9% of the participating hospitals (n=13/109) in 2018. Thirteen other hospitals (11.9%) did not answer the question. In total, 28 clusters were reported: 10 hospitals reported one cluster, one hopital two clusters, one hospital three clusters and one hospital 13 clusters. In total, 164 patients were affected (min-max: 3-57), of which 19 patients (11.6%) were infected. The evolution of the number of outbreaks reported in the national surveillance is presented in Table 12.

Table 12. Evolution of the number of outbreaks reported in the national surveillance of resistant, Belgian acute care hospitals, 2014-2018

	2014	2015	2016	2017	2018
N of hospitals reporting an outbreak (%)	3/40 (7.5)	8/77 (10.4)	7/98 (7.1)	13/103 (12.6)	13/109 (11.9)
N of hospitals not answering the question (%)	0/40 (0.0)	0/77 (0.0)	1/98 (1.0)	4/103 (3.9)	13/109 (11.9)
N of clusters	3	12	12	21	28
N of patients involved	68	136	247	166	164
N of patients colonised (%)	54 (79.4)	115 (84.6)	215 (88.8)	149 (89.8)	145 (88.4)
N of patients infected (%)	14 (20.6)	21 (15.4)	27 (11.2)	17 (10.2)	19 (11.6)

2. VRE in chronic care hospitals

In total, 109 *Enterococcus faecium* (median: 9 per hospital; IQR: 7-17) and 492 *Enterococcus faecalis* (median: 54 per hospital; IQR: 25-83) isolated from clinical samples (excluding faeces samples) were reported.

In 2018, no cases of vanco-R *E. faecalis* were reported in the participating chronic care hospitals. Only one case of vanco-R *E. faecium* was reported. The crude resistance proportion and incidence of vanco-R *E. faecium* was 0.92% and 0.002 cases per 1 000 patient days, respectively.

Between 2014 and 2018 no outbreaks with vanco-R enterococci have been reported by the participating chronic care hospitals.

PART 3. RESISTANCE IN GRAM-NEGATIVE BACTERIA

Similar to the MRSA surveillance, all but four acute care hospital administrative groups (mergers; n=97/101) participated in the 2018 MRGN surveillance with at least one hospital site. In total, 113 acute care hospital mergers or sites and 12 chronic care hospitals/sites provided data. All hospitals provided Type D data and were thus included. With the exception of two acute care hospitals that provided data for only one semester, all hospitals reported annual numbers.

Table 13 presents the participation in the MRGN surveillance by hospital type, region and level of specialty care within the acute care hospital.

Table 13. Participation in the surveillance of multiresistant Gram-negative bacteria by type of hospital, region and hospital size, Belgian acute and chronic care hospitals, 2018

	Flanders	Wallonia	Brussels	Belgium
N of acute care hospitals (%)	**57 (50.4)**	**42 (37.2)**	**14 (12.4)**	**113**
Primary hospitals	48 (84.2)	33 (78.6)	6 (42.9)	87 (77.0)
Secondary hospitals	6 (10.5)	8 (19.1)	4 (28.6)	18 (15.9)
Tertiary hospitals	3 (5.3)	1 (2.4)	3 (21.4)	7 (6.2)
Specialised hospitals	-	-	1 (7.1)	1 (0.9)
N of chronic care hospitals (%)	**5 (41.7)**	**5 (41.7)**	**2 (16.7)**	**12**

N = number

1. Resistant Gram-negative bacteria in acute care hospitals

1.1 RESISTANCE IN *ESCHERICHIA COLI*

The crude resistance proportion of *E. coli* non-susceptible to 3rd generation cephalosporines (3GC I/R) was 10.1% (n=9 719/96 189) (clinical samples only) in 2018. The median resistance proportion of 3GC I/R *E. coli* was significantly lower in Flanders compared to Brussels (p=0.007) and lower in primary hospitals compared to tertiary hospitals (p=0.024) (Table 14).
No noteworthy differences were seen in the median incidence of 3GC I/R *E. coli* between the regions but the incidence was higher in tertiary hospitals compared to primary (p=0.040) and secondary hospitals (p=0.025). The crude incidence of 3GC I/R *E. coli* accounted 5.25 cases per 1 000 admissions or 0.81 cases per 1 000 patient days (Table 14).

In total, 115 cases of *E. coli* non-susceptible to meropenem (meropenem I/R) were reported by 53 (46.9%) acute care hospitals (min-max: 1-10). The crude resistance proportion and incidence of meropenem I/R *E. coli* were 0.12% and 0.062 cases per 1 000 admission, respectively (Table 14; clinical samples only). The median resistance proportion and incidence did not differ significantly between the regions nor between the three levels of specialty care.

Table 14. Resistance proportion and incidence of *Escherichia coli* (clinical samples only) by region and level of specialty care within the hospital: non-susceptibility to third generation cephalosporins and meropenem, Belgian acute care hospitals, 2018

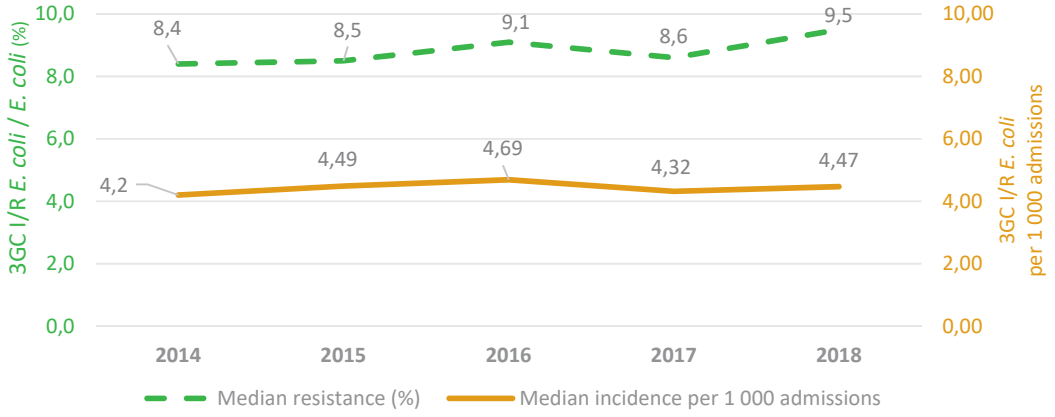
	3GC I/R					Meropenem I/R				
	N hosp	Crude	Mean	Md	P25 - P75	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)										
Belgium	**112**	**10.1**	**10.0**	**9.7**	**7.7 – 12.0**	**113**	**0.12**	**0.14**	**0.00**	**0.00 – 0.17**
Flanders	56	9.8	9.3	8.9	7.1 – 11.7	57	0.11	0.10	0.00	0.00 – 0.16
Wallonia	42	10.0	10.4	9.7	7.3 – 11.8	42	0.13	0.15	0.00	0.00 – 0.17
Brussels	14	11.9	12.1	11.1	10.6 – 14.6	14	0.15	0.25	0.05	0.00 – 0.25
Primary hospitals	86	9.6	9.6	9.5	7.2 – 11.7	87	0.12	0.14	0.00	0.00 – 0.17
Secondary hospitals	18	10.2	10.7	10.9	8.5 – 11.9	18	0.15	0.16	0.13	0.00 – 0.24
Tertiary hospitals	7	12.4	12.7	14.6	9.7 – 15.3	7	0.06	0.06	0.04	0.00 – 0.16
Incidence										
Belgium (per 1 000 pd)	**112**	**0.81**	**0.85**	**0.77**	**0.52 – 0.99**	**113**	**0.009**	**0.011**	**0.000**	**0.000 – 0.016**
Belgium (per 1 000 adm)	**112**	**5.25**	**5.67**	**5.20**	**3.51 – 6.61**	**113**	**0.062**	**0.072**	**0.000**	**0.000 – 0.099**
Flanders (per 1 000 adm)	56	5.38	5.54	5.30	3.84 – 6.37	57	0.058	0.057	0.000	0.000 – 0.088
Wallonia (per 1 000 adm)	42	4.87	5.86	4.42	3.15 – 7.40	42	0.064	0.081	0.000	0.000 – 0.104
Brussels (per 1 000 adm)	14	5.61	5.62	5.66	2.81 – 7.02	14	0.071	0.107	0.029	0.000 – 0.148
Primary (per 1 000 adm)	86	5.33	5.73	5.20	3.54 – 6.58	87	0.068	0.074	0.000	0.000 – 0.099
Secondary (per 1 000 adm)	18	4.03	4.84	4.12	2.81 – 6.33	27	0.061	0.079	0.037	0.000 – 0.128
Tertiary (per 1 000 adm)	7	7.21	7.47	7.02	5.93 – 9.64	8	0.034	0.038	0.026	0.000 – 0.099

N = number, Md = median, pd = patient days, adm = admissions, 3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant; the results of one hospital site providing specialised care are not shown

In a cohort of acute care hospitals that participated at least three years in the surveillance, the median resistance proportion and incidence of 3GC I/R *E. coli* significantly increased between 2017 and 2018 (p<0.001 and p=0.012, respectively). However, between 2014 and 2018 no significant change was noted in the median incidence (IRR: 1.0, 95%CI: 0.99-1.04; p=0.252) (Figure 10).

Between 2015 and 2018 the median resistance proportion and incidence of meropenem I/R *E. coli* did not change in a cohort of acute care hospitals that participated at least three years in the surveillance (all zero values).

Figure 10. ***Escherichia coli*** **non-susceptible to third generation cephalosporins (clinical samples only): median resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2014-2018**



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

1.2 RESISTANCE IN *KLEBSIELLA PNEUMONIAE*

In 2018, the crude resistance proportion and incidence of 3GC I/R *K. pneumoniae* was 24.1% (n=5 192/21 559) or 2.81 per 1 000 admissions, respectively. The median resistance proportion and incidence were lower in Flanders compared to Wallonia (both p<0.001) and Brussels (p=0.001 and p=0.005, respectively). No significant differences were found by level of specialty care provided within the hospitals (Table 15).

Cases of meropenem I/R *K. pneumoniae* (min-max: 1-42) were reported by 70.8% of the hospitals (n=80/113). The crude resistance proportion and incidence of meropenem I/R *K. pneumoniae* was 2.18% or 0.254 cases per 1 000 admissions. The median resistance proportion and incidence were significantly lower in Flanders compared to Wallonia (both p<0.001) and Brussels (both p=0.001). In addition, the median resistance proportion was lower in primary hospitals in comparison to secondary hospitals (p=0.017) (Table 15).

In a cohort of acute care hospitals that participated at least three years in the surveillance, the median resistance proportion and incidence of 3GC I/R *K. pneumoniae* significantly increased between 2017 and 2018 (p=0.002 and p<0.001, respectively). Since 2014, a significant increase in the median resistance proportion (+1.17% per year; p=0.004) and incidence (IRR: 1.08, 95%CI: 1.05-1.12; p<0.001) is seen (Figure 11).

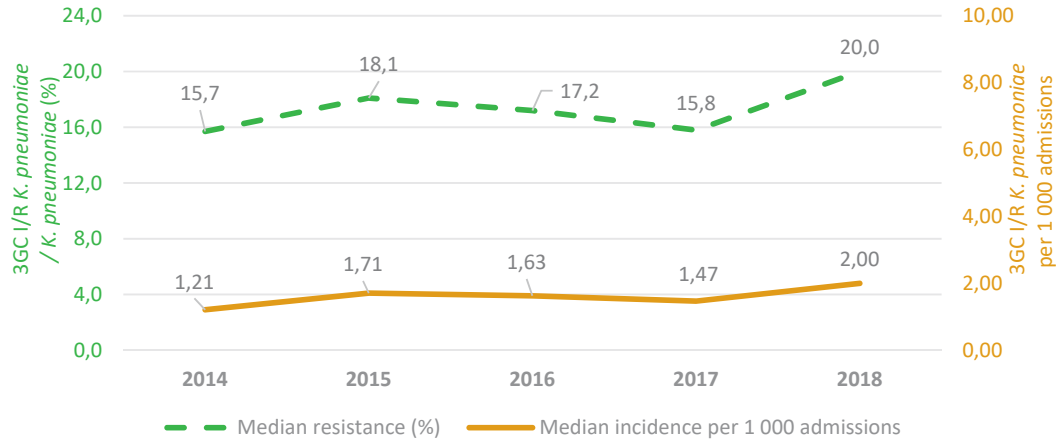
Since 2015, there is a significant increase in the median resistance proportion of meropenem I/R *K. pneumoniae* (+0.27% per year; p=0.022) in a cohort of acute care hospitals that participated at least three years in the surveillance, but the rise in the median incidence was non-significant (IRR: 1.06, 95%CI: 0.97-1.16; p=0.23). In the same cohort, the observed increase in median resistance proportion and incidence between 2017 and 2018 was not significant (p=0.68 and p=0.28, respectively) (Figure 12).

Table 15. Resistance proportion and incidence of *Klebsiella pneumoniae* (clinical samples only) by region and level of specialty care within the hospital: non-susceptibility to third generation cephalosporins and meropenem, Belgian acute care hospitals, 2018

	3GC I/R					Meropenem I/R				
	N hosp	Crude	Mean	Md	P25 - P75	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)										
Belgium	**112**	**24.1**	**24.4**	**21.5**	**15.6 – 31.7**	**113**	**2.18**	**2.22**	**1.32**	**0.00 – 2.89**
Flanders	56	20.2	19.7	17.1	12.9 – 23.6	57	1.29	1.31	0.58	0.00 – 1.57
Wallonia	42	28.6	29.0	28.4	19.2 – 38.2	42	3.35	3.15	2.25	0.97 – 3.27
Brussels	14	27.1	29.8	29.3	23.8 – 36.5	14	2.57	3.10	2.14	1.40 – 4.17
Primary hospitals	86	24.0	24.1	21.0	14.9 – 31.6	87	1.98	2.02	0.86	0.00 – 2.79
Secondary hospitals	18	25.0	25.3	21.9	16.6 – 34.7	18	2.92	3.19	2.38	1.20 – 3.92
Tertiary hospitals	7	23.1	24.4	23.0	18.2 – 30.9	7	2.03	2.19	1.57	1.26 – 3.05
Incidence										
Belgium (per 1 000 pd)	**112**	**0.43**	**0.46**	**0.38**	**0.23 – 0.51**	**113**	**0.039**	**0.045**	**0.022**	**0.000 – 0.053**
Belgium (per 1 000 adm)	**112**	**2.81**	**3.20**	**2.33**	**1.37 – 3.69**	**113**	**0.254**	**0.306**	**0.144**	**0.000 – 0.331**
Flanders (per 1 000 adm)	56	2.15	2.10	1.63	1.09 – 2.72	57	0.138	0.131	0.034	0.000 – 0.200
Wallonia (per 1 000 adm)	42	3.84	4.54	3.14	1.91 – 6.80	42	0.450	0.522	0.235	0.092 – 0.623
Brussels (per 1 000 adm)	14	3.21	3.60	3.21	2.67 – 3.77	14	0.303	0.372	0.183	0.148 – 0.647
Primary (per 1 000 adm)	86	2.73	3.17	2.12	1.29 – 3.55	87	0.225	0.281	0.113	0.000 – 0.316
Secondary (per 1 000 adm)	18	2.47	3.14	2.11	1.64 – 3.44	18	0.289	0.421	0.196	0.092 – 0.416
Tertiary (per 1 000 adm)	7	3.79	3.86	3.60	3.07 – 4.93	7	0.332	0.354	0.274	0.196 – 0.527

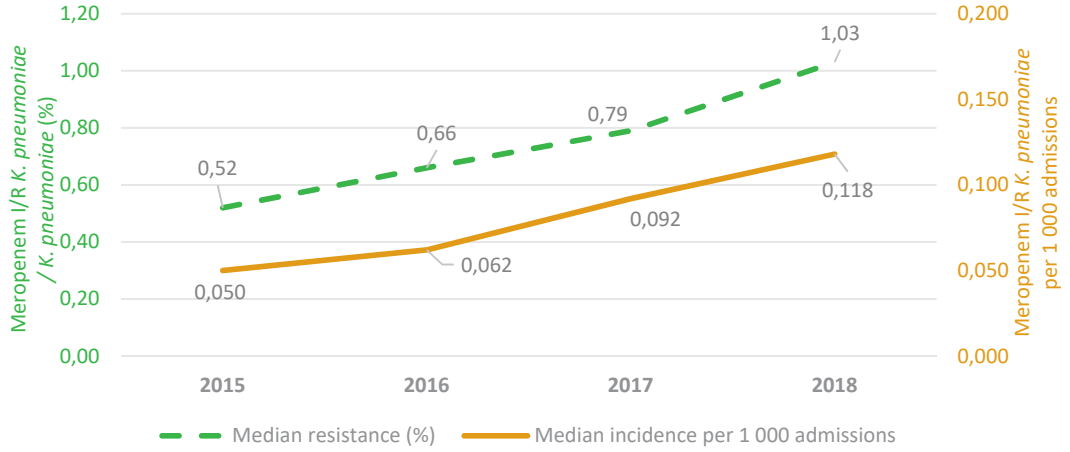
N = number, Md = median, pd = patient days, adm = admissions, 3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant; the results of one hospital site providing specialised care are not shown

Figure 11. *Klebsiella pneumoniae* non-susceptible to third generation cephalosporins (clinical samples only): median resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2014-2018



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

Figure 12. *Klebsiella pneumoniae* non-susceptible to meropenem (clinical samples only): median resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2015-2018



I/R = intermediate susceptibility or resistant

1.3 RESISTANCE IN *ACINETOBACTER BAUMANNII*

Thirty-three hospitals (29.2%) reported at least one meropenem I/R *A. baumannii* (min-max:1-20). The crude resistance proportion and incidence of meropenem I/R *A. baumannii* in clinical samples was 7.6% (n=95/1 256) and 0.05 cases per 1 000 admissions. The median resistance proportion did not differ by region but was significantly higher in tertiary hospitals compared to primary (p<0.001) and secondary hospitals (p=0.019). Similarly, the median incidence was higher in tertiary hospitals compared to primary (p<0.001) and secondary hospitals (p=0.010) (Table 16).

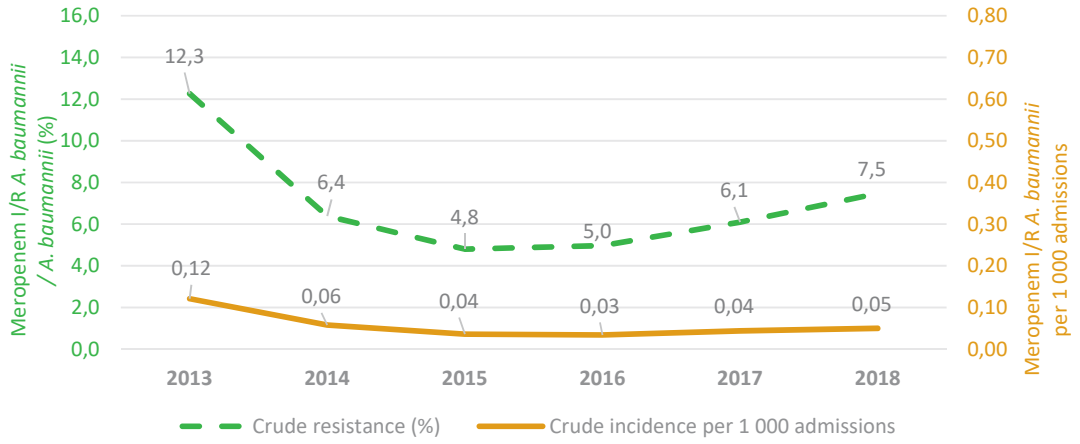
Figure 13 presents the evolution of the crude (median all zero values) resistance proportion and incidence of meropenem I/R *A. baumannii* in a cohort of acute care hospitals that participated at least three times in the surveillance. No significant change in the evolution of the resistance proportion (p=0.60) can be observed between 2013 and 2018. The incidence of meropenem I/R *A. baumannii* significantly decreased between 2013 and 2015 (IRR: 0.75, 95%CI: 0.58-0.96; p=0.023), but remained stable since then (IRR: 1.05, 95%CI: 0.91-1.21; p=0.52).

Table 16. Resistance proportion and incidence of *Acinetobacter baumannii* non-susceptible to meropenem (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2018

	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)					
Belgium	**113**	**7.6**	**5.0**	**0.0**	**0.0 – 4.5**
Flanders	57	5.1	4.2	0.0	0.0 – 2.9
Wallonia	42	6.2	4.2	0.0	0.0 – 1.1
Brussels	14	20.2	11.0	0.0	0.0 – 16.7
Primary hospitals	87	4.8	3.4	0.0	0.0 – 0.0
Secondary hospitals	18	8.1	7.1	0.0	0.0 – 11.1
Tertiary hospitals	7	14.9	20.4	20.0	1.9 – 42.1
Incidence					
Belgium (per 1 000 pd)	**113**	**0.01**	**0.01**	**0.00**	**0.00 – 0.11**
Belgium (per 1 000 adm)	**113**	**0.05**	**0.04**	**0.00**	**0.00 – 0.03**
Flanders (per 1 000 adm)	57	0.04	0.03	0.00	0.00 – 0.03
Wallonia (per 1 000 adm)	42	0.04	0.03	0.00	0.00 – 0.02
Brussels (per 1 000 adm)	14	0.15	0.10	0.00	0.00 – 0.11
Primary (per 1 000 adm)	87	0.03	0.03	0.00	0.00 – 0.00
Secondary (per 1 000 adm)	18	0.04	0.03	0.00	0.00 – 0.05
Tertiary (per 1 000 adm)	7	0.17	0.20	0.08	0.03 – 0.26

N = number, Md = median, pd = patient days, adm = admissions; the results of one hospital site providing specialised care are not shown

Figure 13. *Acinetobacter baumannii* non-susceptible to meropenem (clinical samples only): crude resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2013-2018



I/R = intermediate susceptibility or resistant

1.4 RESISTANCE IN *PSEUDOMONAS AERUGINOSA*

In 2018, the crude resistance proportion and incidence of multidrug-resistant (MDR) *Pseudomonas aeruginosa* was 7.2% (n=1 488/20 743; clinical samples only) and 0.89 cases per 1 000 admissions, respectively. The median resistance proportion and incidence of MDR *P. aeruginosa* were significantly higher in tertiary hospitals compared to primary (p=0.003 and p<0.001, respectively) and secondary hospitals (p=0.022 and p=0.009). No significant differences were found by region (Table 17).

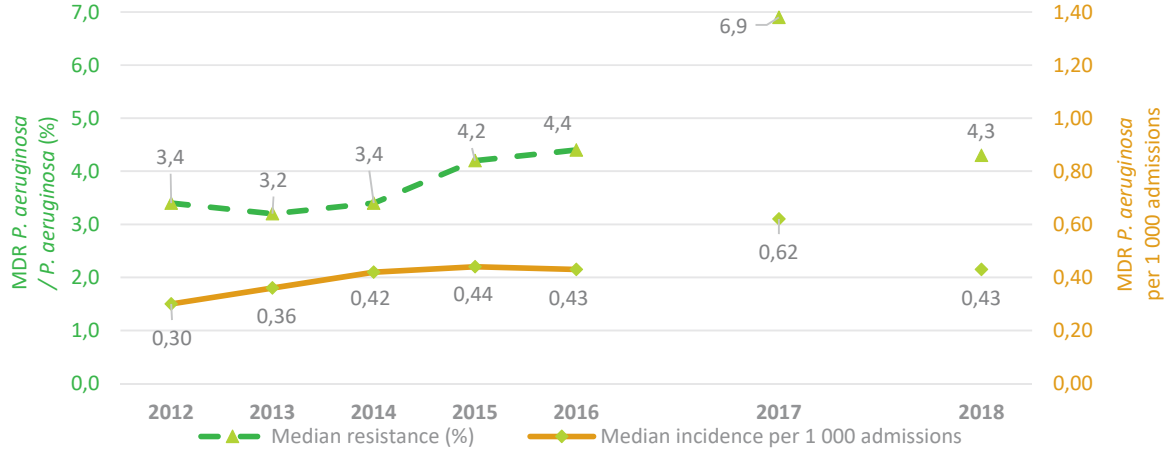
Table 17. Resistance proportion and incidence of multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only) by region and level of specialty care within the hospital, Belgian acute care hospitals, 2018

	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)					
Belgium	**113**	**7.2**	**5.6**	**4.2**	**2.4 – 7.5**
Flanders	57	7.3	5.5	4.8	2.3 – 6.7
Wallonia	42	6.5	5.4	4.0	2.4 – 8.0
Brussels	14	7.9	6.5	5.2	2.7 – 10.4
Primary hospitals	87	5.9	5.0	3.8	2.1 – 6.5
Secondary hospitals	18	5.7	5.7	5.0	2.7 – 8.5
Tertiary hospitals	7	12.4	12.5	13.7	6.6 – 14.8
Incidence					
Belgium (per 1 000 pd)	**113**	**0.12**	**0.10**	**0.06**	**0.03 – 0.12**
Belgium (per 1 000 adm)	**113**	**0.80**	**0.71**	**0.41**	**0.20 – 0.83**
Flanders (per 1 000 adm)	57	0.76	0.63	0.38	0.21 – 0.68
Wallonia (per 1 000 adm)	42	0.74	0.72	0.47	0.18 – 0.92
Brussels (per 1 000 adm)	14	1.09	1.03	0.69	0.30 – 1.81
Primary (per 1 000 adm)	87	0.60	0.59	0.38	0.17 – 0.73
Secondary (per 1 000 adm)	18	0.58	0.73	0.51	0.23 – 0.83
Tertiary (per 1 000 adm)	7	2.19	2.27	2.51	1.22 – 2.54

N = number, Md = median, pd = patient days, adm = admissions; the results of one hospital site providing specialised care are not shown

Definition changes in 2017 and 2018 (see methods) make it difficult to interpret the evolution of MDR *P. aeruginosa.* In a cohort of acute care hospitals that participated at least three years in the surveillance, the median resistance proportion decreased from 6.9% in 2017 to 4.3% in 2018, a resistance level in line with 2016. Likewise, the median incidence diminished from 0.62 to 0.43 cases per 1 000 admission between 2017 and 2018 (Figure 14).

Figure 14. Multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only): median resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2012-2018



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.

2. Resistant Gram-negative bacteria in chronic care hospitals

2.1 RESISTANCE IN *ESCHERICHIA COLI*

In the subgroup of chronic care hospitals and acute care hospital sites with an average length of stay of more than 16 days, the crude resistance proportion was 9.6% for 3GC I/R *E. coli* (n=199/2 066) and 0.24% for meropenem I/R *E. coli* (n=5/2 066). The crude incidence density was 0.35 per 1 000 patient days for 3GC I/R *E. coli* and 0.009 per 1 000 patient days for meropenem I/R *E. coli* (Table 18).

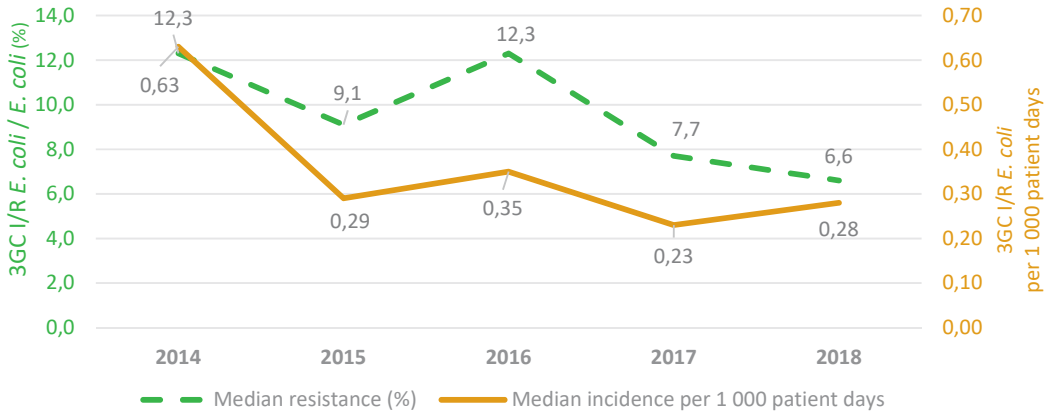
Table 18. Resistance proportion and incidence density of *Escherichia coli* (clinical samples only) by region: non-susceptibility to third generation cephalosporins and meropenem, Belgian chronic care hospitals, 2018

	3GC I/R					Meropenem I/R				
	N hosp	Crude	Mean	Md	P25 - P75	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)										
Belgium	**12**	**9.6**	**8.6**	**9.0**	**3.5 – 13.7**	**12**	**0.24**	**0.18**	**0.00**	**0.00 – 0.12**
Flanders	5	8.3	5.8	4.5	0.0 – 8.7	5	0.00	0.00	0.00	0.00 – 0.00
Wallonia	5	9.2	8.6	9.2	3.9 – 12.1	5	0.17	0.12	0.00	0.00 – 0.24
Brussels	2	14.4	15.6	15.6	12.6 – 18.6	2	1.05	0.75	0.75	0.00 – 1.51
Incidence density per 1 000 patient days										
Belgium	**12**	**0.35**	**0.35**	**0.29**	**0.09 – 0.57**	**12**	**0.009**	**0.010**	**0.000**	**0.000 – 0.009**
Flanders	5	0.26	0.20	0.28	0.00 – 0.30	5	0.000	0.000	0.000	0.000 – 0.000
Wallonia	5	0.36	0.42	0.15	0.10 – 0.65	5	0.006	0.009	0.000	0.000 – 0.018
Brussels	2	0.57	0.57	0.57	0.48 – 0.65	2	0.042	0.039	0.039	0.000 – 0.079

N = number, Md = median, 3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant

In a cohort of chronic care hospitals that participated at least three years in the surveillance, a non-significant trend is observed for both the median resistance proportion (p=0.349) and incidence density (IRR: 1.08, 95%CI: 0.34-3.41; p=0.898) of 3GC I/R *E. coli* (Figure 15).

Figure 15. *Escherichia coli* non-susceptible to third generation cephalosporins (clinical samples only): median resistance proportion and incidence density in a cohort of chronic care hospitals with at least 3 years of participation in the surveillance, 2014-2018



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

2.2 RESISTANCE IN *KLEBSIELLA PNEUMONIAE*

The crude resistance proportion was 35.2% for 3GC I/R *K. pneumoniae* (n=197/559) and 2.33% for meropenem I/R *K. pneumoniae* (n=13/559) in the participating chronic care hospitals. The crude incidence density was 0.35 per 1 000 patient days for 3GC I/R *K. pneumoniae* and 0.023 per 1 000 patient days for meropenem I/R *K. pneumoniae* (Table 19).

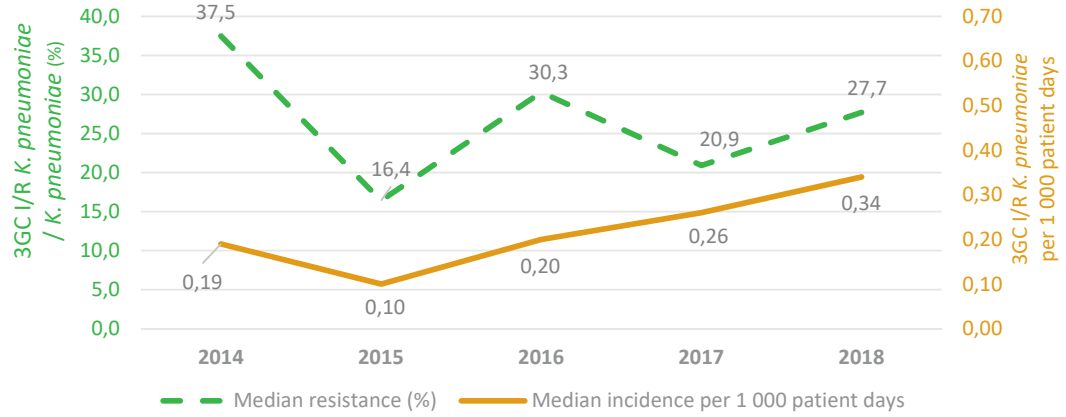
Table 19. Resistance proportion and incidence density of *Klebsiella pneumoniae* (clinical samples only) by region: non-susceptibility to third generation cephalosporins and meropenem, Belgian chronic care hospitals, 2018

	3GC I/R					Meropenem I/R				
	N hosp	Crude	Mean	Md	P25 - P75	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)										
Belgium	**12**	**35.2**	**28.6**	**27.4**	**18.8 – 41.5**	**12**	**2.33**	**2.42**	**1.96**	**0.00 – 3.83**
Flanders	5	28.9	20.3	27.3	5.0 – 27.5	5	1.56	1.38	0.00	0.00 – 1.89
Wallonia	5	33.4	28.6	20.0	19.6 – 28.1	5	2.66	3.57	2.65	2.00 – 6.52
Brussels	2	50.5	49.6	49.6	41.5 – 57.7	2	2.15	2.18	2.18	1.92 – 2.44
Incidence density per 1 000 patient days										
Belgium	**12**	**0.35**	**0.35**	**0.24**	**0.08 – 0.49**	**12**	**0.023**	**0.021**	**0.022**	**0.000 – 0.034**
Flanders	5	0.20	0.17	0.17	0.04 – 0.21	5	0.011	0.011	0.000	0.000 – 0.019
Wallonia	5	0.37	0.42	0.26	0.11 – 0.47	5	0.029	0.027	0.029	0.015 – 0.038
Brussels	2	0.66	0.65	0.65	0.51 – 0.79	2	0.028	0.028	0.028	0.026 – 0.030

N = number, Md = median, 3GC = 3rd generation cephalosporins, I/R = intermediate susceptibility or resistant

In a cohort of chronic care hospitals that participated at least three years in the surveillance, the median resistance proportion of 3GC I/R *K. pneumoniae* showed a non-signficant increase between 2017 and 2018 (p=0.256). The median incidence density showed a significant trend between 2014 and 2018 (IRR: 1.11, 95%CI: 1.08-1.15; p<0.001) (Figure 16).

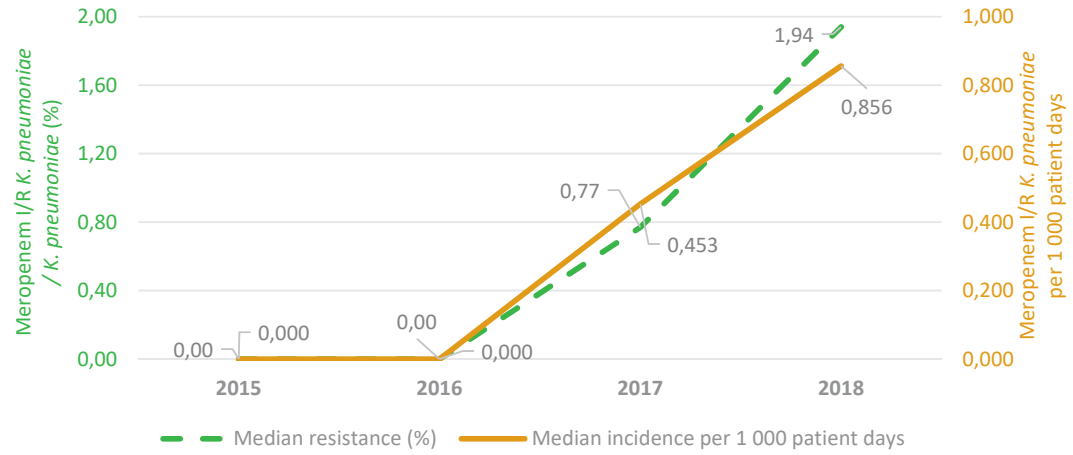
Figure 16. *Klebsiella pneumoniae* non-susceptible to third generation cephalosporins (clinical samples only): median resistance proportion and incidence density in a cohort of chronic care hospitals with at least 3 years of participation in the surveillance, 2014-2018



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

In the same cohort of chronic care hospitals, a steep increase is seen in the median resistance proportion of meropenem I/R *K. pneumoniae* but this rise was statistically non-significant (p=0.022). The same can be concluded for the surge in the median incidence (IRR: 1.46, 95%CI: 0.86-2.49; p=0.16) (Figure 17).

Figure 17. *Klebsiella pneumoniae* non-susceptible to meropenem (clinical samples only): median resistance proportion and incidence in a cohort of chronic care hospitals with at least 3 years of participation in the surveillance, 2015-2018



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* (clinical samples only). Two out of the five chronic care hospitals in Wallonia reported six cases of meropenem I/R *A. baumannii* in total (n=6/14). The crude resistance proportion was 37.5% overall (n=6/16), while the crude incidence density was 0.01 cases of meropenem I/R *A. baumannii* per 1 000 patient days (Table 20).

Table 20. Resistance proportion and incidence density of *Acinetobacter baumannii* non-susceptible to meropenem (clinical samples only) by region, Belgian chronic care hospitals, 2018

	N hosp	Crude	Mean	Md	P25 - P75
Proportion (%)					
Belgium	**12**	**37.5**	**11.7**	**0.0**	**0.0 – 0.0**
Flanders	5	0.0	0.0	0.0	0.0 – 0.0
Wallonia	5	42.9	28.0	0.0	0.0 – 40.0
Brussels	2	0.0	0.0	0.0	0.0 – 0.0
Incidence density per 1 000 patient days					
Belgium	**12**	**0.01**	**0.19**	**0.00**	**0.00 – 0.00**
Flanders	5	0.00	0.00	0.00	0.00 – 0.00
Wallonia	5	0.02	0.46	0.00	0.00 – 0.97
Brussels	2	0.00	0.00	0.00	0.00 – 0.00

N = number, I/R = intermediate susceptibility or resistant

2.4 RESISTANCE IN *PSEUDOMONAS AERUGINOSA*

In total, 5.4% of all reported *P. aeruginosa* were cases of MDR *P. aeruginosa* (n=26/478; clinical samples only). These cases were reported by seven hospitals (58.3%; min.-max.: 1-9). The crude and median incidence density were 0.05 and 0.02 cases of MDR *P. aeruginosa* per 1 000 patient days (Table 21).

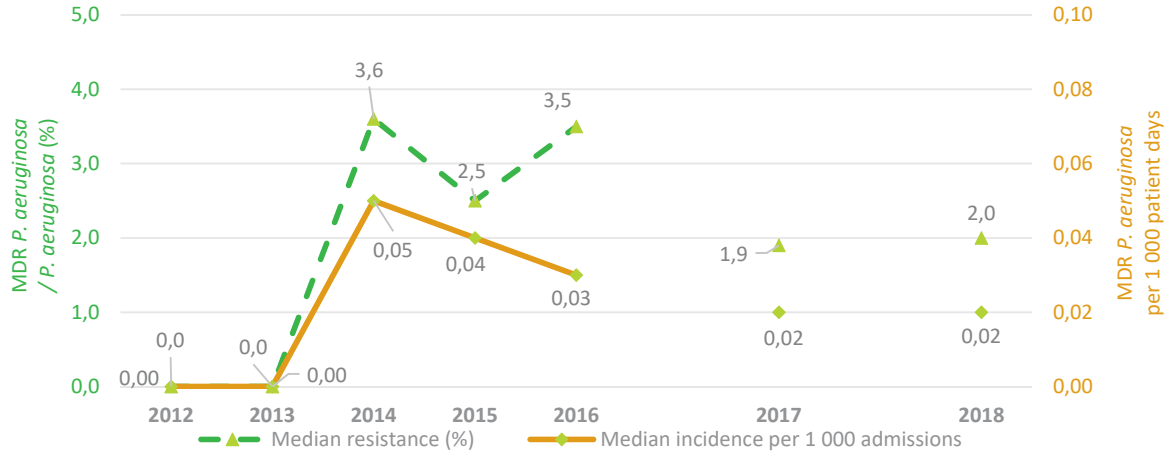
Table 21. Resistance proportion and incidence density of multidrug-resistant *Pseudomonas aeruginosa* (clinical samples only) by region, Belgian chronic care hospitals, 2018

	N hosp	Crude	Mean	Median	P25 - P75
Proportion (%)					
Belgium	**12**	**5.4**	**5.3**	**2.0**	**0.0 – 10.8**
Flanders	5	2.0	3.0	2.0	0.0 – 2.1
Wallonia	5	2.9	2.6	0.0	0.0 – 2.6
Brussels	2	17.8	17.7	17.7	16.7 – 18.8
Incidence density per 1 000 patient days					
Belgium	**12**	**0.05**	**0.06**	**0.02**	**0.00 – 0.10**
Flanders	5	0.02	0.02	0.02	0.00 – 0.04
Wallonia	5	0.02	0.03	0.00	0.00 – 0.03
Brussels	2	0.22	0.23	0.23	0.18 – 0.27

N = number, I/R = intermediate susceptibility or resistant

Figure 18 presents the evolution of the median resistance proportion and incidence density of MDR *P. aeruginosa* in a cohort of chronic care hospitals that participated at least three times in the surveillance.

Figure 18. Multidrug-resistant (MDR) *Pseudomonas aeruginosa* (clinical samples only): median resistance proportion and incidence density in a cohort of chronic care hospitals with at least 3 years of participation in the surveillance, 2012-2018



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.

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 (2018 data to be reported by the end of March 2019) and were 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. Caution is needed when interpreting the numbers and figures presented in this report for the latter as there were only 12 participating chronic care hospitals.

In 2018, the median resistance proportion of MRSA was 11.2% in the participating acute care hospitals. Of all clinical samples reported MRSA positive, 24.7% were collected more than 48 hours after admission, i.e. nosocomial or hospital-acquired MRSA. The median incidence of nosocomial MRSA was 0.46 cases per 1 000 admissions.
Since 2004, a significantly decreasing trend in the median resistance proportion of MRSA and in the median incidence of nosocomial MRSA can be observed. The decrease in both parameters was however not statistically significant between 2017 and 2018 in our Belgian hospitals.

In total, 188 cases of vanco-R *E. faecium* were reported by 47 (43.1%) acute care hospitals (min-max: 1-24). The crude resistance proportion and incidence of vanco-R *E. faecium* was 2.32% and 0.102 cases per 1 000 admissions in the participating acute and chronic care hospitals (median both zero), respectively. No statistically significant trend could be observed between 2014 and 2018.

In the participating acute care hospitals, the median resistance proportion and incidence was 9.7% and 5.20 cases per 1 000 admissions for 3GC I/R *E. coli* in 2018. Both indicators significantly increased between 2017 and 2018. The median resistance proportion and incidence of meropenem I/R *E. coli* however did not change over time (all zero values). In 2018, the crude resistance proportion and incidence of meropenem I/R *E. coli* was 0.12% and 0.062 cases per 1 000 admissions, respectively.

In 2018, the median resistance proportion and incidence of 3GC I/R *K. pneumoniae* in acute care hospitals was 21.5% and 2.33 per 1 000 admissions, respectively. Comparable to 3GC I/R *E. coli*, a significant increase in both parameters could be observed between 2017 and 2018.
Since 2015, there is a significant increase in the median resistance proportion of meropenem I/R *K. pneumoniae* but not in the median incidence. Between 2017 and 2018 both indicators increased non-significantly. In 2018, the median resistance proportion and incidence of meropenem I/R *K. pneumoniae* was 1.32% and 0.144 cases per 1 000 admissions.

No significant change in the evolution of the crude resistance proportion of meropenem I/R *A. baumannii* was observed between 2013 and 2018 in acute care hospitals (median = 0.0%). The incidence of meropenem I/R *A. baumannii* significantly decreased between 2013 and 2015, but remained stable since then. Currently, the crude resistance proportion and incidence of meropenem I/R *A. baumannii* are 7.6% and 0.05 cases per 1 000 admissions in acute care hospitals, respectively.

Definition changes in 2017 and 2018 make it difficult to interpret the evolution of MDR *P. aeruginosa.* In a cohort of acute care hospitals that participated at least three years in the surveillance, the median resistance proportion decreased from 6.9% in 2017 to 4.3% in 2018, a resistance level in line with 2016. Likewise, the median incidence diminished from 0.62 to 0.43 cases per 1 000 admission between 2017 and 2018.

In a cohort of chronic care hospitals with at least 5 years of participation, the overall median MRSA resistance proportion non-significantly increased from 11.1% in 2017 to 15.4% in 2018. The incidence density remained stable.

A non-significant trend in the median resistance proportion is observed between 2017 and 2018 for both 3GC I/R *E. coli* and *K. pneumoniae* and for the median incidence density of 3GC I/R *E. coli*. The median incidence

density of 3GC I/R *K. pneumoniae* however showed a significant increase when considering the period between 2014 and 2018.

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 and only considering invasive sample results of hospitalised patients, EARS-BE found a statistically significant decreasing trend in the mean resistance proportion of MRSA (from 12.8% in 2014 to 8.9% in 2018). The EARS-BE surveillance also highlighted a non-significant increase in the resistance in *K. pneumoniae* to 3GC (from 18.6% to 22.0% between 2014 and 2018) and to carbapenems (from 0.6% to 0.8% between 2014 and 2018). The latter indicator is however decreasing since 2016: from 2.8% in 2016 to 1.2% and 0.8% in 2017 and 2018, respectively.
In contrast to the increasing trend found in the AMR surveillance, EARS-BE reports a significant decrease in 3GC-R in *E. coli* (from 10.1% in 2014 to 8.4% in 2018) [4].

The national surveillance of bloodstream infections (BSI) shows a statistically significant decrease in the crude resistance proportion of MRSA isolated from hospital-associated BSI between 2013 and 2018 (from 21.0% to 10.5%), but reports in the same time period non-significant increasing trends in 3GC-R (from 14.1% to 15.9%) and carbapenem-R (from 0.3% to 0.6%) *E. coli* and 3GC-R (from 25.9% to 35.3%) and carbapenem-R (from 2.4% to 3.8%) *K. pneumoniae*. The crude resistance proportion of both carbapenem-R *E. coli* and *K. pneumoniae* however decreased between 2017 and 2018: from 1.4% to 0.6% and from 5.7% to 3.8%, respectively [5].

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. Conversely, this could have led to under-reporting of antimicrobial resistance, which is more likely to be first detected by screening samples [6].

In contrast to the previous years, the currrent report presents the results of acute care hospitals also by level of specialty care provided within the hospital. Only in the MRGN surveillance differences were found. Both the median resistance proportion and incidence of meropenem I/R *A. baumannii* and of MDR *P. aeruginosa* and the incidence of 3GC I/R *E. coli* were significantly higher in tertiary hospitals compared to primary and secondary hospitals. In addition, the median resistance proportion of 3GC I/R *E. coli* was significantly higher in tertiary hospitals compared to primary hospitals and the resistance proportion of meropenem I/R *K. pneumoniae* was higher in secondary hospitals in comparison to primary hospitals.

As off the 2018 data collection, extended spectrum beta-lactamase (ESBL) and carbapenemase production (CPE) in *E. coli* and *K. pneumoniae* were no longer included in the MRGN surveillance. In replacement, the national reference centre (NRC) for antibiotic resistant gram-negative bacilli launched over a six month period (May to October 2019) a national active surveillance which is coupled with a European survey on carbapenem- and/or colistin-resistant *Enterobacteriaceae* (EURGen-Net network survey) coordinated by European Centre for Disease Prevention and Control (ECDC). The aims of this surveillance are to determine the epidemiological parameters (proportion and incidence rates), to characterize the distribution of major carbapenem-resistant or carbapenemase-producing (CRE/CPE) *E. coli* and *K. pneumoniae* and/or colistin resistance *E. coli* (ColREC) clones and/or mobile resistance/genetic elements and to identify epidemiological risk factors for infection or colonisation with CRE/CPE and/or ColREC [7-8]. The results of this microbiological surveillance are expected soon and will be included in the next AMR surveillance report.

AMR not only has an impact on public and animal health but it also effects the confidence of citizens in the safety of health care, food (in particular of animal origin) and the environment. To tackle this problem, Belgium is currently finalizing a “One Health” national action plan (NAP) 2020-2024 to fight against AMR. The development

of this plan coordinated by the Federal Public Service Health, Food Chain Safety and Environment in close collaboration with Sciensano, the Federal Agency for Medicines and Health Products (FAGG-AFMPS), the Federal Agency for the Safety of the Food Chain (FAVV-AFSCA) and the National Institute for Health and Disability Insurance (RIZIV-INAMI). Representatives of the Federated Entities, of the Belgian Antibiotic Policy Coordination Commission (BAPCOC) and of the knowledge center on antibiotic use and resistance in animals (AMCRA) were also involved in the elaboration of the plan. A preliminary draft of the NAP was presented in November 2019 during a “Stakeholder dialogue”, in the presence of representatives of professional and scientific organizations working in the field of human, animal and environmental health. Using the outcomes and reflections of this meeting, the NAP was finalized by the end of 2019 and will, in a next step, be presented to the political actors involved for validation and funding [9].

One of the strategic objectives of the NAP concerns infection prevention and control (IPC) and aims to sustain the current national strategy for the control of multidrug resistant organisms, to optimize IPC programs in hospitals and to strengthen IPC measures in primary care, nursing homes and other healthcare facilities. As part of the national strategy, the current national surveillances programs for AMR and healthcare-assocated infections will be revised and adapted to current challenges where needed. The implementation of the NAP and progresses achieved will be evaluated yearly using indicators and will be published in a One Health report [9].

Pending these adaptations, Sciensano is already working on harmonizing the data collection for the national AMR surveillance and EARS-BE. For the AMR surveillance, this will imply abandoning an aggregated data collection and going for the collection of detailed laboratory data at isolate/AST test result 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.

In 2020, a limited number of hospitals will participate in a pilot study and test the harmonized AMR/EARS-BE protocol. By submitting their data, the laboratories will automatically participate to the EARS-BE surveillance. Hospitals are however requested to still submit their aggregated MRSA and MRGN (and VRE) data by completing the 2019 AMR surveillance form. The aggregated AMR data will be used to validate the data collected using the joint AMR/EARS-BE protocol and the subsequent data de-duplication and analysis steps [10].

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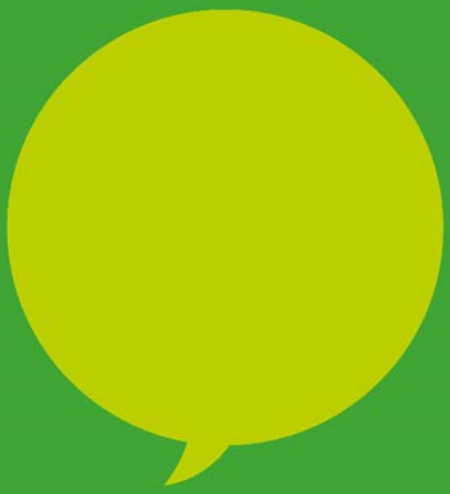

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