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healthy all life long

NSIH

Hotspots of antimicrobial use in human medicine

AMCRA – 19 juni 2019

Boudewijn.Catry@Sciensano.be
Healthcare associated infections & Antimicrobial resistance

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PICTURES = POINT PREVALENCE SURVEYS

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Point Prevalence Survey – Zorginfecties België 2017

Table 2: Crude prevalence of patients with at least one antimicrobial, ECDC point prevalence survey (PPS) 2017, Belgium

ECDC = European Centre for Disease Prevention and Control, CI = confidence interval; N = number of patients with at least one antimicrobial

	Total number of patients	Patients with at least one antimicrobial		
		N	Crude prevalence (%)	95% CI
Total prevalence	11800	3320	28.1	27.3-29.0
Prevalence by hospital type				
Primary	6658	1826	27.4	26.4-28.5
Secondary	2830	793	28.0	26.4-29.7
Tertiary	2312	701	30.3	28.5-32.2
Prevalence by patient specialty				
Medicine	3600	1200	33.3	31.8-34.9
Surgery	2531	916	36.2	34.3-38.1
Intensive care	583	307	52.7	48.6-56.7
Geriatrics	1813	502	27.7	25.6-29.8
Obstetrics/ Maternity	583	73	12.5	9.8-15.2
Healthy neonates	156	3	1.9	0.0-4.1
Neonatology	121	16	13.2	3.1-19.3
Pediatrics	464	153	33.0	28.7-37.3
Psychiatry	823	27	3.3	2.1-4.5
Rehabilitation	903	105	11.6	9.5-13.7
Long-term care	33	8	24.2	9.6-38.9
Mix	28	8	28.6	11.8-45.3
Other	50	2	4.0	0.0-9.4

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(Vandael et al., Sciensano 2018 www.nsih.be)

Outbreak support team MDRO

Table 2: Overview of outbreaks of multidrug resistant organisms (MDRO) where the multidisciplinary outbreak support team (OST) was engaged, Belgium December 2014-2017.

Request made	Region	MDRO	Resistance mechanism (virulence)	Bacterium involved (Genus species or family)
12/18/2014	Flanders	VRE	VanA	*Enterococcus faecium*
1/9/2015	Flanders	CA-MRSA,	(PVL+)	*Staphylococcus aureus*
1/29/2015	Flanders	CPE	VIM	*Enterobacteriaceae*
3/23/2015	Flanders	VRE	VanA	*Enterococcus faecium*
5/21/2015	Flanders	CPE	oxa-48	*Klebsiella pneumoniae*
6/10/2015	Wallonia	CPE	oxa-48	*Klebsiella pneumoniae*
9/24/2015	Brussels	PSAR		*Pseudomonas aeruginosa*
1/18/2016	Flanders	CA-MRSA	(PVL+)	*Staphylococcus aureus*
2/19/2016	Wallonia	CPE	NDM	*Enterobacteriaceae*
2/19/2016	Wallonia	VRE	VanA	*Enterococcus faecium*
4/25/2016	Flanders	CA-MRSA		*Staphylococcus aureus*
5/23/2016	Wallonia	CPE	oxa-48 + NDM	*Klebsiella pneumoniae*
7/5/2016	Wallonia	VRE	VanA	*Enterococcus faecium*
7/1/2016	Flanders	VRE	VanA	*Enterococcus faecium*
12/7/2016	Wallonia	CPE		*Klebsiella pneumonia*
1/18/2017	Flanders	VRE	VanB	*Enterococcus faecium*
1/30/2017	Wallonia	CPE	oxa-48	*Enterobacteriaceae*
3/21/2017	Flanders	CPE		*Enterobacteriaceae*
3/29/2017	Flanders	VRE	VanB	*Enterococcus faecium*
4/21/2017	Wallonia	PSAR		*Pseudomonas aeruginosa*
8/2/2017	Flanders	VRE	VanA	*Enterococcus faecium*
9/1/2017	Flanders	CPE		*Klebsiella oxytoca*

**VRE: Vancomycineresistente Enterococcus; CA-MRSA:* Community Associated Methicilline Resistente *Staphyloccocus aureus; PVL:* Panton-Valentine Leukocidine*; CPE:* Carbapenemase Producer End Enterobacteriaceae; *VIM:* Verona Integron-encoded Beta-Lactamase; oxa-48: Oxacillinase-48; NDM: New Delhi MetalloBetaLactamase; *PSAR: Pseudomonas aeruginosa.*

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77% °Digestive tract

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Catry et al., 2018 dx.doi.org/10.16966/2471-8211.165

Point Prevalence Survey – Belgium 2017
HEALTHCARE ASSOCIATED INFECTIONS – 7.3% of PATIENTS
(Vandael et al., Sciensano 2018 www.nsih.be)

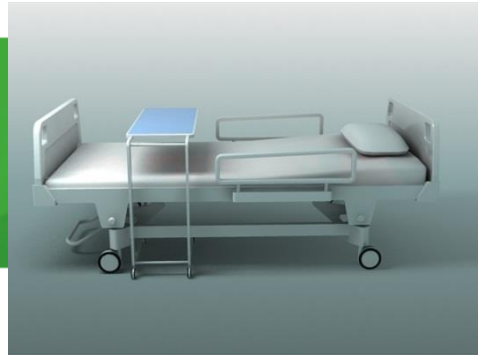
Table 5: Distribution of main groups of healthcare-associated infections (HAI), ECDC point prevalence survey (PPS) 2017, Belgium

ECDC = European Centre for Disease Prevention and Control

Number (%) of infections by main HAI group	Patient Specialty				
	Total	Medicine	Surgery	Intensive care	Geriatrics
Pneumonia	197 (21.6%)	69 (24.6%)	20 (9.1%)	49 (**36.3**%)	43 (**25.9**%)
Other lower respiratory tract infection	45 (4.9%)	10 (3.6%)	2 (0.9%)	14 (10.4%)	10 (6.0%)
Urinary tract infection	194 (21.3%)	57 (20.3%)	39 (17.8%)	12 (8.9%)	54 (**32.5**%)
Surgical site infection	154 (16.9%)	16 (5.7%)	95 (**43.4%**)	15 (11.1%)	5 (3.0%)
Bloodstream infection	105 (11.5%)	40 (14.2%)	21 (9.6%)	24 (17.8%)	15 (0.9%)
Gastro-intestinal infection	87 (9.6%)	32 (11.4%)	15 (6.9%)	9 (6.7%)	22 (13.3%)
Systemic infection	40 (4.4%)	20 (7.1%)	6 (2.7%)	5 (3.7%)	5 (3.0%)
Skin and soft tissue infection	35 (3.8%)	14 (5.0%)	8 (3.7%)	1 (0.7%)	7 (4.2%)
Eye, ear, nose or mouth infection	19 (2.1%)	10 (3.6%)	1 (0.5%)	0	3 (1.8%)
Catheter-related infection	14 (1.5%)	7 (2.5%)	3 (1.4%)	2 (1.5%)	2 (1.2%)
Cardiovascular infection	9 (1.0%)	3 (1.1%)	2 (0.9%)	3 (2.2%)	0
Bone and joint infection	6 (0.7%)	2 (0.7%)	3 (1.4%)	0	0
Central nervous system infection	4 (0.4%)	0	3 (1.4%)	1 (0.7%)	0
Reproductive tract infection	2 (0.2%)	1 (0.4%)	1 (0.5%)	0	0
Specific neonatal cases	0	0	0	0	0
Total	911	281 (30.8%)	219 (24.0%)	135 (14.8%)	166 (18.2%)

HAI = Healthcare associated infection = nosocomial(e) = zorggeassocieerde = zorggerelateerde = zorginfectie ~ ziekenhuisverworven = associeés aux soins = liées aux soins ~ acquis à l'hopitals

Conclusion on 'PPS Pictures'



- HAI prevalence (%) in Belgium
  - Hospitals: 7.3 (28.1% AB use)
  - LTCFs: 3.5 (5.4% AB use)

- Estimated number of patients per year with an HAI in Belgium
  - Hospital: 111 276
  - LTCFs: 170 090

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ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Latour K, 2018

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FILMS = CONTINUOUS SURVEILLANCES

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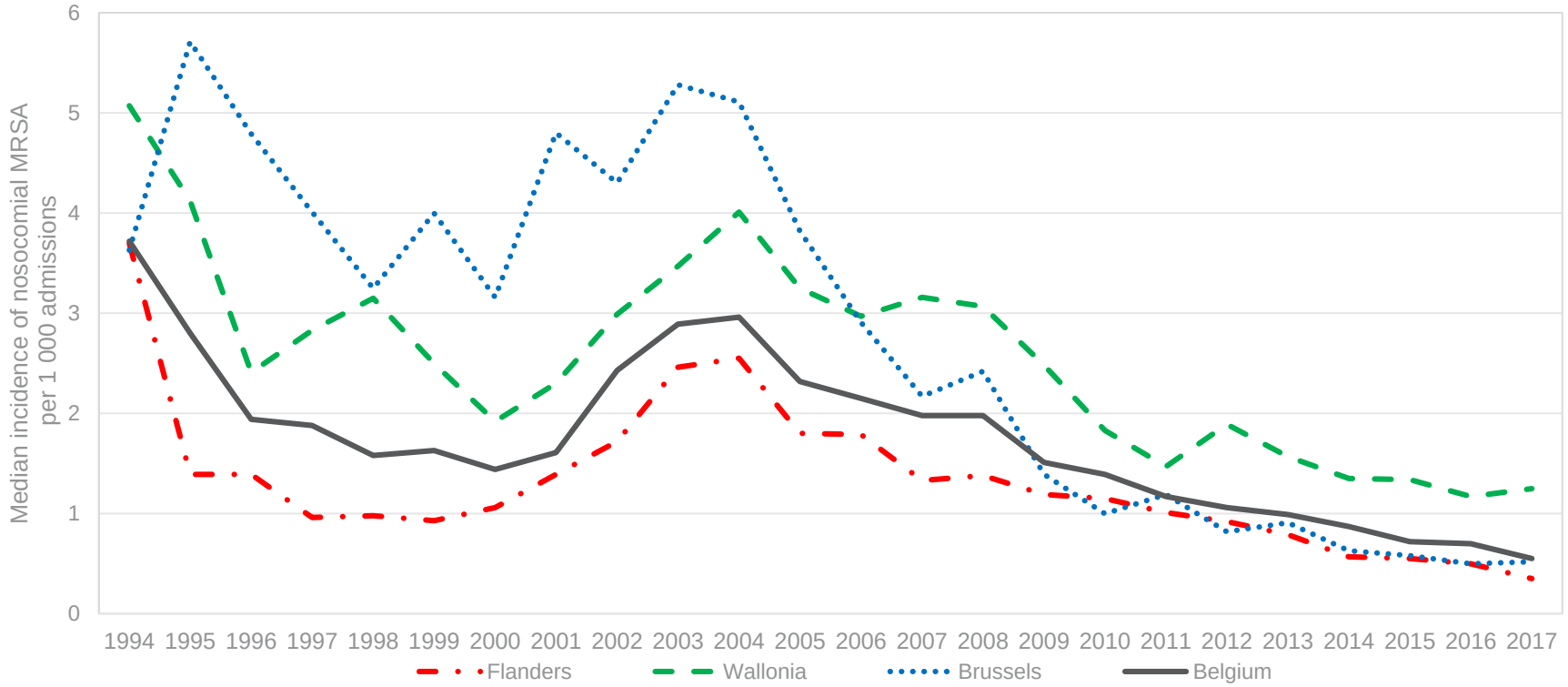
Nosocomial MRSA – methicillin resistant *Staphylococcus aureus*



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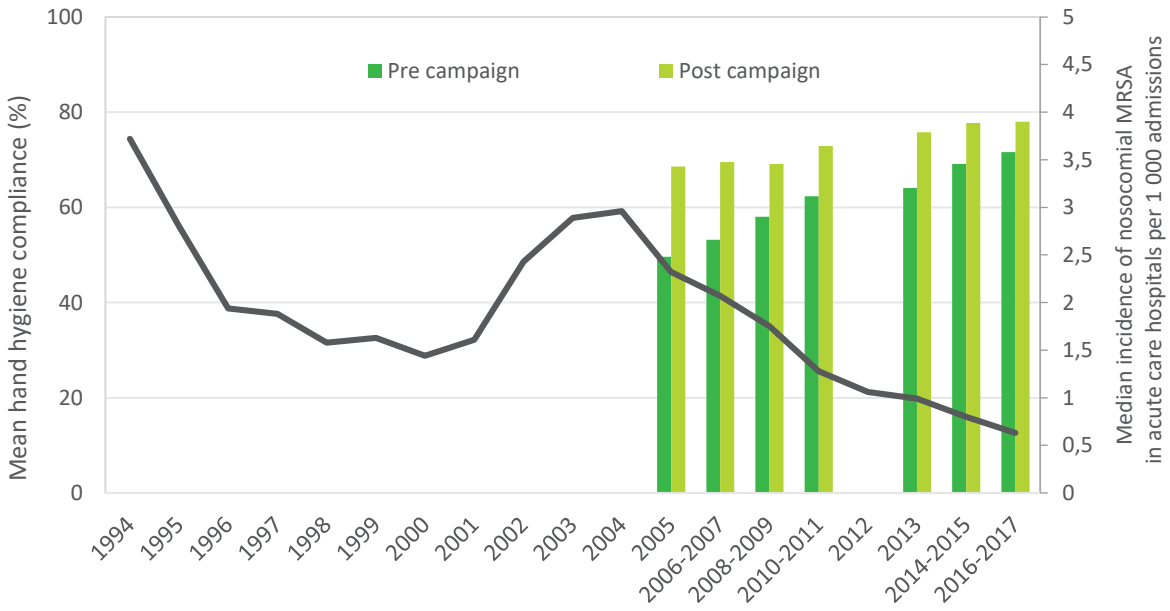
Hand hygiene campaigns – 8th ongoing



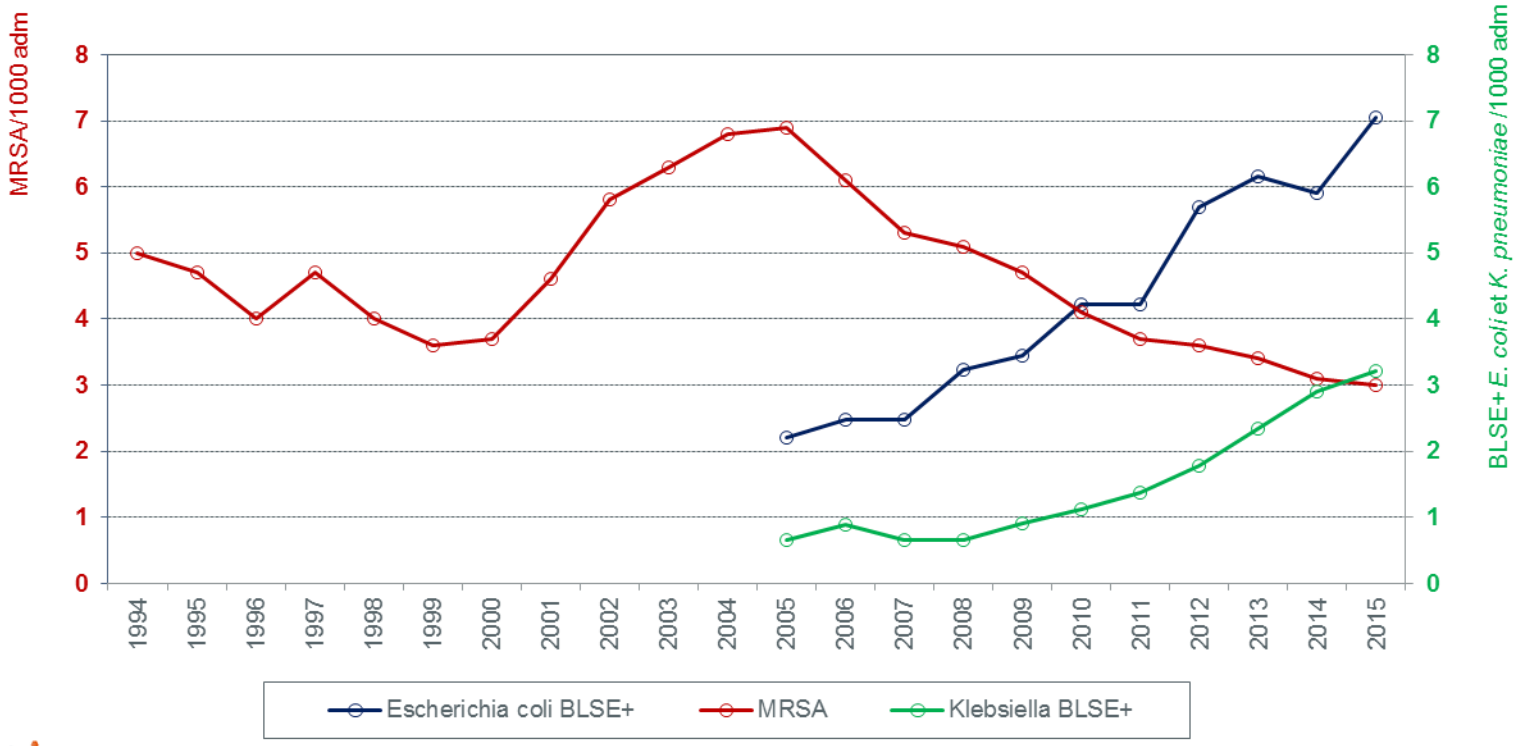
Latour & De Pauw, 2019

MULTIDRUG RESISTANT ORGANISMS

	Microorganism	Resistance
MRSA	*Staphylococcus aureus*	Met(h)icillin
ESBL+	Enterobacteriaceae *(E.coli / Klebsiella / …)*	3de generation cephalosporins
CPE	Enterobacteriaceae	Carbapenems
VRE	*Enterococcus faecalis/faecium*	Vancomycin
MDR	*Pseudomonas/Acinetobacter*	Intrinsic + different classes
CDIF	*Clostridium difficile*	Intrinsic (Anaërobic)
Many other…	*e.g. Candida auris*	Intrinsic antibacterial, multi antifungal resistance

MRSA & ESBL in Belgian hospitals

MRSA and ESBL-positive *E. coli* & *K. pneumoniae* from clinical samples in Belgian acute care hospitals (/1000 admissions)
1994 - 2015



Source: National surveillance, B. Jans

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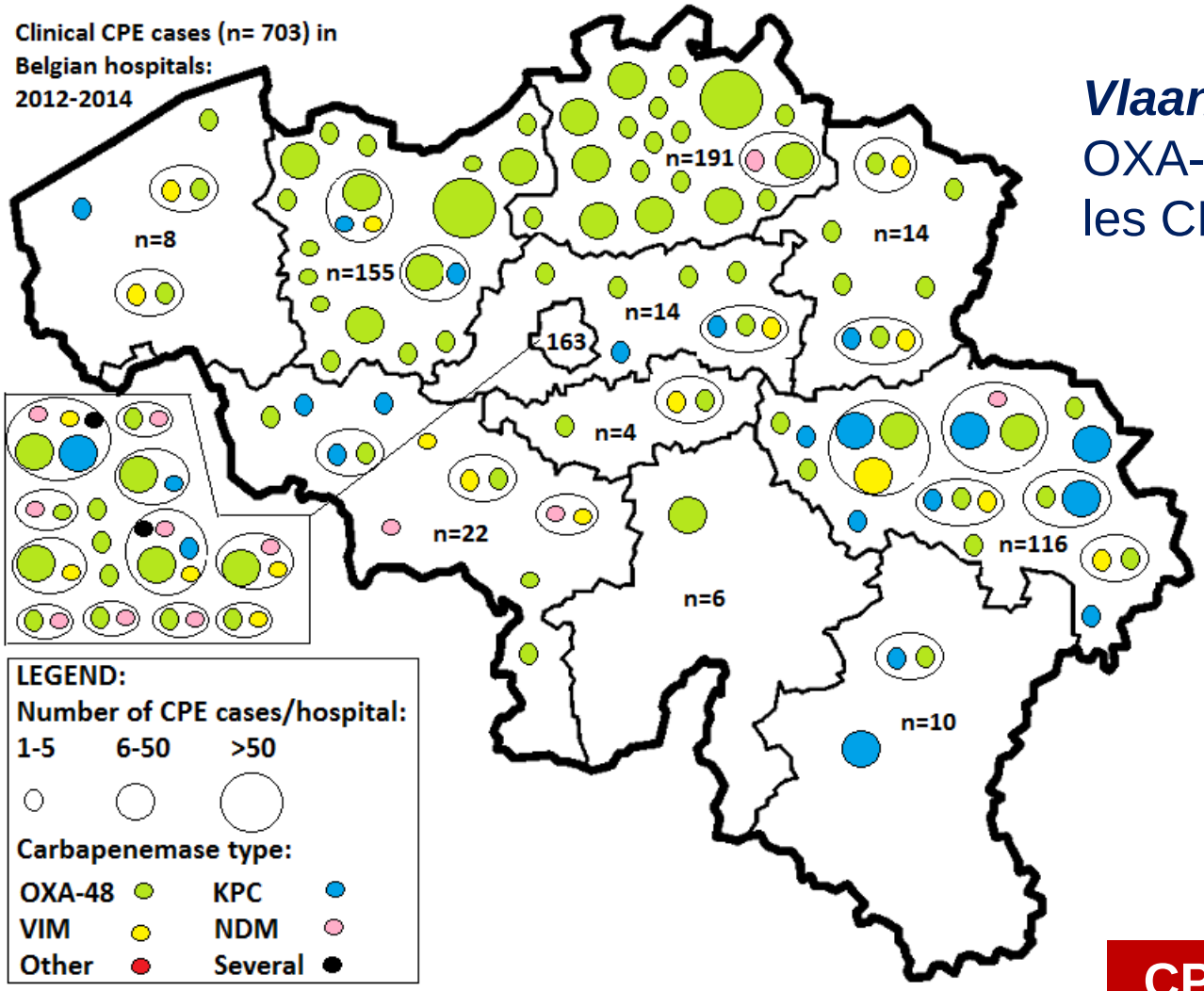
Entérobactéries productrices de carbapénémases (CPE) à partir de prélèvements cliniques: par type de carbapénémase et par province:

2012 - 2014



Vlaanderen:

OXA-48 = 95% de tous les CPE

Bruxelles:

OXA-48: 64%
KPC: 18%
NDM: 10%
VIM: 6%

Wallonie:

KPC = 49%
OXA-48= 39%

CPE en MRS (2015): 1 seul porteur (OXA-48)

CHU UCL NAMUR

Remark: For confidentiality reasons, the locations of the bullets repr
individual hospitals do not correspond to the real location of the hosp
province.

E. coli – nosocomial - acute care hospitals

Figure 10. **Extended spectrum beta-lactamase producing (ESBL+) *Escherichia coli* (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, 2005-2017**

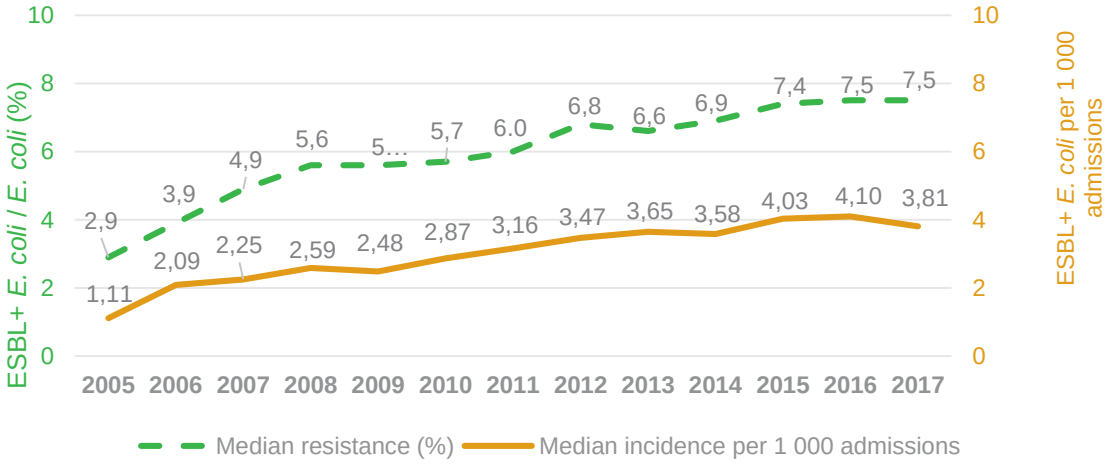
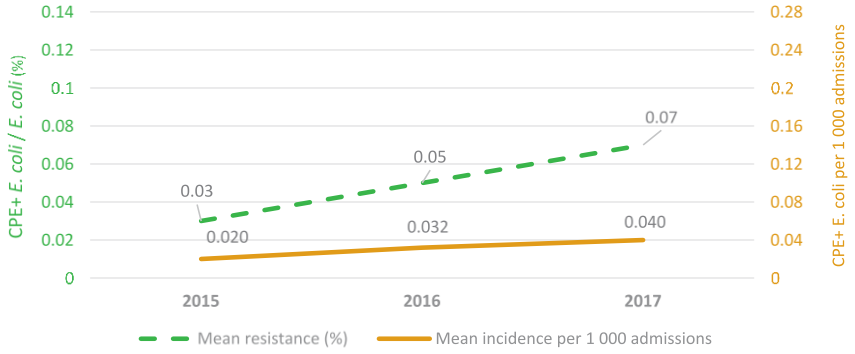


Figure 12. **Carbapenemase producing (CPE+) *Escherichia coli* (clinical samples only): mean resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2015-2017**



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Latour K, in press

K. pneumonia – nosocomial - acute care hospitals

Figure 14. **Extended spectrum beta-lactamase producing (ESBL+) *Klebsiella pneumoniae* (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, 2005-2017**

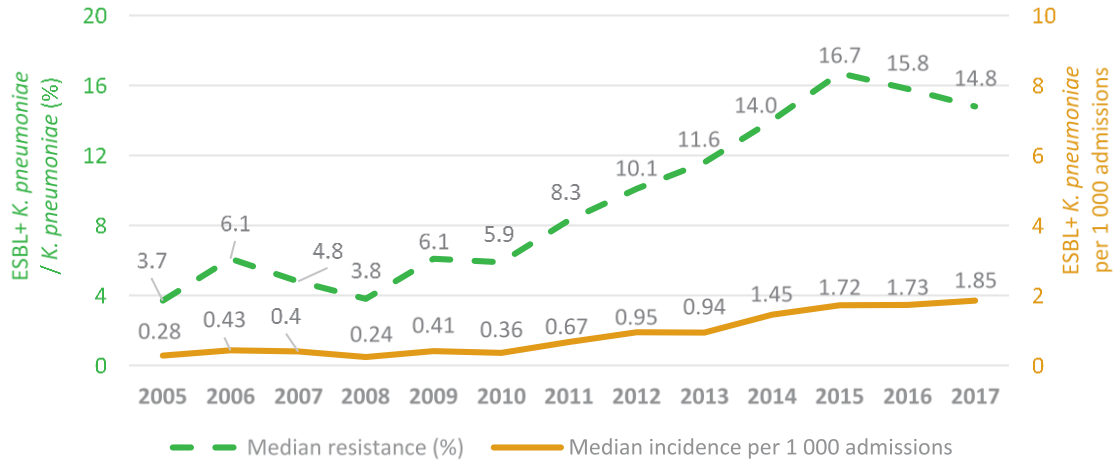
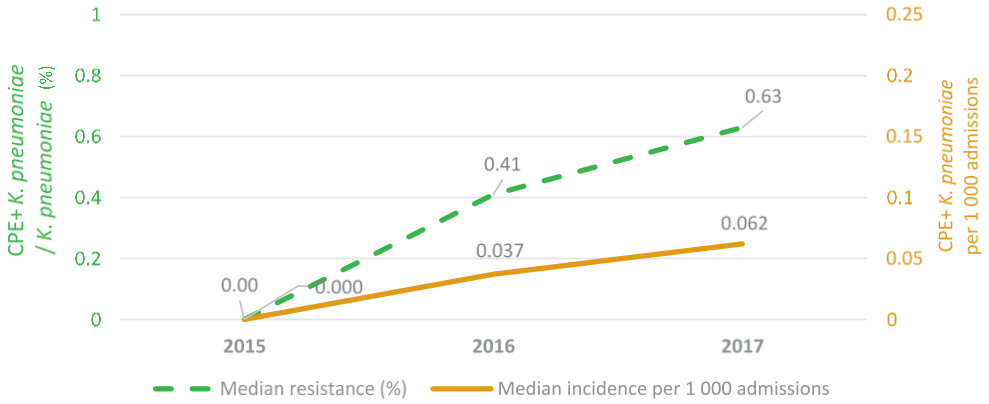


Figure 16. **Carbapenemase producing (CPE+) *Klebsiella pneumoniae* (clinical samples only): median resistance proportion and incidence in a cohort of acute care hospitals with at least 3 years of participation in the surveillance, 2015-2017**



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Latour K, in press

Blood stream infections

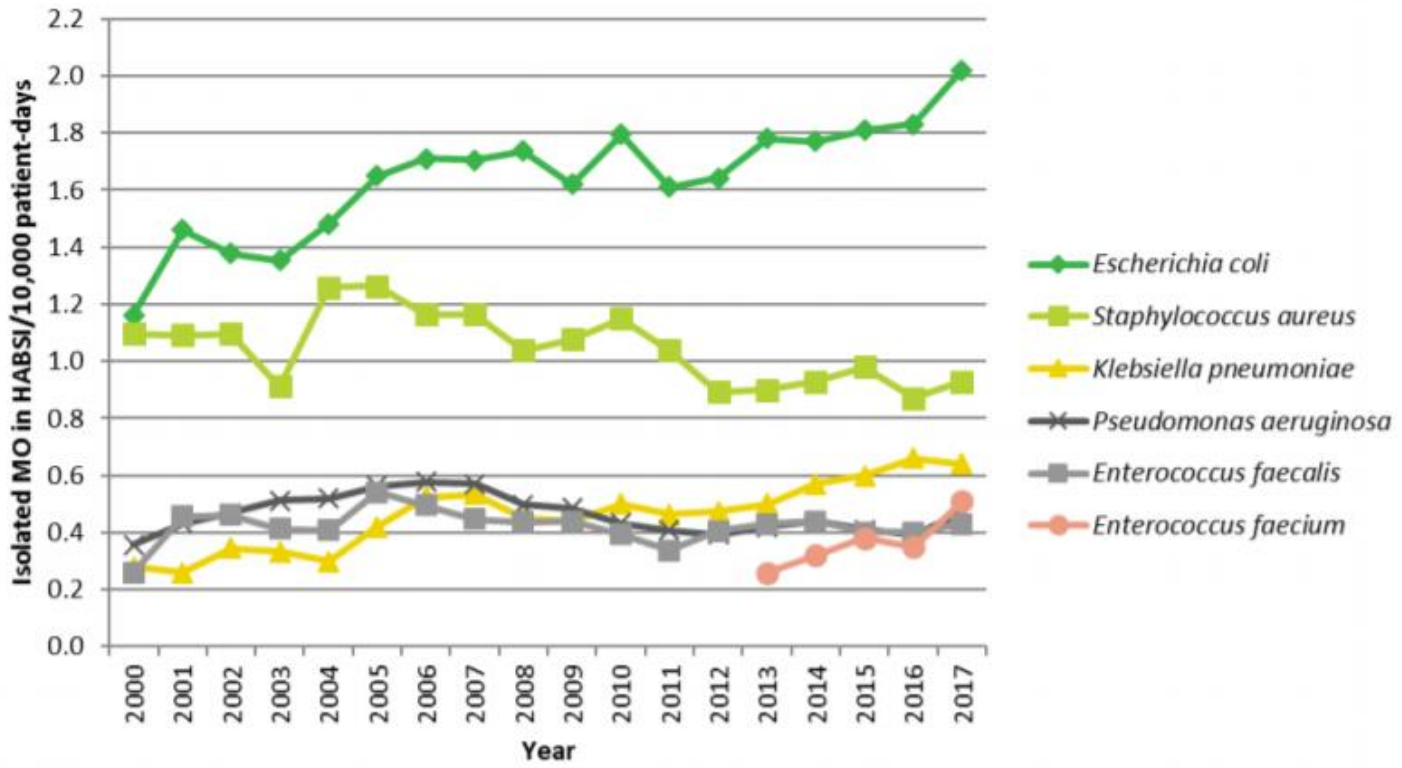

Figure 2: Hospital-associated bloodstream infections mean incidence per microorganism, Belgium 2000-2017 (HABSI, hospital-associated bloodstream infections; MO, microorganism)

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Duysburgh E, 2012

Preliminary EARS-net results 2018 – partially (!) results

Figure ESC.3.1 *Escherichia coli*, Antimicrobial resistance within BLOOD/CSF and URINE isolates, EARS-BE 2018 criteria, BE, 2018

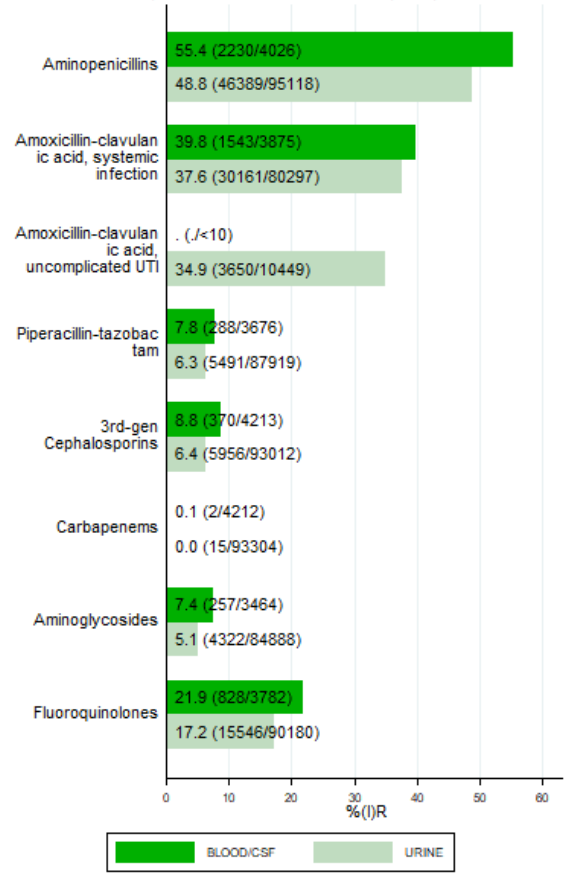
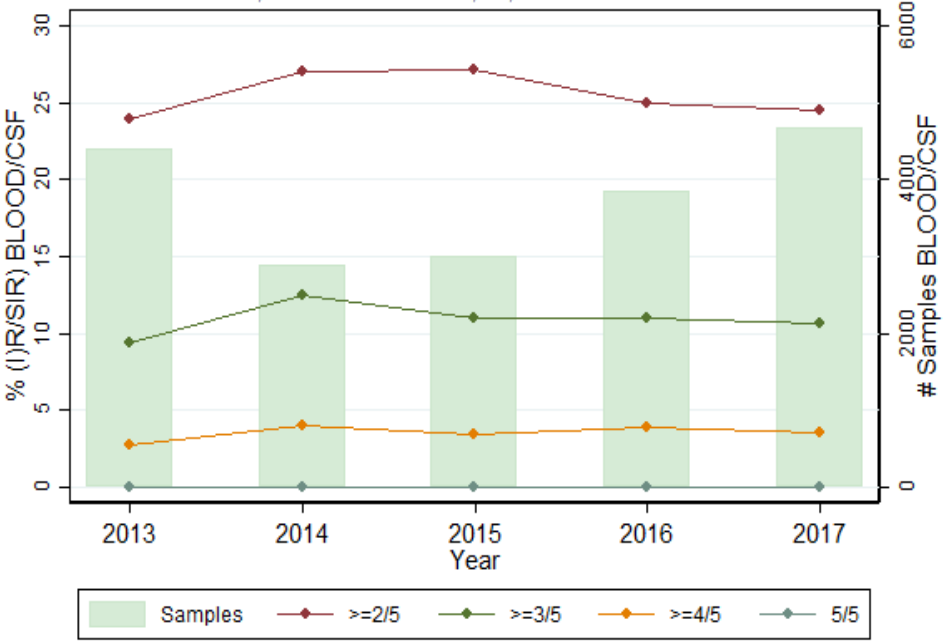


Figure ESC.1.1 *Escherichia coli*, Evolution of combined antimicrobial resistance (Aminopenicillins, 3rd-gen Cephalosporins, Carbapenems, Aminoglycosides, Fluoroquinolones) within BLOOD/CSF isolates, EARS-BE 2017 criteria, BE, 2013-2017



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Catteau L & Mertens K, 2018 & personal communication

Preliminary EARS-net results 2018 – partially (!) results

Figure KLE.3.1 *Klebsiella pneumoniae*, Antimicrobial resistance within BLOOD/CSF and URINE isolates, EARS-BE 2018 criteria, BE, 2018

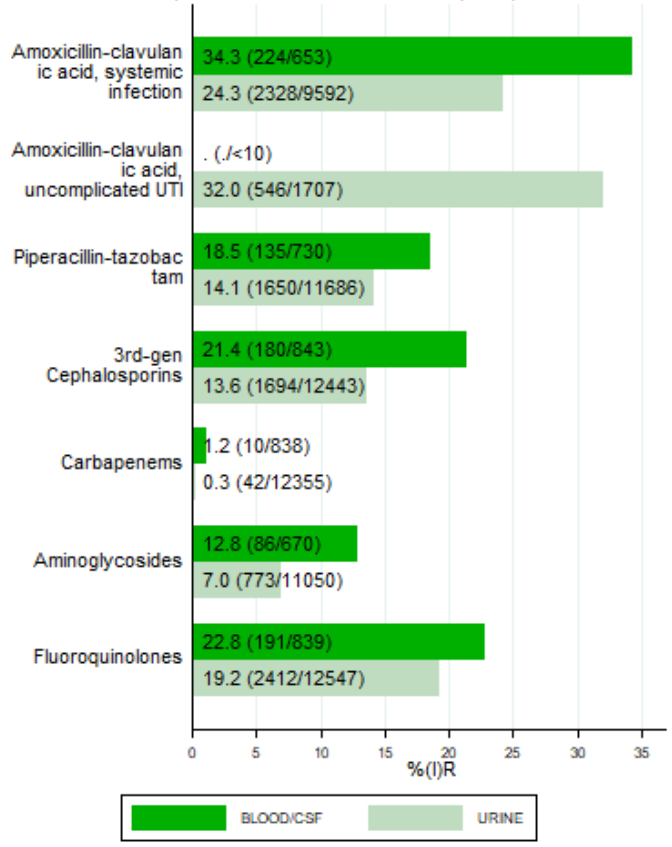
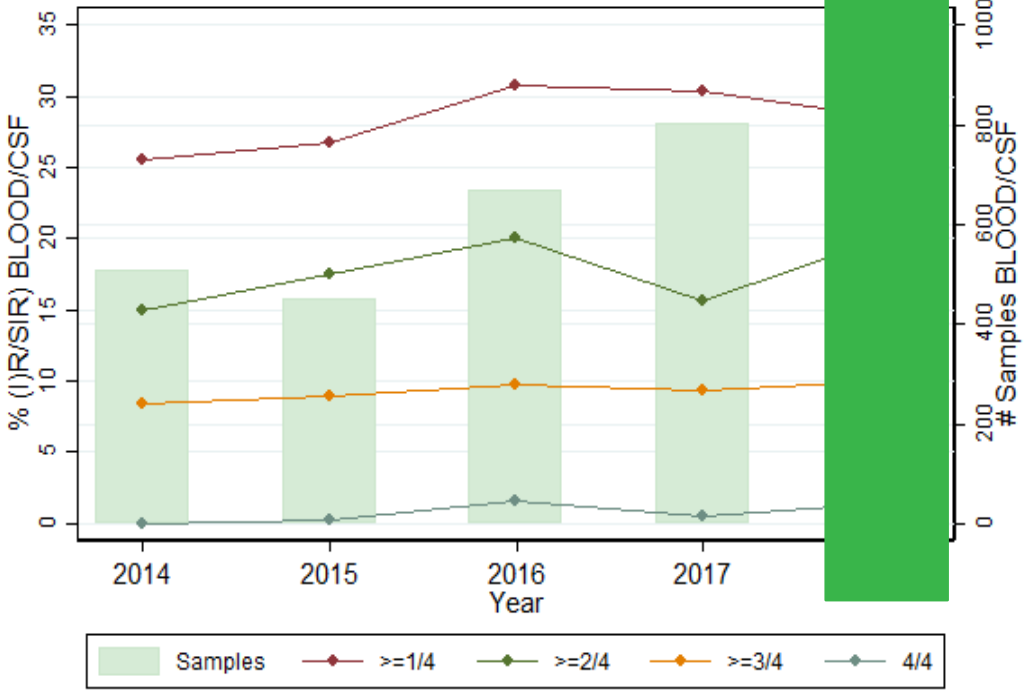
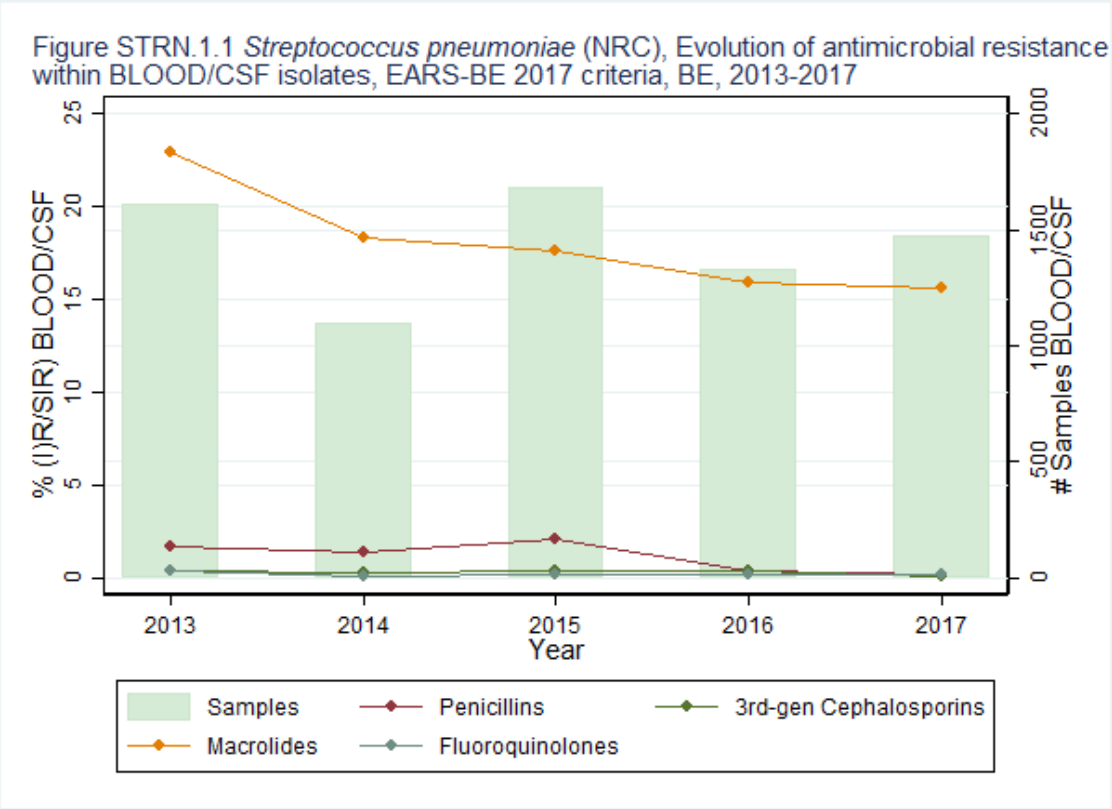


Figure KLE.1.1 *Klebsiella pneumoniae*, Evolution of combined antimicrobial resista (3rd-gen Cephalosporins, Carbapenems, Aminoglycosides, Fluoroquinolones) wit CSF isolates, EARS-BE 2018 criteria, BE, 2014-2018



Catteau L & Mertens K, personal communication

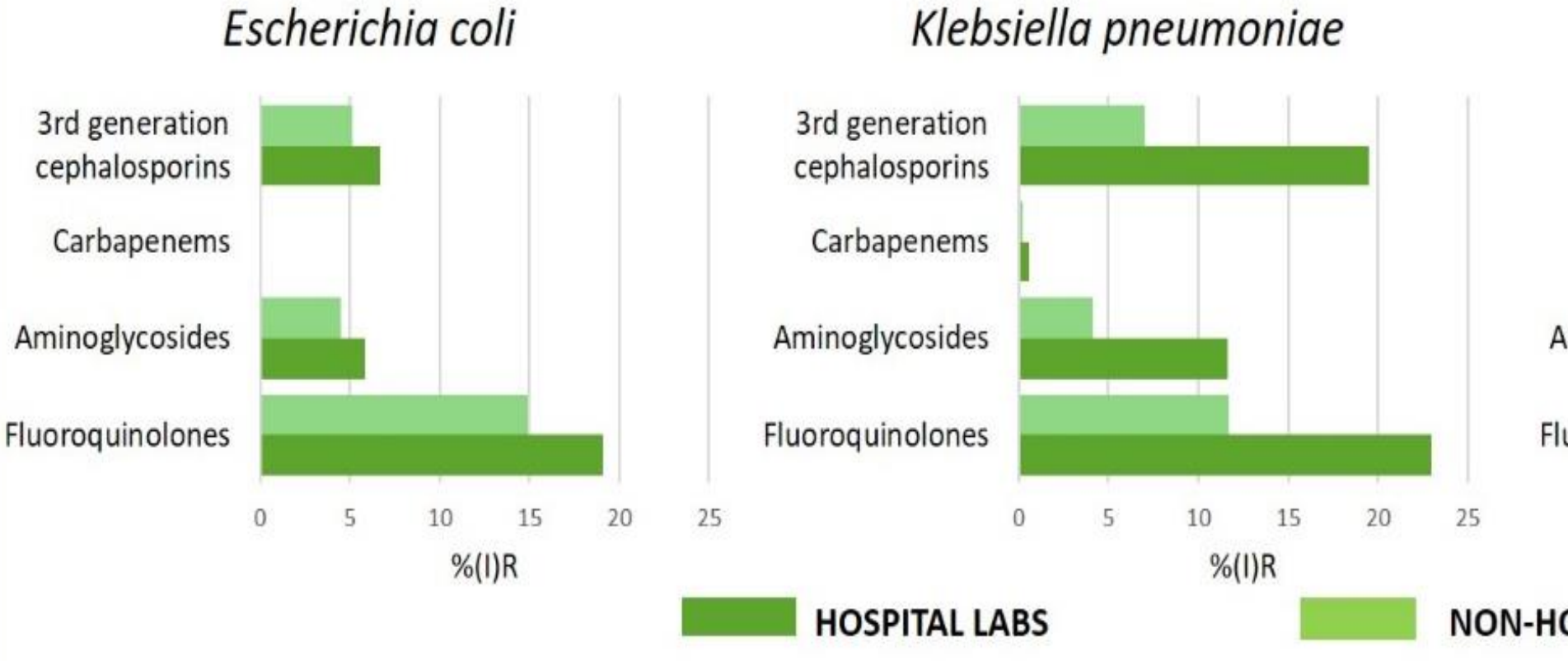
Ears-net 2017 - Community acquired



Mertens K, 2018

Sample type versus patient type

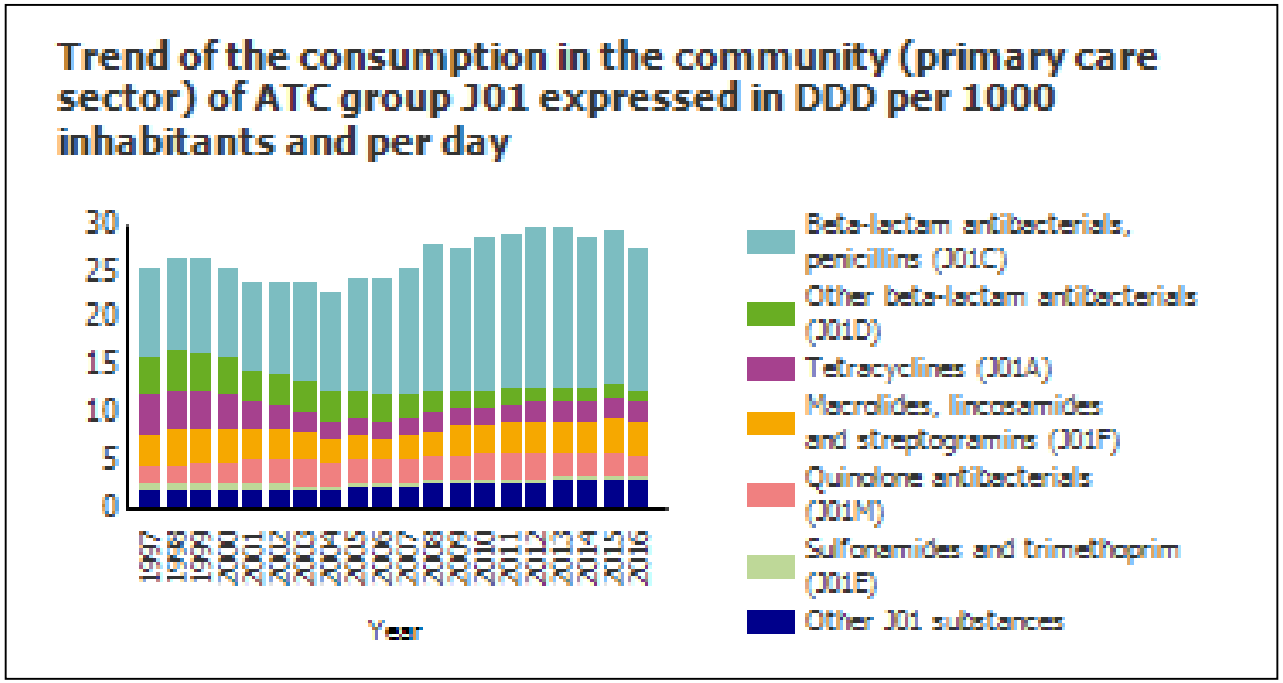
Figure 1B. *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* isolates in Belgian hospital and non hospital labs (EARS-BE 2017 criteria)



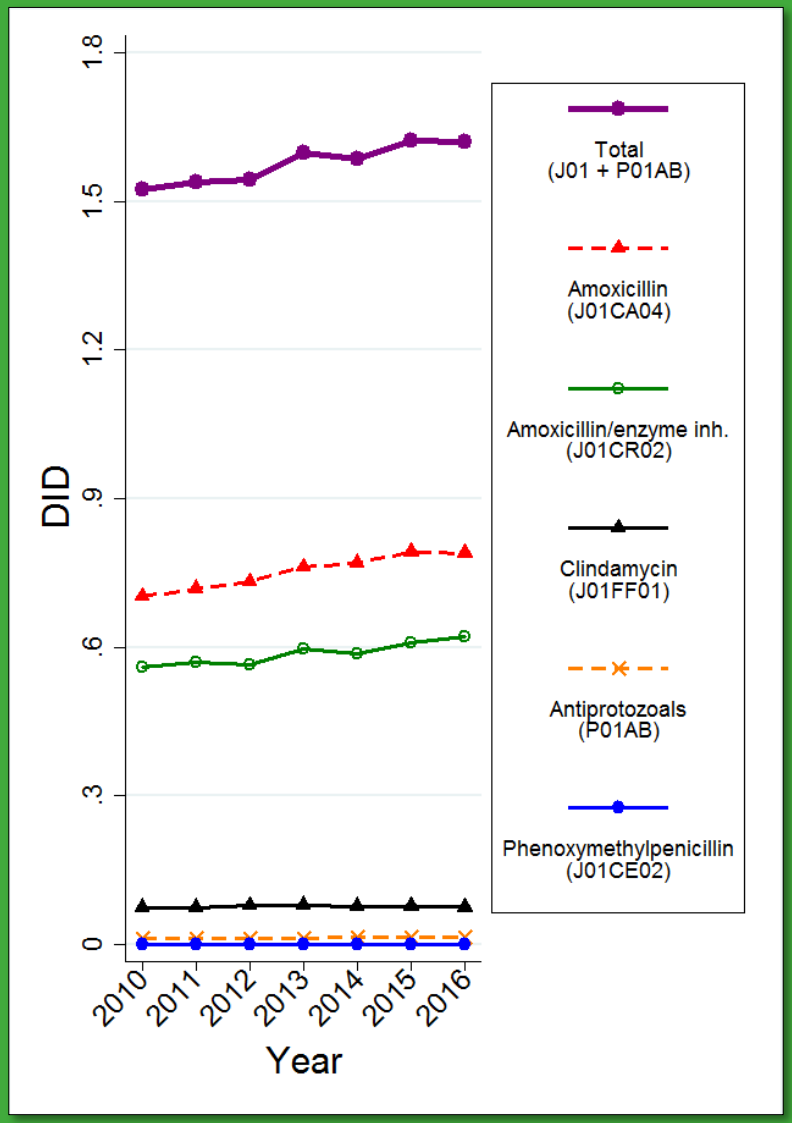
Catteau L & Mertens K, 2019 AAC

ESAC-Net: ambulant care 2016

ATC	DID in 2015	DID 2016
J01	29.30	27.51
J02+D01BA	3.14	3.11



Vandael E. et al., 2018



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DENTISTS

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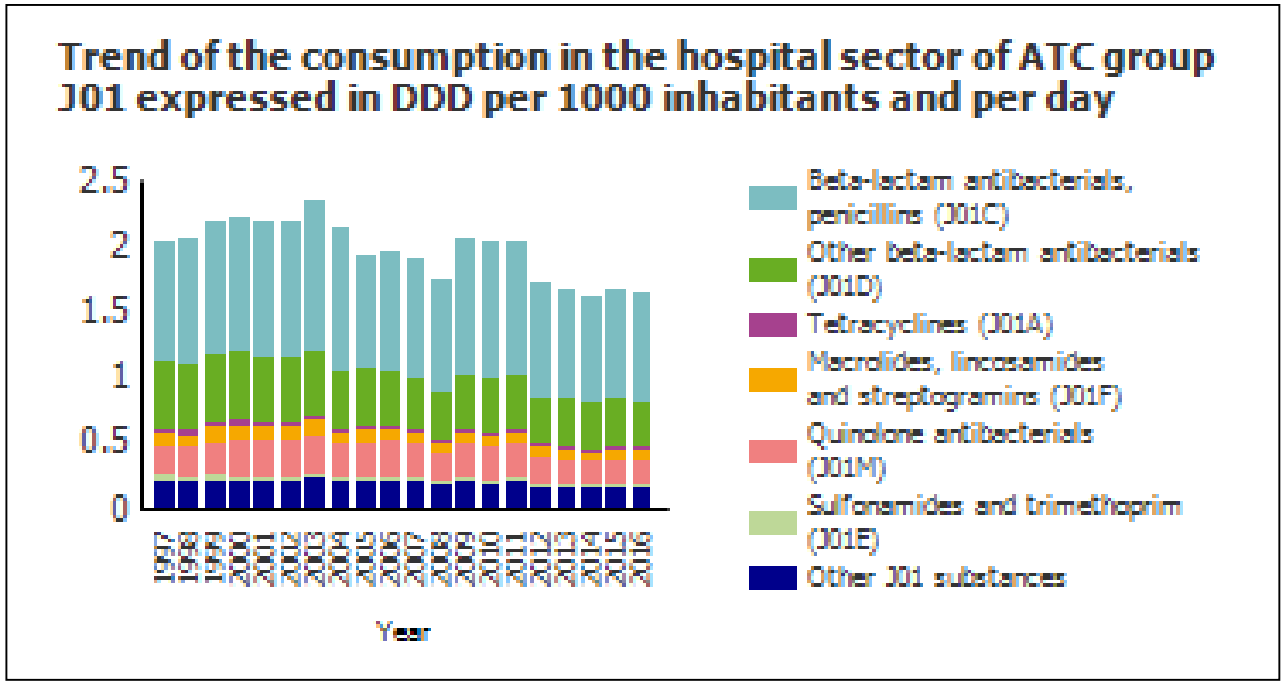
Struyf Thomas et al., in press.

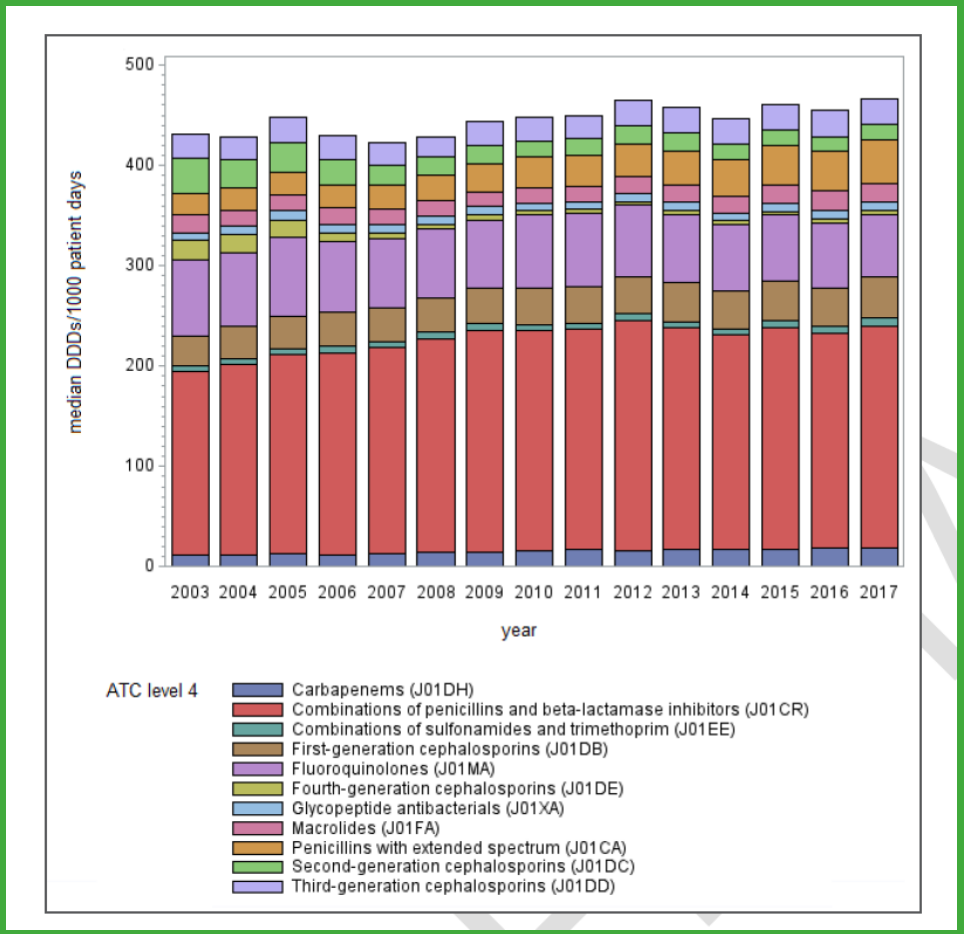
ESAC-Net: hospitals 2016

ATC	DID in 2015	DID 2016
J01	1.67	1.63
J02+D01BA	0.09	0.08



Vandael E. et al., 2018

HOSPITALS 2003-2017



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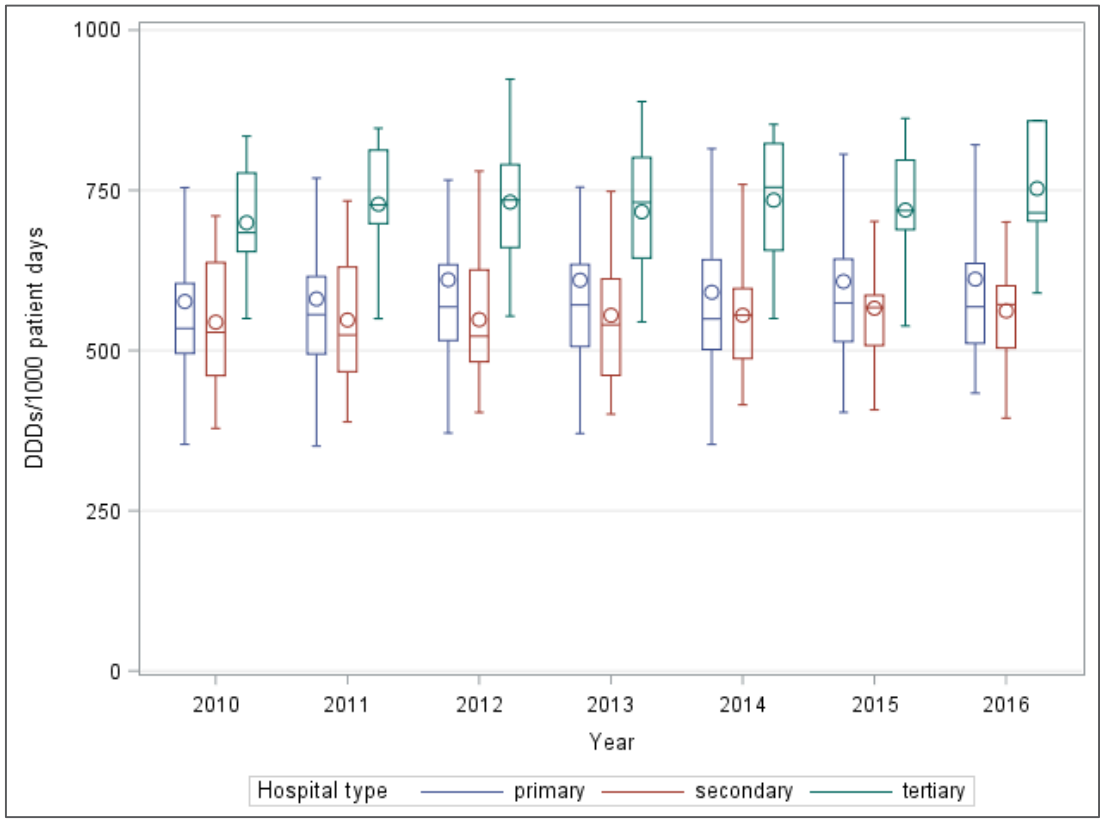
Vandael E. et al., 2018

TYPE OF HOSPITALS



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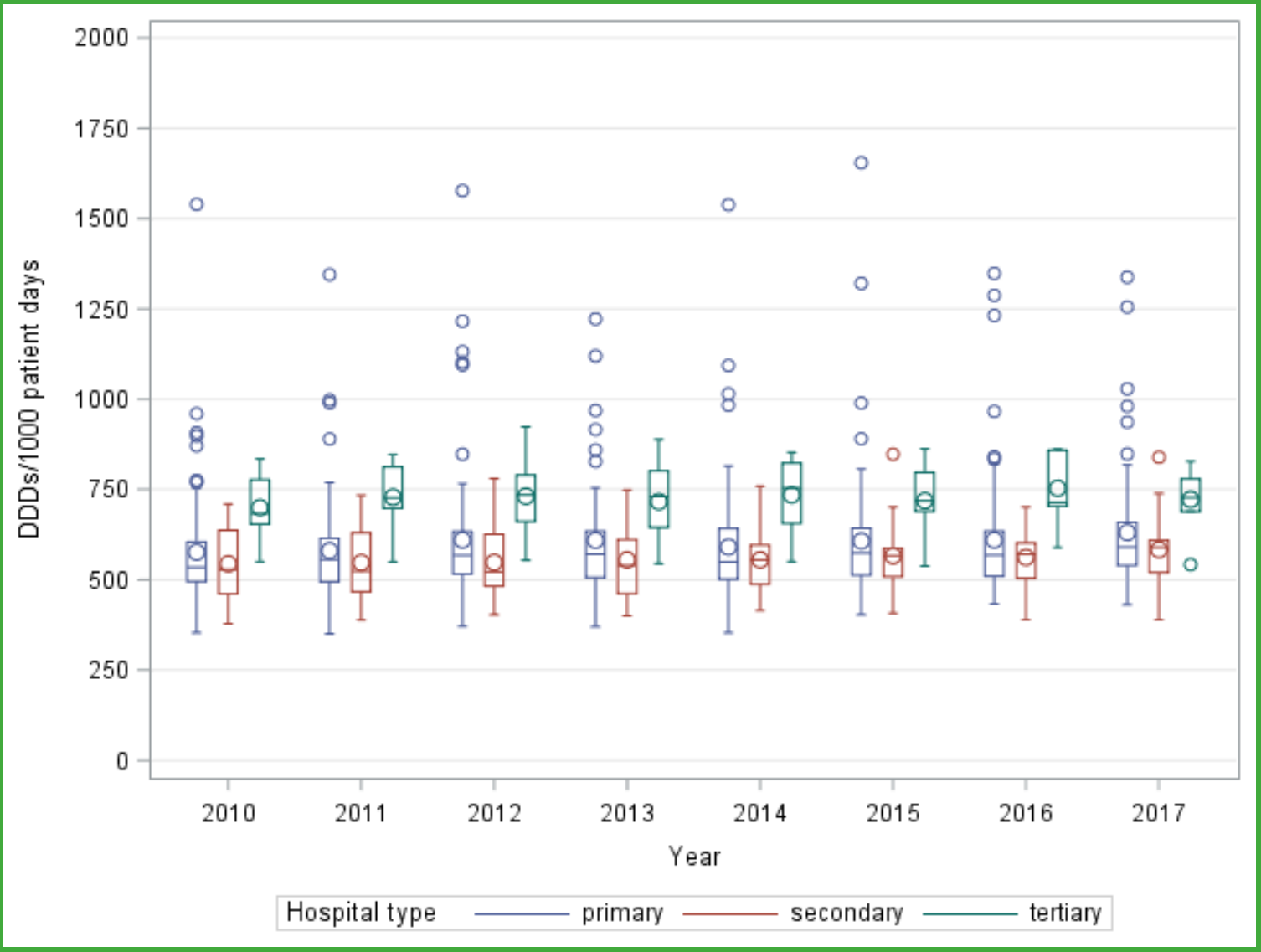
HOSPITALS + OUTLIERS

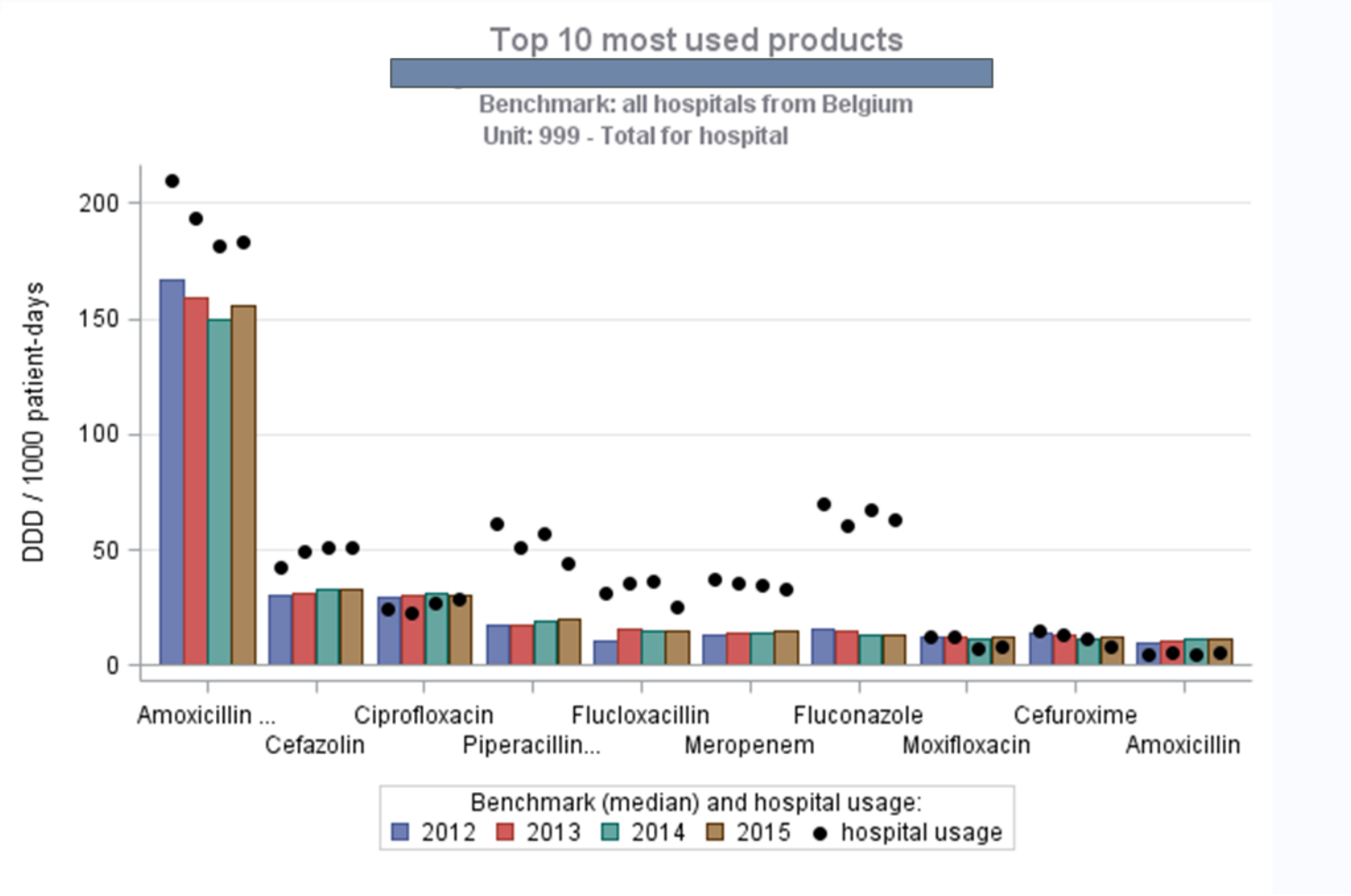


Vandael E. et al., 2018

ATC-code (level 4)	Name	Number of hospitals	DDDs/1000 patient days			
			Median in 2016 over all hospitals	% of the median J01 consumption in 2016	% change 2003-2016	% change 2015-2016
J01AA	Tetracyclines	102	2.44	0.42	-11.98	-1.98
J01BA	Amphenicols	90	2.18	0.38	-42.23	-8.93
J01CA	Penicillins with extended spectrum	102	40.07	6.94	86.44	4.07
J01CE	Beta-lactamase sensitive penicillins	99	5.89	1.02	30.43	8.88
J01CF	Beta-lactamase resistant penicillins	102	24.21	4.20	47.04	5.68
J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	102	213.77	37.04	16.91	-2.91
J01DB	First-generation cephalosporins	102	38.84	6.73	30.96	-0.55
J01DC	Second-generation cephalosporins	102	15.06	2.61	-56.32	-4.34
J01DD	Third-generation cephalosporins	102	26.01	4.51	6.74	0.46
J01DE	Fourth-generation cephalosporins	80	3.13	0.54	-83.83	0.57
J01DF	Monobactams	73	0.40	0.07	-76.74	-24.53
J01DH	Carbapenems	102	19.16	3.32	60.09	5.88
J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	102	6.73	1.17	17.09	1.64
J01FA	Macrolides	102	18.85	3.27	6.30	2.91
J01FF	Lincosamides	102	10.63	1.84	69.65	5.04
J01GB	Aminoglycosides	102	6.74	1.17	-64.12	-6.65
J01MA	Fluoroquinolones	102	64.22	11.13	-15.66	-3.82
J01XA	Glycopeptide antibacterials	102	9.25	1.60	24.43	10.97
J01XB	Polymyxins	78	1.19	0.21	340.74	40.00
J01XD	Imidazole derivatives	98	7.26	1.26	-9.34	-7.70
J01XE	Nitrofuran derivatives	102	9.85	1.71	11.66	-2.48
J01XX	Other antibacterials	102	3.08	0.53	107.88	-0.35

ATC = Anatomical Therapeutic Chemical classification; DDD = Defined Daily Dose

https://www.healthstat.be



Courtesy Vandael E.

The FDA's Antimicrobial Drugs Advisory Committee (ADMAC) and the Drug Safety and Risk Management Advisory Committee met jointly to discuss the use of fluoroquinolone antibacterial drugs for treatment of acute bacterial sinusitis (ABS), acute bacterial exacerbation of chronic bronchitis in those with chronic obstructive pulmonary disease (ABECB-COPD), and uncomplicated urinary tract infection.

Fluoroquinolone labeling currently has warnings about the risks for ***tendonitis, tendon rupture, central nervous system effects, peripheral neuropathy, myasthenia gravis exacerbation, QT prolongation and Torsades de Pointes, phototoxicity, and hypersensitivity.*** *But panel members called for stronger wording, with some suggesting the risks be called out with a black box warning.*

The panel also voted overwhelmingly that the benefits and risks for the systemic fluoroquinolone antibacterial drugs ***do not support the current labeled indications for the treatment of ABS*** *(unanimous),* ***ABECB-COPD*** *(2 yes, 18 no, 1 abstention), or* ***uncomplicated urinary tract infection*** *(1 yes, 20 no).*

Fluoroquinolones currently approved for one or more of these illnesses are ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin, and gemifloxacin.

http://www.medscape.com/viewarticle/854067 - Nov 6 2015

Table 8: Median consumption of antibacterials for systemic use (J01) in 2016 per hospital unit (acute care Belgian hospitals), expressed in defined daily doses (DDDs)/1000 patient days

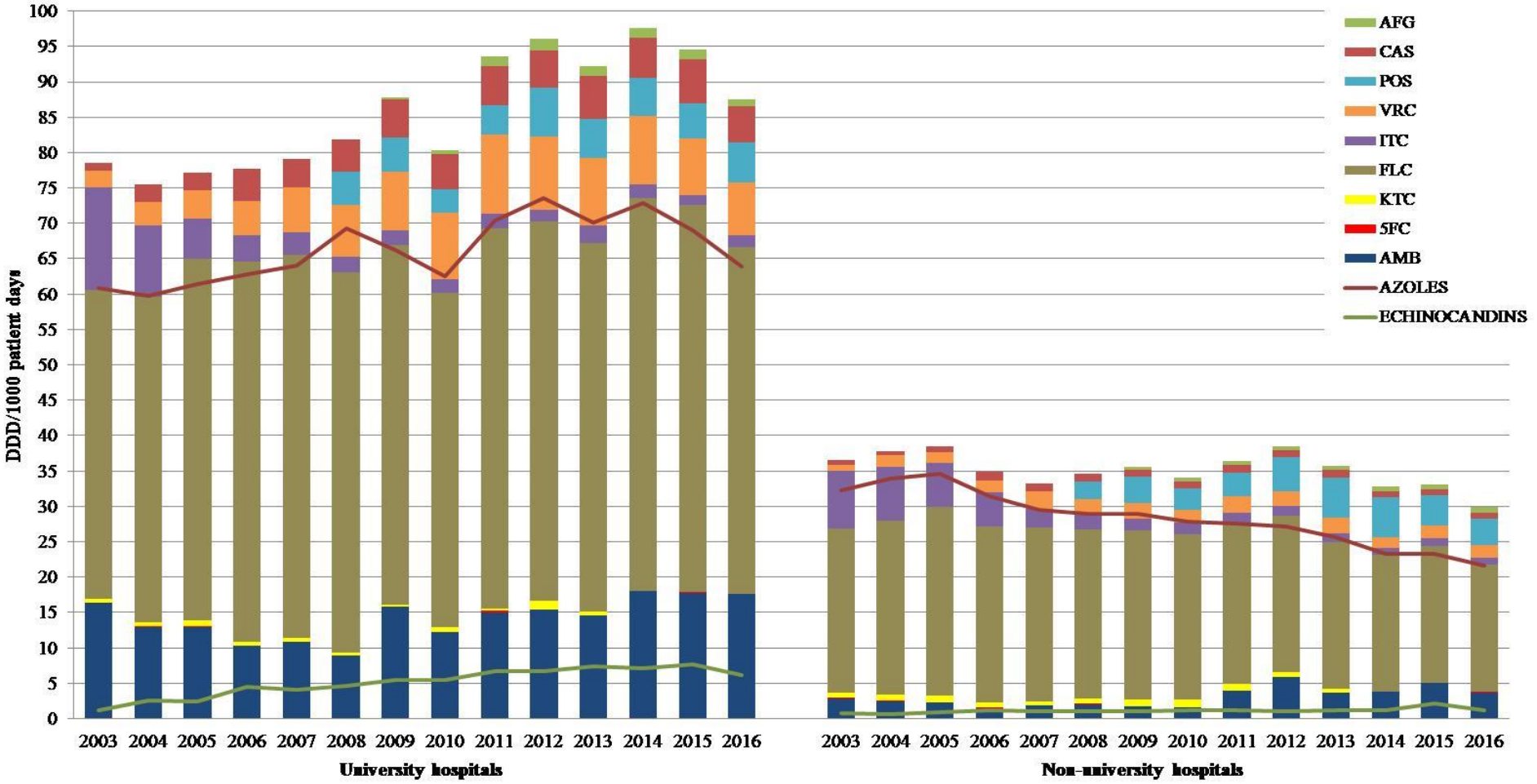
	Median consumption in DDDs/1000 patient days in 2016	Number of hospitals included
Intensive care	1261.0	101
Burn unit	740.4	5
Pediatrics	682.2	94
Internal medicine (including infectious diseases)	658.0	102
Surgery	646.2	102
Geriatrics	510.0	98
Specialized care: cardio-pulmonary	277.7	16
Maternity	242.7	96
Specialized care: chronic - polypathology	206.0	19
Specialized care: locomotive	177.1	65
Specialized care: neurological	154.0	24
Specialized care: chronic - palliative care	125.7	45
Neonatology, intensive care	117.5	19
Specialized care: psycho-geriatrics	104.4	15
Neonatology, non-intensive	50.3	80
Overall consumption in the hospital	577.1	102

The antibiotic consumption was substantially higher in tertiary hospitals (N=7, median: 715.0 DDDs/1000 patient days) than in other hospitals. In Table 9, the median antibiotic consumption in 2016 is displayed per type, per size and per region of Belgian acute care hospitals.

Table 9: Median consumption of antibacterials for systemic use (J01) in 2016 per type, size and region (acute care Belgian hospitals), expressed in defined daily doses (DDDs)/1000 patient days

	Median consumption in DDDs/1000 patient days in 2016	Number of hospitals included
Per type		
Primary	568.1	77
Secondary	571.8	17
Tertiary	715.0	7
Per size		
Large (>600 beds)	578.7	27
Medium (400-600 beds)	554.8	26
Small (<400 beds)	598.8	49
Per region		
Brussels	584.1	12
Flanders	560.2	54
Wallonia	589.2	36

ANTIMYCOTICS



Goemaere B. et al., 2019

Newsflash – 2019 Sciensano

Assessment of the burden of antimicrobial resistance in Europe & Belgium

Catry B., Vandael E., Latour K., Mertens K, Devleesschauwer B.

A recent international study estimated the burden of disease of antimicrobial resistance, for the first time at EU/EEA level and applying the Disability adjusted life years (DALY) methodology. Data from both the European Centre for Disease Prevention and Control point prevalence survey of health-care-associated infections and antimicrobial use (ECDC PPS, 2011-2012) and data from the eight bacterial species frequently isolated from blood or cerebrospinal fluid (invasive isolates) reported to the European antimicrobial resistance surveillance network (EARS-Net 2015) were combined. Remind that this approach is an underestimation of the total burden for the community at large, since for this analysis only the predominant types of healthcare associated infections (ca 88%) and only acute care hospitals were included. Throughout Europe, this study concluded that an estimated number of 33 000 casualties are annually attributed to antimicrobial resistance. For Belgium, this number has been estimated at 530 deaths annually. Among these, 240 and 70 could be attributed to third-generation cephalosporin resistant *Escherichia coli* and *Klebsiella pneumoniae* (excluding those resistant to colistin and/or carbapenem), respectively, and 133 to MRSA (methicillin resistant *Staphylococcus aureus*). Further actions should focus on a reduction of inappropriate antimicrobial consumption and adequate preventive measures including hand hygiene and other infection control policies.

Further reading: https://ecdc.europa.eu/en/news-events/33000-people-die-every-year-due-infections-antibiotic-resistant-bacteria

The article is available here: www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30605-4/fulltext

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BAPCOC
Belgian Antibiotic Policy Coordination Committee

PROTOCOL:

AntiMicrobial consumption data of Belgian hospitals linked with DIAgnoses (AM-DIA project)

Vandael E. et al., 2019

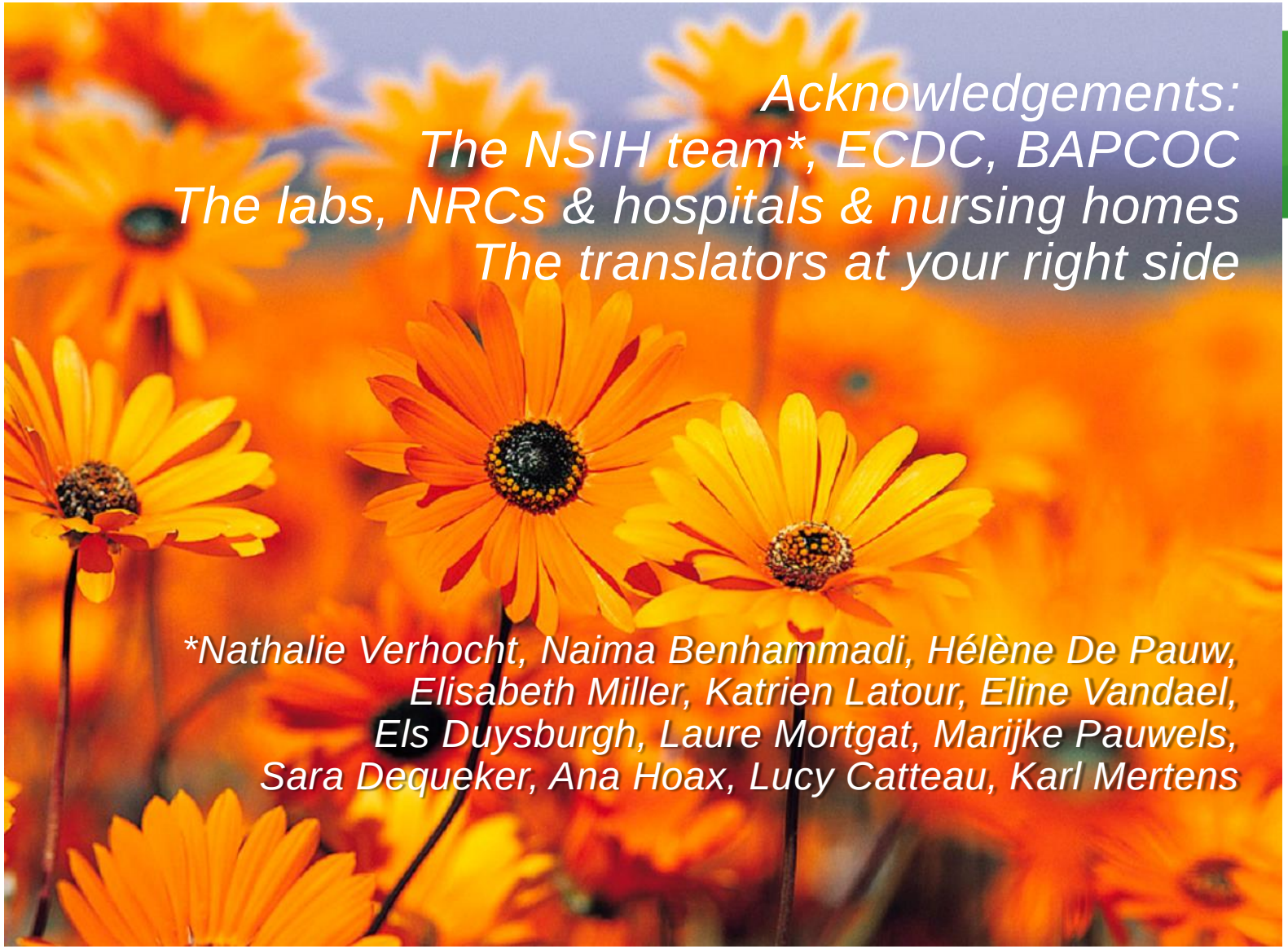
Conclusion on 'Films'

- Selection pressure
  - Hospitals (500/1000 PD) >>> Ambulant care (30/1000 DID)

- Acute Care Hospitals:
  - Intensive care units – internal medicine – pediatrics - geriatrics
  - Tertiary hospitals +++
  - 530 casualties / year in Belgium due to AMR (underestimation)

- Digestive tract concerns: Enterobacteriaceae, enterococci, *C. difficile*, …

The large majority of people treated with antimicrobials do NOT have an infection at the moment of treatment.



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