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HEALTHCARE-ASSOCIATED INFECTIONS AND ANTIMICROBIAL RESISTANCE

ANTIMICROBIAL CONSUMPTION IN BELGIUM

10-year evolution (2010-2019) in the community, nursing homes and hospitals

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ABBREVIATIONS

- ABUH = Antibiotic Use in Hospitals
- AMR = Antimicrobial resistance
- ATC = Anatomical Therapeutic Chemical Classification
- BAPCOC = Belgian Antibiotic Policy Coordination Commission
- BeH-SAC = Belgian Hospitals – Surveillance of Antimicrobial Consumption
- BelVet-SAC = Belgian Veterinary Surveillance of Antibacterial Consumption
- CI = confidence intervals
- DDA = daily dose administrated
- DDD = Defined Daily Dose
- DID = DDDs/1000 inhabitants/days
- EU/EEA = European Union/European Economic Area countries
- ECDC = European Center for Disease Prevention and Control, Stockholm, SE
- EFSA = European Food Safety Authority
- EMA = European Medicines Agency
- ESAC-Net = European Surveillance of Antimicrobial Consumption Network
- FAMHP = Federal agency for medicines and health product (FAGG-AFMPS)
- FTE = full-time equivalent
- Global/ECDC-PPS = Point Prevalence Studies of antimicrobial consumption, resistance and healthcare-associated infections in acute hospitals
- H database (NIHDI) = data delivered by insurance companies on the number of patient days
- HALT = Point prevalence survey of Healthcare-associated infections and Antimicrobial use in Long-Term care facilities (HALT-PSY: in psychiatric institutions)
- ICU = intensive care unit
- IM = intramuscular
- IV = intravenous
- IQR = interquartile range
- MDRO = multidrug resistant organisms
- NAP = National AMR action plan
- NIHDI = National Institute for Health and Disability Insurance (RIZIV-INAMI)
- OPAT = Outpatient parenteral antimicrobial therapy
- PH database (NIHDI) = data delivered by insurance companies on the consumption of pharmaceutical products in hospitals
- PID = packages/1000 inhabitants/days
- PO = per os (oral)
- SC = subcutaneous
- SHA database (NIHDI) = data delivered by insurance companies for each anonymized stay in hospitals
- WHO = World Health Organization

EXECUTIVE SUMMARY

Antimicrobial consumption is monitored in Belgium following national and international protocols through longitudinal or cross-sectional studies. Longitudinal studies rely on existing administrative data with few details that are continuously collected, whereas cross-sectional studies collect details on the applied preventive or curative regimen at a given point in time (point prevalence study).

The objective of this national report is to present an overview of the trends in antimicrobial consumption in the last decade (2010-2019) for the different human settings (community, nursing homes, hospitals), based on the results of following surveillances and studies:

- European Surveillance of Antimicrobial Consumption Network (ESAC-Net)
- Belgian Hospitals – Surveillance of Antimicrobial Consumption (BeH-SAC)
- Point prevalence survey of healthcare-associated infections and antimicrobial use in long-term care facilities (HALT) and in psychiatric institutions (HALT-PSY)
- Global (https://www.global-pps.com/) and European (ECDC-PPS) Point Prevalence Studies of antimicrobial consumption, resistance and healthcare-associated infections in acute hospitals

	ESAC-Net	BeH-SAC	HALT / HALT-PSY	ECDC-PPS	Global-PPS
Data source	Reimbursement data	Reimbursement data	Data collected locally	Data collected locally	Data collected locally
Type of study	Surveillance	Surveillance	Point prevalence study	Point prevalence study	Point prevalence study
Setting	Community (including nursing homes) and hospitals (aggregated data)	Acute, categorical and psychiatric hospitals (data per hospital)	HALT: long-term care facilities (mainly nursing homes), HALT-PSY: psychiatric hospitals and psychiatric wards in acute hospitals	Acute hospitals (inpatient wards)	Acute hospitals (inpatient wards)
Main indicator	Defined daily doses (DDDs)/1000 inhabitants/day (DID)	DDDs/1000 patient days, DDDs/1000 admissions	Prevalence (%) of residents with at least one antimicrobial prescription on the day of the PPS	Prevalence (%) of patients with at least one antimicrobial prescription on the day of the PPS	Prevalence (%) of patients with at least one antimicrobial prescription on the day of the PPS
Start year in Belgium	1997	2003	2010	2011	2015
Included years in the present report	2010-2019	2010-2019	HALT: 2010, 2013, 2016; HALT-PSY: 2017	Surveys in 2011 and 2017	Surveys in 2015, 2017, 2019

Antimicrobial agents are classified using the Anatomical Therapeutic Chemical (ATC) classification of the World Health Organization (WHO) Collaborating Centre for Drugs Statistics and Methodology. The following ATC codes were included as antimicrobial agents: A07AA (intestinal anti-infectives), D01BA (antifungals for systemic use), J01 (antibacterials for systemic use), J02 (antimycotics for systemic use), J04A (drugs for treatment of tuberculosis), J05 (antivirals), P01AB (nitroimidazole-derived antiprotozoals). Consumed units/packages per drug were translated in defined daily doses (DDDs) based on the DDD classification of WHO (version December 2020). Administration routes included are oral (PO), intravenous (IV), intramuscular (IM), subcutaneous (SC), inhalation and rectal. Other topical use (e.g. transdermal via ointments) were excluded in the present report. Trends analysis of the total consumption over 10 years (2010-2019) were performed using linear regression. P-values <0.05 were considered as a significant trend. Other indicators have been included to follow up the rational use of antimicrobial

agents as outlined in national (Belgian Antibiotic Policy Coordination Commission (BAPCOC)) and international action plans and recommendations. The main results per sector are summarized below.

Community (including nursing homes)	Hospitals
Overall (reimbursed) antibiotic consumption: • 2010-2019: significant **<u>decrease</u>** in DID[a] **<u>(-14%)</u>** • 23.1 DID in 2010 to 19.8 DID in 2019 (20.6 DID in 2019 if non-reimbursed consumption of fluoroquinolones (estimation) is taken into account) • Comparison with neighboring countries: - EU/EEA mean in 2019: 18.0 DID (2010-2019: -5%) - The Netherlands in 2019: 8.7 DID (2010-2019: -13%) - France in 2019: 23.3 DID (2010-2019: +0.4%)	**Overall (reimbursed) antibiotic consumption:** *All hospitals* • 2010-2019: significant **<u>decrease</u>** in DID **<u>(-13%)</u>** • 1.76 DID in 2010 to 1.54 DID in 2019 • Comparison with neighboring countries: - EU/EEA mean in 2019: 1.77 DID (2010-2019: +0%) - The Netherlands in 2019: 0.80 DID (2010-2019: -14%) - France in 2019: 1.74 DID (2010-2019: -4%) *Acute hospitals (inpatients wards[$])* • 2010-2019: significant **<u>increase</u>** in DDDs/1000 patient days **<u>(+3%)</u>**, 442.8 in 2010 to 457.8 in 2019 • 2010-2018: significant **<u>decrease</u>** in DDDs/1000 admissions **<u>(-6%)</u>**, 3486 in 2010 to 3276 in 2018
Top 5 most used products in 2019: amoxicillin, amoxicillin + clavulanic acid, nitrofurantoin, azithromycin, cefuroxime	**Top 5 most used products in 2019:** *Acute hospitals (non-psychiatric inpatient wards)* amoxicillin + clavulanic acid, cefazolin, piperacillin + tazobactam, flucloxacillin, ciprofloxacin
Ratio amoxicillin/amoxicillin + clavulanic acid: From 0.85 (46/54) in 2010 to 1.04 (51/49) in 2019	**Ratio amoxicillin/amoxicillin + clavulanic acid:** *All hospitals* From 0.08 (7/93) in 2010 to 0.14 (12/88) in 2019
Indicator broad-spectrum antibiotic use[b]: 2.38 in 2010 to 1.94 in 2019 (% of all antibiotics: 54.3% in 2010 to 48.1% in 2019)	**Indicator broad-spectrum antibiotic use[c]:** *Acute hospitals (non-pediatric, non-psychiatric inpatient wards)* 32.1% in 2010 to 31.3% in 2019 (not significant)
Overall antimycotic and antifungal consumption: • 2010-2019: significant **<u>decrease</u>** in DID **<u>(-9%)</u>** • 3.3 DID in 2010 to 3.0 DID in 2019 • Among the highest consumers of antimycotics and antifungals in EU/EAA countries (2019: EU/EEA mean 1.0 DID, the Netherlands 1.3 DID, France 1.3 DID)	**Overall antimycotic and antifungal consumption:** *All hospitals* • 2010-2019: significant **<u>decrease</u>** in DID **<u>(-28%)</u>** • 0.13 DID in 2010 to 0.09 DID in 2019 • Comparison with neighboring countries in 2019: EU/EEA mean 0.12 DID, France 0.21 DID
Observed prevalence of residents with at least one antimicrobial prescription on one day: *Nursing homes* 4.3% in 2010, 5.1% in 2013, 5.6% in 2016	**Observed prevalence of patients with at least one antimicrobial prescription on one day:** *Acute hospitals (inpatients wards)* 28.9% in 2011, 27.4% in 2015, 27.0% in 2017, 27.8% in 2019 *Psychiatric hospitals* 3.8% in 2017
Quality indicators BAPCOC policy plan 2014-2019 (1)	
From 800 prescriptions/1000 inhabitants/year in 2014 to 600 in 2020 and 400 in 2025 Not possible to assess with the ESAC-Net data, based on packages/1000 inhabitants in 2019 (734) estimated at ±700 prescriptions/1000 inhabitants/year → target not yet reached	**Choice of the antibiotic in line with the local guidelines in ≥90% of the cases (therapeutic use)** Global PPS: 80.7% in 2015, 81.7% in 2017, 83.7% in 2019 → steady improvement, but target not yet reached
Reduction in % fluoroquinolones from 10% in 2014 to 5% in 2018 Estimated at 6.7% in 2019 (taking non-reimbursed consumption (estimation) into account) → improvement, but target not yet reached	**Indication of the antimicrobial noted in the medical file in ≥90% of the cases** Global-PPS 2015: 79.9%, ECDC/Global-PPS 2017: 81.9%, Global-PPS 2019: 85.2% → steady improvement, but target not yet reached
Ratio amoxicillin/amoxicillin + clavulanic acid from 1 (50/50) in 2014 to 4 (80/20) in 2018 Still 1.04 (51/49) in 2019 → target not yet reached	**Choice of the antibiotic for surgical prophylaxis (SP) in line with the local guidelines in ≥90% of the cases** Global PPS: 70.8% in 2015, 73.8% in 2017, 79.8% in 2019 → steady improvement, but target not yet reached
	Duration of the surgical prophylaxis (SP) treatment in line with the local guidelines in ≥90% of the cases Global PPS: 28.1% of SP >1 day in 2015, 25.3% in 2017, 18.9% in 2019 → steady improvement

a. DID: Defined daily doses (DDDs)/1000 inhabitants/day

b. total DDDs J01(CR+DC+DD+(F-FA01)+MA)/J01(CA+CE+CF+DB+FA01)

c. % DDDs J01(CR05+DD+DE+DF+DH+MA+XA+XB+XX08+XX09+XX11)/J01

$ inpatient wards include surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care (ICU), specialized care and psychiatry (outpatient wards and day hospitalizations excluded)

*** Values underlined & in bold: significant trend as obtained by linear regression (p-values <0.05)**

2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDDs) were used (2)

A significant decrease/improvement is seen in the (reimbursed) antibiotic consumption in the community, but the Belgian consumption (expressed in DDDs/1000 inhabitants/day) is still high in comparison with other EU/EEA countries. The ratio amoxicillin / amoxicillin+clavulanic acid only slightly improved over time. Based on total sales data, we estimate that the total consumption of fluoroquinolones in 2019 is still responsible for 6.7% of the total antibiotic consumption (-37% in comparison with 2017 and -16% in comparison with 2018). Worrisome, following the more strict reimbursement criteria for fluoroquinolones, the consumption of fluoroquinolones without reimbursement has strongly increased. The use of antimycotics and antifungals in the community in Belgium is among the highest of all participating EU/EEA countries in ESAC-Net. Although a significant decrease over time is seen, the antimycotic consumption in Belgium is still 3 to 6 times higher than our neighboring countries.

In hospitals, the antibiotic and antimycotic/antifungal consumption is in line with the EU/EEA mean if expressed in DDDs/1000 inhabitants/day. In acute hospitals, expressed in DDDs/1000 patient days, there was a significant increase in antibiotic consumption between 2010 and 2019 (probably explained by the evolution towards shorter hospital stays with a more intensive antibiotic treatment on less patient days). The percentage of broad-spectrum use (±31%) did only slightly improve over the last decennium (not significant). For several results (total antibiotic consumption, antibiotic consumption on ICU, % broad-spectrum use, % IV use) a high variation was found between acute hospitals, also when compared per type of hospital (primary, secondary, tertiary). High outliers should be further targeted to understand the reasons behind these outlying results and identify possible points for improvement. Strikingly, only half of antimicrobial prescriptions in 2019 had a stop/review date documented in the medical record (Global-PPS). It is advised that a legal framework is provided requiring prescribers to document a stop/review date. Preferably, this would be integrated in the hospital's electronic systems to enable information exchange with the hospital pharmacy.

Although improvement is seen over the last few years, none of the targets of the quality indicators set up by BAPCOC in their 2014-2019 action plan were reached based on 2019 data, indicating that the efforts need to be pursued. Actions are planned to further sensibilize prescribers to use antibiotics in a prudent way, with special attention for the use of broad-spectrum antibiotics. Antimicrobial consumption data linked with indications would help to evaluate this consumption in a more thorough way and to provide more detailed feedback to prescribers.

Certain agents have been shown to be (temporary) unavailable from the Belgian market, and often this is the case for older small-spectrum agents (out of patent). This scenario promotes the irrational use of more last line agents and should be avoided to decrease the resistance selection for these newer compounds. Data on shortages of antimicrobial agents in Belgium over the last five years (January 2015 - January 2020) were collected from the *PharmaStatus* database from the Federal agency for medicines and health product (FAMHP). In this period, 44 antibiotic products (ATC codes) were implicated. Especially when only one alternative exists, a shortage can have a substantial impact. FAMHP is consulting several companies to find sustainable solutions to bring unavailable antimicrobial agents on the Belgian market again.

A new national One Health action plan against antimicrobial resistance (2020-2024) is currently being finalized. This action plan contains different approaches to improve the prudent use of antimicrobial consumption and new indicators to follow-up the impact of these approaches on antimicrobial consumption and resistance. It also planned to publish a One Health national report over all sectors (human and animals) in the coming years with combined results on antimicrobial consumption and resistance.

SAMENVATTING

Antimicrobiële consumptie wordt in België gemonitord volgens nationale en internationale protocollen door middel van longitudinale en cross-sectionele studies. Longitudinale studies zijn gebaseerd op beschikbare administratieve data met weinig details die continue verzameld kunnen worden, terwijl cross-sectionele studies details verzamelen over de toegepaste preventieve en curatieve behandelingen op één punt in de tijd (puntprevalentiestudie).

Het objectief van dit nationaal rapport is om een overzicht te presenteren van de trends in antimicrobiële consumptie in het laatste decennium (2010-2019) voor de verschillende humane settings (ambulante zorg, woonzorgcentra, ziekenhuizen), op basis van de resultaten van de volgende surveillances en studies:

- Europese Surveillance van Antimicrobiële Consumptie Netwerk (ESAC-Net)
- Belgische ziekenhuizen – Surveillance van Antimicrobiële Consumptie (BeH-SAC)
- Puntprevalentiestudie van zorggerelateerde infecties en antimicrobieel gebruik in chronische zorginstellingen (HALT) en psychiatrische instellingen (HALT-PSY)
- Global (https://www.global-pps.com/) and Europese (ECDC-PPS) puntprevalentiestudies van antimicrobiële consumptie, resistentie en zorggerelateerde infecties in acute ziekenhuizen

	ESAC-Net	**BeH-SAC**	**HALT / HALT-PSY**	**ECDC-EPP**	**Global-EPP**
Databron	Terugbetalings-data	Terugbetalings-data	Data lokaal verzameld	Data lokaal verzameld	Data lokaal verzameld
Type van studie	Surveillance	Surveillance	Puntprevalentie-studie	Puntprevalentie-studie	Puntprevalentie-studie
Setting	Ambulante zorg (inclusief woonzorgcentra) en ziekenhuizen (geaggregeerde data)	Acute, categorische en psychiatrische ziekenhuizen (data per ziekenhuis)	HALT: chronische zorginstellingen (vnl. woonzorgcentra), HALT-PSY: psychiatrische ziekenhuizen en psychiatrische afdelingen in acute ziekenhuizen	Acute ziekenhuizen (intramurale afdelingen)	Acute ziekenhuizen (intramurale afdelingen)
Belangrijkste indicator	Dagdosissen (DDD's)/1000 inwoners/dag (DID)	DDD's/1000 ligdagen, DDD's/1000 opnames	Prevalentie (%) van residenten met minstens één antimicrobieel voorschrift op de dag van de PPS	Prevalentie (%) van patiënten met minstens één antimicrobieel voorschrift op de dag van de PPS	Prevalentie (%) van patiënten met minstens één antimicrobieel voorschrift op de dag van de PPS
Startjaar in België	1997	2003	2010	2011	2015
Geïncludeerde jaren in het huidige rapport	2010-2019	2010-2019	HALT: 2010, 2013, 2016; HALT-PSY: 2017	Studies in 2011 en 2017	Studies in 2015, 2017, 2019

Antimicrobiële middelen worden geclassificeerd volgens de Anatomische Therapeutische Chemische (ATC) classificatie van de Wereldgezondheidsorganisatie (WHO). De volgende ATC-codes worden geïncludeerd als antimicrobiële middelen: A07AA (intestinale anti-infectie middelen), D01BA (antifungale middelen voor systemisch gebruik), J01 (antibiotica voor systemisch gebruik), J02 (antimycotica voor systemisch gebruik), J04A (geneesmiddelen voor de behandeling van tuberculose), J05 (antivirale middelen), P01AB (antiparasitaire middelen: nitroimidazole-derivaten). Verbruikte eenheden/verpakkingen per geneesmiddel worden vertaald in dagdosissen (DDD's: *defined daily doses*) gebaseerd op de DDD classificatie van het WHO (versie december

2020). De volgende routes van toediening worden geïncludeerd: per os (PO), intraveneus (IV), intramusculair (IM), subcutaan (SC), inhalatie en rectaal. Ander topisch gebruik (bvb. transdermaal via zalven) werd niet meegenomen in het huidige rapport. Trendanalyses van de totale consumptie over 10 jaar (2010-2019) werden uitgevoerd met behulp van lineaire regressie. P-waardes <0.05 werden beschouwd als significant. Andere indicatoren, zoals beschreven in nationale (Belgische Commissie voor de coördinatie van het antibioticabeleid (BAPCOC)) en internationale actieplannen en richtlijnen, werden onderzocht om het rationeel gebruik van antimicrobiële middelen op te volgen. De belangrijkste resultaten worden hieronder samengevat.

Ambulante zorg (inclusief woonzorgcentra)	**Ziekenhuizen**
Totale (terugbetaalde) consumptie van antibiotica: • 2010-2019: significante **daling** in DID[a] **(-14%)** • van 23.1 DID in 2010 naar 19.8 DID in 2019 (20.6 DID in 2019 als het niet-terugbetaald gebruik van fluoroquinoles (schatting) wordt meegerekend) • Vergelijking met buurlanden: - EU/EEA gemiddelde in 2019: 18.0 DID (2010-2019: -5%) - Nederland in 2019: 8.7 DID (2010-2019: -13%) - Frankrijk in 2019: 23.3 DID (2010-2019: +0.4%)	**Totale (terugbetaalde) consumptie van antibiotica:** *Alle ziekenhuizen* • 2010-2019: significante **daling** in DID **(-13%)** • van 1.76 DID in 2010 naar 1.54 DID in 2019 • Vergelijking met buurlanden: - EU/EEA gemiddelde in 2019: 1.77 DID (2010-2019: +0%) - Nederland in 2019: 0.80 DID (2010-2019: -14%) - Frankrijk in 2019: 1.74 DID (2010-2019: -4%) *Acute ziekenhuizen (intramurale afdelingen[$])* • 2010-2019: significante **stijging** in DDD's/1000 ligdagen **(+3%)**, van 442.8 in 2010 naar 457.8 in 2019 • 2010-2018: significante **daling** in DDD's/1000 opnames **(-6%)**, van 3486 in 2010 naar 3276 in 2018
Top 5 meest gebruikte producten in 2019: amoxicilline, amoxicilline + clavulaanzuur, nitrofurantoïne, azithromycine, cefuroxime	**Top 5 meest gebruikte producten in 2019:** *Acute ziekenhuizen (niet-psychiatrische intramurale afdelingen)* amoxicilline + clavulaanzuur, cefazoline, piperacilline + tazobactam, flucloxacilline, ciprofloxacine
Ratio amoxicilline/amoxicilline + clavulaanzuur: Van 0.85 (46/54) in 2010 naar 1.04 (51/49) in 2019	**Ratio amoxicilline/amoxicilline + clavulaanzuur:** *Alle ziekenhuizen* Van 0.08 (7/93) in 2010 naar 0.14 (12/88) in 2019
Indicator breedspectrum antibiotica gebruik[b]: Van 2.38 in 2010 naar 1.94 in 2019 (% van alle antibiotica: van 54.3% in 2010 naar 48.1% in 2019)	**Indicator breedspectrum antibiotica gebruik[c]:** *Acute ziekenhuizen (niet-pediatrische, non-psychiatrische intramurale afdelingen)* Van 32.1% in 2010 naar 31.3% in 2019 (niet significant)
Totale consumptie van antimycotica en antifungale middelen: • 2010-2019: significante **daling** in DID **(-9%)** • Van 3.3 DID in 2010 naar 3.0 DID in 2019 • Eén van de hoogste verbruikers van antimycotica en antifungale middelen in EU/EAA landen (2019: EU/EEA gemiddelde 1.0 DID, Nederland 1.3 DID, Frankrijk 1.3 DID)	**Totale consumptie van antimycotica en antifungale middelen:** *Alle ziekenhuizen* • 2010-2019: significante **daling** in DID **(-28%)** • Van 0.13 DID in 2010 naar 0.09 DID in 2019 • EU/EEA gemiddelde 2019: 0.12 DID, Frankrijk 0.21 DID
Geobserveerde prevalentie van residenten met minstens één voorschrift voor een antimicrobieel middel op één dag: *Woonzorgcentra:* 4.3% in 2010, 5.1% in 2013, 5.6% in 2016	**Geobserveerde prevalentie van patiënten met minstens één voorschrift voor een antimicrobieel middel op één dag:** *Acute ziekenhuizen (intramurale afdelingen)* 28.9% in 2011, 27.4% in 2015, 27.0% in 2017, 27.8% in 2019 *Psychiatrische ziekenhuizen* 3.8% in 2017
Kwaliteitsindicatoren BAPCOC actieplan 2014-2019 (1)	
Van 800 voorschriften/1000 inwoners/jaar in 2014 naar 600 in 2020 en 400 in 2025 Niet mogelijk om te beoordelen op basis van ESAC-Net data, indien gebaseerd op aantal verpakkingen/1000 inwoners in 2019 (734): geschat op ±700 voorschriften/1000 inwoners/jaar → doelstelling nog niet behaald	**Keuze van het antibioticum in lijn met de lokale richtlijnen in ≥90% van de gevallen (therapeutisch gebruik)** Global EPP: 80.7% in 2015, 81.7% in 2017, 83.7% in 2019 → geleidelijke verbetering, maar doelstelling nog niet behaald
Reductie in % fluoroquinolones van 10% in 2014 naar 5% in 2018 Geschat op 6.7% in 2019 (niet-terugbetaald verbruik (schatting) in rekening gebracht) → verbetering, maar doelstelling nog niet behaald	**Indicatie van het antimicrobieel middel genoteerd in het medisch dossier in ≥90% van de gevallen** Global-PPS 2015: 79.9%, ECDC/Global PPS 2017: 81.9%, Global-PPS 2019: 85.2% → geleidelijke verbetering, maar doelstelling nog niet behaald

Ratio amoxicilline/amoxicilline + clavulaanzuur van 1 (50/50) in 2014 naar 4 (80/20) in 2018 Nog steeds 1.04 (51/49) in 2019 → doelstelling nog niet behaald	**Keuze van het antibioticum voor chirurgische profylaxe in lijn met de lokale richtlijnen in ≥90% van de gevallen** Global PPS: 70.8% in 2015, 73.8% in 2017, 79.8% in 2019 → geleidelijke verbetering, maar doelstelling nog niet behaald
	Duur van de chirurgische profylaxe behandeling in lijn met de lokale richtlijnen in ≥90% van de gevallen Global PPS: 28.1% van de chirurgische behandelingen >1 dag in 2015, 25.3% in 2017, 18.9% in 2019 → geleidelijke verbetering

a. DID: *Defined daily doses* (DDD's)/1000 inwoners/dag
b. totaal DDD's J01(CR+DC+DD+(F-FA01)+MA)/J01(CA+CE+CF+DB+FA01)
c. % DDD's J01(CR05+DD+DE+DF+DH+MA+XA+XB+XX08+XX09+XX11)/J01
$ intramurale afdelingen: chirurgie, interne geneeskunde, geriatrie, pediatrie, intensieve en niet-intensieve neonatologie, materniteit, infectieuze ziektes, intensieve zorgen (ICU), gespecialiseerde zorg en psychiatrie (poliklinische afdelingen en daghospitalisaties geëxcludeerd)
*** Waardes onderlijnd en in het vet: significante trend geanalyseerd met lineaire regressie (p-waardes <0.05)**
2020 editie van het Anatomische Therapeutische Chemische (ATC) classificatie systeem and Defined Daily Doses (DDD's) werd gebruikt (2)

Er wordt een significante daling/verbetering gezien in het (terugbetaald) antibioticaverbruik in de ambulante zorg, maar dit verbruik (uitgedrukt in DDD's/1000 inwoners/dag) ligt nog steeds hoog in vergelijking met andere EU/EAA landen. De ratio amoxicilline/amoxicilline + clavulaanzuur is slechts licht verbeterd doorheen de tijd. Gebaseerd op totale verkoopsdata schatten we dat het totale verbruik van fluoroquinolones in 2019 nog steeds verantwoordelijk is voor 6.7% van het totale antibioticaverbruik (-37% in vergelijking met 2017 en -16% in vergelijking met 2018). Opmerkelijk, volgend op de meer strikte terugbetalingscriteria voor fluoroquinolones, is het verbruik van fluoroquinolones zonder terugbetaling sterk gestegen. Het verbruik van antimycotica en antifungale middelen in de ambulante zorg bedraagt één van de hoogste van alle deelnemende EU/EEA landen in ESAC-Net. Ondanks dat er een significante daling wordt gezien doorheen de tijd, is het verbruik van antimycotica in België nog steeds 3 tot 6 keer hoger dan in onze buurlanden.

In ziekenhuizen ligt het verbruik van antibiotica en antimycotica/antifungale middelen in lijn met het EU/EEA gemiddelde indien uitgedrukt in DDD's/1000 inwoners/dag. In acute ziekenhuizen was er een significante stijging in het verbruik van antibiotica, uitgedrukt in DDD's/1000 ligdagen, tussen 2010 en 2019 (waarschijnlijk verklaard door de evolutie naar kortere ziekenhuisopnames met een intensievere antibioticabehandeling op minder dagen). Het percentage van breedspectrum verbruik (±31%) is slechts licht verbeterd doorheen het laatste decennium (niet significant). Voor verschillende resultaten (totale antibioticaverbruik, antibioticaverbruik op intensieve zorgen, % breedspectrum verbruik, % IV verbruik) werd er een grote variatie gevonden tussen acute ziekenhuizen, ook wanneer vergeleken per type van ziekenhuis (primair, secundair, tertiair). Hoge uitschieters zouden verder onderzocht moeten worden om de redenen achter de uitliggende resultaten te begrijpen en om verbeterpunten te identificeren. Opvallend, in 2019 werd slechts bij de helft van de antimicrobiële voorschriften een stop- of herbeoordelingsdatum gedocumenteerd in het medisch dossier (Global-PPS). Er zou een wettelijk kader moeten komen om voorschrijvers te verplichten een einddatum of herbeoordelingsdatum te documenteren. Dit is bij voorkeur ingebed in de elektronische systemen van het ziekenhuis, zodat informatie met de ziekenhuisapotheek kan worden uitgewisseld.

Ondanks dat er een verbetering wordt gezien over de laatste jaren, werd geen enkele van de doelstellingen voor de kwaliteitsindicatoren opgezet door BAPCOC in hun 2014-2019 actieplan behaald op basis van 2019 data, wat aantoont dat de inspanningen verder gezet moeten worden. Acties zijn gepland om voorschrijvers verder te sensibiliseren om antibiotica voorzichtig te gebruiken met speciale aandacht voor het gebruik van breedspectrum antibiotica. Antimicrobiële verbruiksdata gelinkt met indicaties zouden kunnen helpen om het verbruik grondiger te kunnen evalueren en meer gedetailleerde feedback te kunnen voorzien voor voorschrijvers.

Er werd aangetoond dat verschillende antimicrobiële middelen tijdelijk onbeschikbaar waren op de Belgische markt. Het ging in de meeste gevallen om oudere eng-spectrum middelen (waarbij het patent verlopen is). Dit scenario werkt het irrationeel verbruik van laatste lijn middelen in de hand en zou vermeden moeten worden om de resistentiedruk voor deze nieuwere producten te verlagen. Er werden data verzameld over de

onbeschikbaarheden van antimicrobiële middelen in de laatste 5 jaar (januari 2015 - januari 2020) uit de *FarmaStatus* databank van het Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten (FAGG). Er waren in deze periode 44 verschillende antibiotica (ATC-codes) onbeschikbaar. Vooral in de gevallen dat er maar één alternatief voorradig is, kan een tekort een belangrijke impact hebben. Het FAGG consulteert verschillende bedrijven om duurzame oplossingen te vinden om onbeschikbare antimicrobiële middelen terug op de Belgische markt te brengen.

Op dit moment wordt er een nieuw nationaal *One Health* actieplan tegen antimicrobiële resistentie (2020-2024) gefinaliseerd. Dit actieplan bevat verschillende strategieën om het voorzichtig gebruik van antimicrobiële middelen te verbeteren en nieuwe indicatoren om de impact van deze strategieën op antimicrobiële consumptie en resistentie op te volgen. Er zijn eveneens plannen om in de komende jaren een nationaal *One Health* rapport te publiceren over alle sectoren (humaan en dieren) met gecombineerde resultaten over antimicrobiële consumptie en resistentie.

RESUME

En Belgique, la consommation d'antimicrobiens est surveillée selon des protocoles nationaux et internationaux au moyen d'études longitudinales et cross-sectionnelles. Les études longitudinales sont basées sur les données administratives disponibles avec le peu de détails qui peuvent être collectés, alors que les études cross-sectionnelles collectent des détails sur les traitements préventifs et curatifs appliqués à un point donné dans le temps (étude de prévalence ponctuelle).
L'objectif de ce rapport national est de présenter un aperçu des tendances dans la consommation d'antimicrobiens au cours de la dernière décennie (2010-2019) pour les différents cadres humains (soins ambulatoires, maisons de repos et de soins (MRS), hôpitaux), sur la base des résultats des surveillances et études suivantes:

- Surveillance européenne du réseau de consommation d'antimicrobiens (ESAC-Net)
- Hôpitaux belges – Surveillance de la consommation d'antimicrobiens (BeH-SAC)
- Etude de prévalence ponctuelle (EPP) des infections associées aux soins et de l'usage des antibiotiques dans les institutions de soins chronique (HALT) et dans les institutions psychiatriques (HALT-PSY)
- Etudes de prévalence ponctuelles globales (https://www.global-pps.com/) et européennes (ECDC-EPP) de la consommation d'antimicrobiens, de la résistance antimicrobienne et des infections liées aux soins dans les hôpitaux aigus.

	ESAC-Net	**BeH-SAC**	**HALT / HALT-PSY**	**ECDC-EPP**	**Global-EPP**
Source des données	Données de remboursement	Données de remboursement	Données collectées localement	Données collectées localement	Données collectées localement
Type d'étude	Surveillance	Surveillance	Etude de prévalence ponctuelle	Etude de prévalence ponctuelle	Etude de prévalence ponctuelle
Cadre	Soins ambulatoires (y compris les MRS) et les hôpitaux (données agrégées)	Hôpitaux aigus, catégoriques et psychiatriques (données par hôpital)	HALT: institutions de soins chroniques (principalement: MRS); HALT-PSY: hôpitaux psychiatriques et unités psychiatriques d'hôpitaux aigus	Hôpitaux aigus (unités intramuros)	Hôpitaux aigus (unités intramuros)
Indicateur principal	Doses quotidiennes (DDD)/1000 résidents/jour (DID)	DDD/1000 journées d'hospitalisation, DDD/1000 admissions	Prévalence (%) de résidents recevant au moins une prescription d'antimicrobien le jour de l'EPP	Prévalence (%) de résidents recevant au moins une prescription d'antimicrobien le jour de l'EPP	Prévalence (%) de résidents recevant au moins une prescription d'antimicrobien le jour de l'EPP
Année de lancement en Belgique	1997	2003	2010	2011	2015
Années incluses dans le présent rapport	2010-2019	2010-2019	HALT: 2010, 2013, 2016; HALT-PSY: 2017	Les études de 2011 et 2017	Les études de 2015, 2017 et 2019

Les antimicrobiens sont classifiés selon la classification anatomique, thérapeutique et chimique (ATC) de l'Organisation mondiale de la santé (OMS). Les codes ATC suivants sont inclus comme antimicrobiens: A07AA

(agents d'anti-infection intestinale), D01BA (antifongiques à usage systémique), J01 (antibiotiques à usage systémique), J02 (antimycotiques à usage systémique), J04A (médicaments destinés au traitement de la tuberculose), J05 (antiviraux), P01AB (antiparasitaires: dérivés des nitroimidazoles). Les unités/emballages utilisés par médicament sont traduits en doses quotidiennes (DDD: *defined daily doses*) basées sur la classification DDD de l'OMS (version décembre 2020). Les voies d'administration suivantes sont incluses: per os (PO), intraveineuse (IV), intramusculaire (IM), sous-cutanée (SC), inhalation et rectale. Un autre usage topique (p. ex. transdermique via des pommades) n'a pas été repris dans le présent rapport. Des analyses de tendances de la consommation totale sur 10 ans (2010-2019) ont été réalisées à l'aide de la régression linéaire. Les valeurs P<0.05 ont été considérées comme significatives. D'autres indicateurs, tels que décrits dans les plans d'action et directives nationaux (Commission belge de coordination de la politique antibiotique (BAPCOC)) et internationaux, ont été analysés pour suivre l'utilisation rationnelle des antimicrobiens. Les principaux résultats sont résumés ci-dessous.

Soins ambulatoires (y compris les MRS)	Hôpitaux
Consommation totale (remboursée) d'antibiotiques: • 2010-2019: **baisse** significative des DID[a] **(-14%)** • de 23.1 DID en 2010 à 19.8 DID en 2019 (20.6 DID en 2019 si la consommation non remboursée de fluoroquinolones (estimation) est prise en compte) • Comparativement aux pays voisins: - moyenne EU/EEA en 2019: 18.0 DID (2010-2019: -5%) - Pays-Bas en 2019: 8.7 DID (2010-2019: -13%) - France en 2019: 23.3 DID (2010-2019: +0.4%)	**Consommation totale (remboursée) d'antibiotiques:** *Tous les hôpitaux* • 2010-2019: **baisse** significative des DID **(-13%)** • de 1.76 DID en 2010 à 1.54 DID en 2019 • Comparativement aux pays voisins: - moyenne EU/EEA en 2019: 1.77 DID (2010-2019: +0%) - Pays-Bas en 2019: 0.80 DID (2010-2019: -14%) - France en 2019: 1.74 DID (2010-2019: -4%) *Hôpitaux aigues (unités intramuros[$])* • 2010-2019: **augmentation** significative des DDD/1000 journées d'hospitalisation **(+3%)**, de 442.8 en 2010 à 457.8 en 2019 • 2010-2018: **baisse** significative des DDD/1000 admissions **(-6%)**, de 3486 en 2010 à 3276 en 2018
Top 5 des produits le plus utilisés en 2019: amoxicilline, amoxicilline + acide clavulanique, nitrofurantoïne, azithromycine, cefuroxime	**Top 5 des produits le plus utilisés en 2019:** *Hôpitaux aigus (unités intramuros non psychiatriques)* amoxicilline + acide clavulanique, cefazoline, piperacilline + tazobactam, flucloxacilline, ciprofloxacine
Ratio amoxicilline/amoxicilline + acide clavulanique: De 0.85 (46/54) en 2010 à 1.04 (51/49) en 2019	**Ratio amoxicilline/amoxicilline + acide clavulanique:** *Tous les hôpitaux* De 0.08 (7/93) en 2010 à 0.14 (12/88) en 2019
Indicateur utilisation antibiotiques spectre large[b]: De 2.38 en 2010 à 1.94 en 2019 (% de tous les antibiotiques: de 54.3% en 2010 à 48.1% en 2019)	**Indicateur utilisation antibiotiques spectre large[c]:** *Hôpitaux aigus (unités intramuros non pédiatriques, non psychiatriques)* De 32.1% en 2010 à 31.3% en 2019 (non significatif)
Consommation totale d'antimycotiques et d'antifongiques: • 2010-2019: **baisse** significative des DID **(-9%)** • De 3.3 DID en 2010 à 3.0 DID en 2019 • L'un des plus grands consommateurs d'antimycotiques et d'antifongiques dans les pays EU/EAA (2019: moyenne EU/EEA 1.0 DID, Pays-Bas 1.3 DID, France 1.3 DID)	**Consommation totale d'antimycotiques et d'antifongiques:** *Tous les hôpitaux* • 2010-2019: **baisse** significative des DID **(-28%)** • De 0.13 DID en 2010 à 0.09 DID en 2019 • Comparativement aux pays voisins en 2019: la moyenne EU/EEA: 0.12 DID, France 0.21 DID
Prévalence observée chez les résidents ayant au moins une prescription d'antimicrobien sur un jour: *Maisons de repos et de soins :* 4.3% en 2010, 5.1% en 2013, 5.6% en 2016	**Prévalence observée chez les patients ayant au moins une prescription d'antimicrobien sur un jour:** *Hôpitaux aigus (unités intramuros)* 28.9% en 2011, 27.4% en 2015, 27.0% en 2017, 27.8% en 2019 *Hôpitaux psychiatriques* 3.8% en 2017
Indicateurs de qualité plan d'action BAPCOC 2014-2019 (1)	
De 800 prescriptions/1000 résidents/an en 2014 à 600 en 2020 et 400 en 2025 Pas possible à estimer sur la base des données ESAC-Net, si basées sur le nombre d'emballages/1000 résidents en 2019 (734): estimé à ±700 prescriptions/1000 résidents/an → l'objectif pas encore atteint	**Choix de l'antibiotique conforme aux directives locales dans ≥90% des cas (l'usage thérapeutique)** Global-EPP: 80.7% en 2015, 81.7% en 2017, 83.7% en 2019 → amélioration constante, mais l'objectif pas encore atteint

Réduction en % des fluoroquinolones de 10% en 2014 à 5% en 2018 Estimé à 6.7% en 2019 (consommation non remboursée (estimation) prise en compte) → amélioration, mais l'objectif pas encore atteint	**Indication de l'antimicrobien notée dans le dossier médical dans ≥90% des cas** Global-EPP 2015: 79.9%, ECDC/Global-EPS 2017: 81.9%, Global-EPP 2019: 85.2% → amélioration constante, mais l'objectif pas encore atteint
Ratio amoxicilline/amoxicilline + acide clavulanique de 1 (50/50) en 2014 à 4 (80/20) en 2018 Toujours 1.04 (51/49) en 2019 → l'objectif pas encore atteint	**Choix de l'antibiotique pour la prophylaxie chirurgicale conforme aux directives locales dans ≥90% des cas** Global-EPP: 70.8% en 2015, 73.8% en 2017, 79.8% en 2019 → amélioration constante, mais l'objectif pas encore atteint
	Durée de la prophylaxie chirurgicale conforme aux directives locales dans ≥90% des cas Global-EPP: 28.1% des traitements chirurgicaux >1 jour en 2015, 25.3% en 2017, 18.9% en 2019 → amélioration constante

a. DID: *Defined daily doses* (DDD)/1000 résidents/jour
b. Total DDD J01(CR+DC+DD+(F-FA01)+MA)/J01(CA+CE+CF+DB+FA01)
c. % DDD J01(CR05+DD+DE+DF+DH+MA+XA+XB+XX08+XX09+XX11)/J01
$ Unités intramuros: chirurgie, médecine interne, gériatrie, pédiatrie, néonatologie intensive et non intensive, maternité, maladies infectieuses, soins intensifs (ICU), soins spécialisés et psychiatrie (unités polycliniques et hospitalisations de jour exclues)
*** Valeurs soulignées et en gras: tendance significative analysée avec régression linéaire (valeurs p <0.05)**
L'édition 2020 du système de classification anatomique, thérapeutique et chimique (ATC) et des Defined Daily Doses (DDD) a été utilisée (2)

Une diminution significative/amélioration de la consommation d'antibiotiques (remboursés) est constatée dans les soins ambulatoires, mais cette consommation (exprimée en DDD/1000 habitants/jour) reste élevée par rapport aux autres pays de l'EU/EAA. Le ratio amoxicilline/amoxicilline + acide clavulanique ne s'est que légèrement amélioré avec le temps. Sur la base des données relatives aux ventes totales, nous estimons que la consommation totale de fluoroquinolones en 2019 représente encore 6,7% de la consommation totale d'antibiotiques (-37 % par rapport à 2017 et -16 % par rapport à 2018). Il est inquiétant de constater que, suite au renforcement des critères de remboursement des fluoroquinolones, la consommation de fluoroquinolones non remboursées a augmenté beaucoup. La consommation d'antimycotiques et d'antifongiques dans le cadre des soins ambulatoires est l'une des plus élevées de tous les pays de l'EU/EAA participant au réseau ESAC-Net. Malgré une diminution significative au fil du temps, la consommation d'antimycotiques en Belgique est encore 3 à 6 fois plus élevée que dans nos pays voisins.

Dans les hôpitaux, la consommation d'antibiotiques et d'antimycotiques/antifongiques est conforme à la moyenne de l'EU/EAA lorsqu'elle est exprimée en DDD/1000 habitants/jour. Dans les hôpitaux de soins aigus, on a constaté une augmentation significative de la consommation d'antibiotiques exprimée en DDD/1000 journées d'hospitalisation entre 2010 et 2019 (ce qui s'explique probablement par l'évolution vers des séjours hospitaliers plus courts avec un traitement antibiotique plus intensif sur un nombre de jours plus restreint). Le taux de consommation à large spectre (±31%) ne s'est que légèrement amélioré au cours de la dernière décennie (non significatif). Pour différents résultats (utilisation totale d'antibiotiques, utilisation d'antibiotiques dans les unités de soins intensifs, % d'utilisation à large spectre, % d'utilisation IV), une grande variation a été constatée entre les hôpitaux de soins aigus, également par rapport au type d'hôpital (primaire, secondaire, tertiaire). Les valeurs aberrantes élevées doivent faire l'objet d'une enquête plus approfondie afin d'en comprendre les raisons et d'identifier les domaines à améliorer. Il est à noter qu'en 2019, seule la moitié des prescriptions d'antimicrobiens avaient une date de fin de traitement ou de réévaluation inscrite dans le dossier médical du patient (Global-EPP). Un cadre légal devrait être mis en place pour obliger les prescripteurs à documenter une date de fin ou de réévaluation. De préférence, cela serait intégré dans les systèmes électroniques de l'hôpital pour permettre l'échange d'informations avec la pharmacie de l'hôpital.

Bien qu'une amélioration ait été constatée ces dernières années, aucun des objectifs concernant les indicateurs de qualité fixés par la BAPCOC dans leur plan d'action 2014-2019 n'a été atteint sur base des données de 2019, ce qui montre que les efforts doivent être poursuivis. Des actions sont prévues pour sensibiliser davantage les prescripteurs à une utilisation prudente des antibiotiques, en accordant une attention particulière à l'utilisation des antibiotiques à large spectre. Les données sur la consommation d'antimicrobiens liées aux indications pourraient

aider à évaluer la consommation de manière plus approfondie et à fournir un feed-back plus détaillé aux prescripteurs.

Il a été démontré que plusieurs antimicrobiens étaient temporairement indisponibles sur le marché belge. La plupart d'entre eux étaient des médicaments plus anciens à spectre étroit (dont le brevet avait expiré). Ce scénario favorise la consommation irrationnelle de produits de dernière ligne et doit être évité afin de réduire la pression de résistance pour ces produits plus récents. Des données ont été recueillies sur l'indisponibilité des agents antimicrobiens au cours des 5 dernières années (janvier 2015 - janvier 2020) dans la base de données PharmaStatut de l'Agence fédérale des médicaments et des produits de santé (AFMPS). Il y avait 44 antibiotiques différents (codes ATC) non disponibles pendant cette période. Une pénurie peut avoir un impact important, en particulier dans les cas où il n'y a qu'une seule alternative disponible. L'AFMPS consulte plusieurs entreprises pour trouver des solutions durables afin d'apporter des agents antimicrobiens non disponibles sur le marché belge à nouveau.

Actuellement, un nouveau plan d'action national "One Health" contre l'antibiorésistance (2020-2024) est en cours de finalisation. Ce plan d'action comprend plusieurs stratégies visant à améliorer l'utilisation prudente des agents antimicrobiens et de nouveaux indicateurs pour surveiller l'impact de ces stratégies sur la consommation d'antimicrobiens et la résistance aux antimicrobiens. Il est également prévu de publier dans les prochaines années un rapport national "One Health" couvrant tous les secteurs (humain et animal) avec des résultats combinés sur la consommation d'antimicrobiens et la résistance.

BACKGROUND

The emerge of micro-organisms that are resistant to the action of one or more antimicrobial agents, referred to as antimicrobial resistance (AMR), is a worldwide threat that requires immediate attention. Although the incidence of resistant bacteria on the skin (e.g. methicillin resistant *Staphylococcus aureus*) is decreasing, the incidence of other resistant bacteria especially found in the gut is clearly increasing (3). AMR leads to an increased burden in terms of morbidity and mortality, also in Belgium (4,5). Cassini et al. calculated that each year in Europe 33000 persons die due to an infection with a resistant micro-organism. Most of these infections are associated with healthcare. In Belgium, the number of deaths attributed to AMR was estimated at 530 per year (6). This number is an underestimation, since only the most prominent resistant bacteria and predominant type of infections were taken into account. Moreover, the costs of AMR to the Belgian health system are approximately 24 million euros each year (7).

There is a link between the level of antimicrobial consumption, especially inappropriate consumption, and the level of AMR (8–10). Therefore the responsible and prudent use of antimicrobials should be encouraged. The 'One Health Action Plan against Antimicrobial Resistance' of the European Commission (June 2017) underlines the importance of surveillance of antimicrobial use in the member states (11). A recent study of the European Centre for Disease Prevention and Control (ECDC) indicated that recent efforts in antibiotic stewardship and infection prevention and control are slowing down (rather than decreasing) the emerge of resistant bacteria, so further investment in these efforts is needed (12).

Specifically in Belgium, the Belgian Antibiotic Policy Coordination Commission (BAPCOC) was launched in 1999 at a federal level to follow-up the AMR threat and to set up actions to improve antimicrobial use and infection prevention and control in the different settings (community, hospitals, nursing homes and animal sector) (1). In the last two decades, several actions were successfully implemented (e.g. public awareness campaigns, antibiotic management teams in hospitals, hand hygiene campaigns, outbreak support team for multidrug resistant organisms (MDRO)). Nevertheless, a country visit of ECDC and the European Commission in 2017 made clear that a revised and more coordinated One Health approach is needed to combat this complex AMR threat with also attention for the environmental aspects (13). In addition, the Belgian Health Care Knowledge Centre (KCE, https://kce.fgov.be/) performed an elaborated review of the current antibiotic policy in Belgium and listed several recommendations for improvement (14). Based on these recommendations, a One Health National AMR Action Plan (NAP, 2020-2024) was compiled and the final version is currently being validated at political level.

Antimicrobial consumption data are monitored following national and international protocols through longitudinal or cross-sectional studies. Longitudinal studies rely on administrative data with few details but continuously collected, whereas cross-sectional studies collect very detailed data at a given point in time (point prevalence study). Several systems are already in place (e.g. European Surveillance of Antimicrobial Consumption Network (ESAC-Net, ECDC), Belgian Hospitals – Surveillance of Antimicrobial Consumption (BeH-SAC), Belgian Veterinary Surveillance of Antibacterial Consumption (BelVet-SAC)) (15–17). So far, the results have been published in different places. An overall report for the different settings is a target in the new NAP (2020-2024). The objective of this national report is to present an overview of the trends in antimicrobial consumption in the last decade (2010-2019) for the different human settings (the community, nursing homes, hospitals), based on the results of several surveillances and studies. In addition, references to more detailed data related to antimicrobial consumption are provided.

METHODS

DATA COLLECTIONS

In this national report, the results of the following surveillances/studies are presented:

- European Surveillance of Antimicrobial Consumption Network (ESAC-Net)
- Belgian Hospitals – Surveillance of Antimicrobial Consumption (BeH-SAC)
- Point prevalence survey of healthcare-associated infections and antimicrobial use in long-term care facilities (HALT) and in psychiatric institutions (HALT-PSY)
- Global and ECDC Point Prevalence Studies (PPS) of antimicrobial consumption, resistance and healthcare-associated infections in acute hospitals

Below, each methodology is discussed more in detail. An overview of the different Belgian databases is presented in Table 1.

ESAC-NET

ESAC-Net is the European network of national surveillance systems of antimicrobial consumption, organized by ECDC (follow-up of the ESAC project, previously coordinated at the University of Antwerp till 2011 (18)). Using a shared methodology, different European countries are collecting antimicrobial consumption data in the community and/or hospital sector. The database contains aggregated data, meaning consumption in the whole community sector and consumption in all hospitals without further specification. In ESAC-Net, the consumption is expressed in Defined Daily Doses (DDDs) per 1000 inhabitants per day (DID) or packages per 1000 inhabitants per day (PID), using the country population (Eurostat data (19)) as a denominator for both the community and the hospital sector. More information on the methodology can be found in the ESAC-Net protocol (15).

Specifically for Belgium, reimbursement data from the National Institute for Health and Disability Insurance (NIHDI) are used to send Belgian data to ECDC. Each year in July, NIHDI transfers the database (data received from the insurance companies, Farmanet data for the community, PH data for the hospitals) to Sciensano. Sciensano is responsible for the data validation and the transferal to ECDC. The data for the community include all antimicrobial packages delivered in community pharmacies (including all nursing homes who receive their medication from a community pharmacy, which is the majority in Belgium). Hospital data include all deliveries in hospital pharmacies. A consequence of using NIHDI data is that only reimbursed consumption is included. As approximately 99% of the Belgian population has a health insurance, an extrapolation from 99% to 100% is performed to correct for this. Nevertheless, a small underestimation, especially for certain products with limited reimbursement (e.g. fluoroquinolones since May 2018, products that are imported from other countries) should be taken into account. For the community sector, the consumption is besides DID also expressed in PID. The tarification per unit in Belgian nursing homes (delivery per unit and no longer per package), introduced in the second half of 2015, cannot be taken into account with this indicator. Consequently, starting from 2015, the consumption in PID is slightly underestimated (in 2015 ±2% of the total DDDs of antibiotics in the community were delivered per unit). The estimation of non-reimbursed consumption of fluoroquinolones in 2018 and 2019 is based on a comparison between total sales data (IQVIA, previously known as IMS, includes reimbursed and non-reimbursed consumption) and NIHDI data (Farmanet, only reimbursed consumption), with 2017 used as reference year *[personal communication from NIHDI to Sciensano]*.

For the hospital sector, there is a larger delay in the NIHDI data with an underestimation of approximately 15% for the last reported year (in the database that is requested in July for the previous year). Therefore, an extra

extrapolation of 15% is performed for the consumption in hospitals for the last reported year. In the following data delivery, the data are retrospectively corrected with the exact consumption. Consequently, the antimicrobial consumption in hospitals in ESAC-Net for the last reported year (2019) is still an estimation. The ESAC-Net database of November 2020 was used for the analyses in this national report.

BEH-SAC

Since 2007 a national surveillance of antimicrobial consumption has been set up in Belgian hospitals with - in comparison with ESAC-Net - more detailed data per hospital, making benchmarking possible. Between 2007 and 2014, in the ABUH (Antibiotic Use in Hospitals) project, acute and large (≥150 beds) chronic hospitals were obligated to annually upload their consumption data on a web-based data collection application of Sciensano (formerly WIV-ISP) called NSIHweb (20). In 2018, BeH-SAC was introduced with a revised methodology. In line with the 'only collect data once' principle (Royal Decree May 5, 2014), reimbursement data of NIHDI are used in combination with a new reporting system on Healthstat. The objectives of BeH-SAC are:

- To develop and offer a scientifically standardized methodology to Belgian hospitals, to follow-up their antimicrobial consumption in a quantitative way through time (in complement to their own local and in-depth monitoring).
- To give Belgian hospitals the opportunity to benchmark, based on their antimicrobial consumption, with similar hospitals.
- To provide national and regional data (with an acceptable delay in time) to be able to evaluate the antimicrobial consumption in Belgian hospitals.

The reimbursement data collected from NIHDI consist of consumption (PH database) and denominator data (number of patient days (H database) and admissions (SHA database)), collected per year/trimester and per hospital/unit. In BeH-SAC, the antimicrobial consumption is expressed in DDDs/1000 patient days and DDDs/1000 admissions. The same limitations as for ESAC-Net apply: only reimbursed use is taken into account. Non-reimbursed off-label use or imported antimicrobials agents are not considered, leading to a small underestimation. No extrapolations are performed in BeH-SAC and only complete data are presented. More details on the methodology can be found in the protocol (16). The BeH-SAC database of January 2021 was used for the analyses in this national report. For the analyses of 2018 and 2019, the data of one tertiary hospital (total number of tertiary hospitals in 2010-2019: n=7) were excluded because a significant underestimation in the reimbursement data of this hospital was discovered for these years (technical problem at level of the hospital that is currently being solved).
The methodology and preliminary results of a validation study of BeH-SAC are presented in Appendix 1.

HALT

HALT is a European PPS (cross-sectional) of healthcare-associated infections and antimicrobial consumption in long-term facilities, coordinated by ECDC (follow-up of the ESAC project, previously coordinated at the University of Antwerp (18)). In Belgium, three HALT studies have taken place so far (HALT-1: May-September 2010, HALT-2: April-May 2013, HALT-3: September-November 2016). In this report, the Belgian results for nursing homes (HALT-1 to 3) and the European results (HALT-3) for all included long-term care facilities (nursing homes, residential homes and mixed facilities) are presented. The participation is Belgium was voluntary, all interested facilities could participate (convenience sample). The data were collected from each facility on one single day by a local data collector. Data on both institutional and resident level (including antimicrobial use) were collected. More information on the methodology is available in the HALT protocol (21).
In addition, the HALT-PSY protocol was designed for a psychiatric setting (psychiatric hospitals and psychiatric wards in acute hospitals) (22). The set-up is similar as the HALT studies, but customized to this specific patient

population. The first Belgian HALT-PSY study took place in October-November 2017. A summary of the results is presented in this report.

GLOBAL- AND ECDC-PPS

Similar as the HALT study in long-term care facilities, PPS (cross-sectional) are organized in acute hospitals. In 2011 and 2016-2017, ECDC organized a European PPS in acute hospitals focused on the prevalence of healthcare-associated infections and antimicrobial consumption. The Global-PPS on antimicrobial consumption and resistance, organized in 2015, 2017 and 2019 by BAPCOC/the University of Antwerp, has a similar approach. Detailed information on the methodology of each study can be found in the protocols of the ECDC-PPS (23) and Global-PPS (24).

In 2017, the ECDC- and Global-PPS were simultaneously organized in Belgian acute care hospitals. A random selection was made for the ECDC-PPS. In addition, other hospitals could voluntary participate in either the ECDC-PPS or the Global-PPS. Data had to be collected on one single day for each ward in the participating hospitals. All patients present at the ward at 8h00 a.m. and not discharged from the ward at the time of the survey had to be included. Data were collected on the hospital/ward (including the full-time equivalent (FTE) antimicrobial stewardship consultants, interpreted as the time that a consultant/pharmacist is specifically employed and paid for antimicrobial stewardship tasks) and patient level (including the consumption of antimicrobial agents). Several quality indicators were registered, e.g. if the reason of antimicrobial treatment was documented in the patient's notes, if a stop/review date was documented, and if the antibiotic prescription was being compliant with the local guidelines.

In this report, the Belgian results for the ECDC-PPS 2011, the Global-PPS 2015, the combined results of the ECDC-PPS and Global-PPS 2017, the Global-PPS 2019, and the European results of the ECDC-PPS 2017 are presented.

Table 1: Overview of the data sources used in this national report

	ESAC-Net	BeH-SAC	HALT/HALT-PSY	ECDC-PPS	Global-PPS
Data source	Reimbursement data	Reimbursement data	Data collected locally	Data collected locally	Data collected locally
Type of study	Surveillance	Surveillance	Point prevalence study	Point prevalence study	Point prevalence study
Setting	Community (including nursing homes) and hospitals (aggregated data)	Acute, specialised and psychiatric hospitals (data per hospital)	Long-term care facilities (mainly nursing homes), HALT-PSY: psychiatric hospitals and psychiatric wards in acute hospitals	Acute hospitals (inpatient wards)	Acute hospitals (inpatient wards)
Main indicator	DDDs/1000 inhabitants/day (DID)	DDDs/1000 patient days, DDDs/1000 admissions	Prevalence (%) of residents with at least one antimicrobial prescription on the day of the PPS	Prevalence (%) of patients with at least one antimicrobial prescription on the day of the PPS	Prevalence (%) of patients with at least one antimicrobial prescription on the day of the PPS
Included antimicrobial agents (ATC)	A07AA, D01BA, J01, J02, J04A, J05, P01AB	A07AA, D01BA, J01, J02, J04A, J05, P01AB	A07AA, D01BA, J01, J02, J04, P01AB	A07AA, D01BA, J01, J02, J04 (excluding treatment of mycobacteria), P01AB	A07AA, D01BA, J01, J02, J04A, J05, P01AB, P01B
Start year in Belgium	1997	2003	2010	2011	2015
Included years in the present report	2010-2019	2010-2019	HALT: 2010, 2013, 2016, HALT-PSY: 2017	Surveys in 2011 and 2017	Surveys in 2015, 2017 and 2019
Reporting	ESAC-Net interactive database (25), ESAC-Net report (26)	Healthstat: national and hospital feedback reports (27)	ECDC and national reports (28–30)	ECDC and national reports (31,32), hospital feedback reports	National/EU reporting (32,33); raw data in excel; one point, longitudinal and merged feedback reports

ATC = Anatomical Therapeutic Chemical classification; BeH-SAC = Belgian Hospitals - Surveillance of Antimicrobial Consumption; DDD = Defined Daily Dose; ECDC = European Center for Disease Prevention and Control; ESAC-Net = European Surveillance of Antimicrobial Consumption Network; Global/ECDC-PPS = Point Prevalence Study of antimicrobial consumption, resistance and healthcare-associated infections in acute hospitals; HALT = Point prevalence survey of Healthcare-associated infections and Antimicrobial use in Long-Term care facilities (HALT-PSY: in psychiatric institutions)

A07AA (intestinal anti-infectives), D01BA (antifungals for systemic use), J01 (antibacterials for systemic use), J02 (antimycotics for systemic use), J04 (antimycobacterials), J04A (drugs for treatment of tuberculosis), J05 (antivirals), P01AB (nitroimidazole-derived antiprotozoals), P01B (antimalarials)

DATA DEFINITIONS AND ANALYSIS

Antimicrobial agents are classified using the Anatomical Therapeutic Chemical (ATC) classification of the World Health Organization (WHO) Collaborating Centre for Drugs Statistics and Methodology, version December 2020 (2). Table 1 presents the included ATC codes per study. Administration routes that are included are oral (PO), intravenous (IV), intramuscular (IM), subcutaneous (SC), inhalation and rectal. Other topical use (e.g. transdermal via ointments) were excluded in the present report.

The indicators for broad-spectrum use were calculated in line with the outcome indicators jointly proposed by ECDC, the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) (34).

- For the community: the total DDDs of broad-spectrum penicillins, cephalosporins, macrolides and fluoroquinolones divided by the total DDDs of narrow-spectrum penicillins, cephalosporins and macrolides (J01(CR+DC+DD+(F-FA01)+MA) / J01(CA+CE+CF+DB+FA01))
- For hospitals: the percentage of consumed DDDs of broad-spectrum antibacterials among all antibacterials for systemic use (J01). The following products were included as broad-spectrum: piperacillin in combination with a beta-lactamase inhibitor (J01CR05), third- and fourth-generation cephalosporins (J01DD and J01DE), monobactams (J01DF), carbapenems (J01DH), fluoroquinolones (J01MA), glycopeptides (J01XA), polymyxins (J01XB), daptomycin (J01XX09) and oxazolidinones: linezolid (J01XX08) and tedizolid (J01XX11).

The Access, Watch and Reserve antibiotic classes are defined in accordance with the AWaRe classification of the WHO (version December 2019) (35). This antibiotic classification identifies three stewardship groups for optimal use and potential for antimicrobial resistance selection pressure: Access, Watch and Reserve.

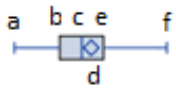
Consumed units/packages per drug were translated in defined daily doses (DDDs) based on the DDD classification of WHO (version December 2020) (2). Because the list of DDDs is updated every year and the calculations are retrospectively adjusted, this can lead to a variation in the published results over time. In 2019, there was an important adjustment in the DDD for several antibiotics (including amoxicillin, amoxicillin + clavulanic acid, meropenem, ciprofloxacin) which had an important impact on the Belgian results (based on the total antibiotic consumption in the community in 2017: 25.9 DID before the DDD adjustments and 21.1 DID after applying the new DDDs).
In addition, a national list of daily dose administrated (DDA) was used for BeH-SAC (version May 2019, validated by the working group Hospital Medicine of BAPCOC) (36). Compared to DDDs, DDAs are more in line with the actual doses administrated in Belgian acute hospitals.

Hospitals were classified in accordance with the list of hospitals of the Belgian Ministry of Health (Dienst Datamanagement - Directoraat-Generaal Gezondheidszorg, version December 2020) and in line with the definitions of ECDC (23,37). Hospitals in Belgium are divided in general and categorical hospitals (in the past indicated as chronic hospitals, n=8 in 2019). General hospitals are further classified in acute (n=104 in 2019) and psychiatric hospitals (n=59 in 2019). Furthermore, acute hospitals can be divided per type: primary (general, n=80 in 2019), secondary (general with a university character, n=17 in 2019) and tertiary (university, n=7 in 2019) hospitals.

In BeH-SAC, data presented for all inpatient wards include surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care (ICU), specialized care and psychiatry. Outpatient wards and day hospitalizations were excluded. In some chapters, where indicated, psychiatry units and neonatology/pediatric units were also excluded from the results.

Data on shortages of antimicrobial agents in Belgium in the last five years (January 2015 - January 2020) were collected from the PharmaStatus database from the Federal agency for medicines and health product (FAMHP) (38). PharmaStatus is a platform where pharmacists, wholesaler-distributors and pharmaceutical companies can communicate about shortages and commercialization of medicines in Belgium.

Data-analyses were performed with SAS Enterprise Guide 7.1. Median, interquartile range (IQR), range (minimum-maximum), 95th percentile (P95) and 5th percentile (P5) were calculated where appropriate. Boxplots and violin plots are used to present the evolution of the consumption in hospitals and the variability between hospitals. Outliers (outside 1.5x IQR) are not presented in the boxplots. Line graphs are used to indicate the evolution of the consumption and stacked bar plots to visualize the distribution of the consumption per antibiotic subclass.
Legend boxplot: a. maximum (without outliers, 1.5x interquartile range), b. 75 percentile (P75), c. median, d. mean, e. 25 percentile (P25), f. minimum (without outliers, 1.5x interquartile range)



Trends analysis of the total consumption over 10 years (2010-2019) were performed using linear regression. P-values <0.05 were considered as a significant trend (indicated with ↑ or ↓) and p-values <0.001 as a very significant trend (↑↑ or ↓↓).

In the PPS and HALT, the observed prevalence of patients/residents with at least one antimicrobial was calculated by dividing the number of patients/residents receiving at least one antimicrobial by the total number of eligible patients/residents. Patients/residents presenting with multiple antimicrobials on the PPS day were thus counted only once. Observed prevalences are presented along with their 95% confidence intervals (95%CI), where available.

RESULTS

COMMUNITY/PRIMARY CARE (INCLUDING NURSING HOMES)

Between 2010 and 2019, there was a significant decrease in the (reimbursed) antibiotic consumption (J01) in the community from 23.1 DID to 19.8 DID (-14.3%). The same significant decreasing trend was seen in PID (from 2.53 PID in 2011 to 2.01 PID in 2019, however slightly underestimated starting from 2015 due to the implementation of tarification per unit in Belgian nursing homes). The largest absolute decrease over this period was detected for fluoroquinolones (J01MA, -2.1 DID), penicillins in combination with beta-lactamase inhibitors (J01CR, -1.1 DID) and second-generation cephalosporins (J01DC: -0.3 DID). The consumption of macrolides (J01FA, +0.5 DID) and lincosamides (J01FF, +0.1 DID) increased.

In the last year (2019 in comparison with 2018), the overall antibiotic consumption further decreased (20.8 DID in 2018 and 19.8 DID in 2019). This was mainly due to a large decline (-0.6 DID, -51.3% in comparison with 2018) in the (reimbursed) consumption of fluoroquinolones (J01MA). A change in reimbursement criteria for fluoroquinolones starting from May 2018 onwards (reimbursement limited to a specific list of infections and conditions in the community (39)) coincided with this trend. The (reimbursed) consumption of all types of fluoroquinolones remarkably decreased (ofloxacin: -54.2%, 0.02 DID in 2019, 3.5% of J01MA; ciprofloxacin: -44.3%, 0.29 DID in 2019, 50.9% of J01MA; norfloxacin: -70.0%, 0.01 DID in 2019, 1.8% of J01MA; levofloxacin: -35.1%, 0.10 DID in 2019, 17.5% of J01MA; moxifloxacin: -63.2%, 0.15 DID in 2019, 26.3% of J01MA). The percentage (reimbursed) fluoroquinolone consumption of the total antibiotic consumption (% J01MA/J01) declined from 10.3% in 2017 to 5.6% in 2018 and to 2.9% in 2019. Worrisome, following the more strict reimbursement criteria for fluoroquinolones, the consumption of fluoroquinolones without reimbursement has increased significantly. Based on total sales data, we estimate that the total consumption of fluoroquinolones in 2019 (±1.4 DID, 6.7% of J01) has declined with 16% in comparison with 2018 (±1.6 DID, 7.7% of J01) and 37% in comparison with 2017 (2.2 DID). Taken this non-reimbursed consumption of fluoroquinolones into account, the total antibiotic consumption (J01) was estimated at 20.6 DID in 2019 (-10.8% in comparison with 2010).
There was an decrease in the (reimbursed) consumption of other antibacterial subgroups in comparison with 2018, especially for J01CR 'Combinations of penicillins, incl. beta-lactamase inhibitors' (-0.36 DID, -7.1%) and J01FA 'Macrolides' (-0.08 DID, -2.5%; mainly clarithromycin: -8.4%, azithromycin: increase of +2.1%). The consumption of J01XE ' Nitrofuran derivatives' (+0.08 DID, +3.4%) and J01CA 'Penicillins with extended spectrum' (+0.03 DID, +0.6%) increased. In 2019, Belgium had the second highest consumption of J01XE ' Nitrofuran derivatives' in the community (2.41 DID) compared to other European Union (EU)/European Economic Area (EEA) countries (the Netherlands: 1.30 DID, France: 0.17 DID) (25). In Belgium, nitrofurantoin is the first-line treatment for acute cystitis (40).

The top 5 of most used antibiotic products in 2019 consisted of amoxicillin (J01CA04, 4.82 DID), amoxicillin in combination with clavulanic acid (J01CR02, 4.70 DID), nitrofurantoin (J01XE01, 2.41 DID), azithromycin (J01FA10, 1.98 DID) and cefuroxime (J01DC02, 1.17 DID). Within the subgroups of penicillins, the ratio of amoxicillin (J01CA04) versus amoxicillin in combination with a beta-lactamase inhibitor (J01CR02) changed from 0.85 (46/54) in 2010 to 1.04 (51/49) in 2019.

The ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and macrolides decreased from 2.38 in 2010 to 1.94 in 2019. Over all 30 EU/EEA countries participating in ESAC-Net, the mean of this ratio in 2019 was 2.84 (country range 0.1-20.1) (26). In Belgium, the percentage of this broad-spectrum consumption of penicillins,

cephalosporins, macrolides and fluoroquinolones of the total antibiotic consumption changed from 54.3% in 2010 to 48.1% in 2019.

In Figure 2, the evolution of the total antibiotic consumption in Belgium is compared with our neighboring countries (the Netherlands in 2019: 8.7 DID, change 2010-2019: -13%; France in 2019: 23.3 DID, change 2010-2019: +0.4%) and with the EU/EEA mean (18.0 DID in 2019, change 2010-2019: -5%). The antibiotic consumption in Belgium is still higher than the EU/EEA mean and twice as high as the consumption in the Netherlands, but lower than in France.

Detailed results on the consumption of other antimicrobial products can be found in Table 3. The (reimbursed) consumption of antimycotics for systemic use (J02) in the community in 2019 remained similar as the previous year (-0.01 DID, -0.8%). Over a 10-year period, the total antimycotic consumption significantly decreased from 1.49 DID in 2010 to 1.18 DID in 2019 (fluconazole: 0.67 DID, itraconazole: 0.49 DID). Although a significant decrease over time is seen, the antimycotic consumption in Belgium is still 3 to 6 times higher than our neighboring countries (see Figure 3). The same is true for the consumption of terbinafine (D01BA02, 1.78 DID in 2018, 2-3 times higher than our neighboring countries). With a total consumption of 3.0 DID in 2019 (2010-2019: significant decrease, -9%), Belgium is among the highest consumers of antimycotics and antifungals (J02 and D01B) out of all participating EU/EEA countries in ESAC-Net (EU/EEA mean in 2019: 1.0 DID, country range 0.4-3.0, the Netherlands 1.3 DID, France 1.3 DID) (26).

Table 2: Evolution (2010-2019) of antibiotic consumption in the community (nursing homes included) per antibiotic subclass (ESAC-Net 2019, Belgium)

ATC	Name antibiotic class	DDDs/1000 inhabitants/day (DID)													
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Change (%) 2018-2019	Evolution 2010-2019	10-year trend[a]	% total J01 use (2019)
J01AA	Tetracyclines	2.10	2.09	2.11	2.16	2.1	2.03	1.99	1.92	1.88	1.86	-1.06		↓↓	9.39
J01BA	Amphenicols	0.03	0.03	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02	0.00		↓	0.10
J01CA	Penicillins with extended spectrum	4.85	4.92	5.16	5.21	4.87	5.01	5.01	4.73	4.79	4.82	0.63			24.34
J01CE	Beta-lactamase sensitive penicillins	0.09	0.05	0.03	0.03	0.03	0.03	0.03	0.02	0.02	0.01	-50.00		↓	0.05
J01CF	Beta-lactamase resistant penicillins	0.26	0.26	0.25	0.26	0.25	0.25	0.26	0.25	0.26	0.27	3.85			1.36
J01CR	Combinations of penicillins. incl. beta-lactamase inhibitors	5.76	5.91	6.02	4.37	4.76	4.8	4.92	4.74	5.06	4.70	-7.11		↓	23.74
J01DB	First-generation cephalosporins	0.13	0.12	0.12	0.11	0.1	0.1	0.08	0.05	0.05	0.03	-40.00		↓↓	0.15
J01DC	Second-generation cephalosporins	1.47	1.40	1.41	1.42	1.32	1.34	1.24	1.12	1.2	1.17	-2.50		↓	5.91
J01EE	Combinations of sulfonamides and trimethoprim. incl. derivatives	0.26	0.30		0.27	0.18	0.21	0.20	0.19	0.21	0.21	0.00		↓	1.06
J01FA	Macrolides	2.62	2.86	3.05	2.99	3.04	3.27	3.24	3.03	3.17	3.09	-2.52		↑	15.61
J01FF	Lincosamides	0.30	0.31	0.34	0.35	0.35	0.37	0.38	0.38	0.4	0.42	5.00		↑↑	2.12
J01GB	Aminoglycosides	0.01	0.01	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.00			0.05
J01MA	Fluoroquinolones	2.69	2.73	2.77	2.64	2.55	2.57	2.4	2.17	1.17 1.63[c]	0.57 1.37[c]	-51.28		↓	2.88
J01XB	Polymyxins	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00			0.05
J01XE	Nitrofuran derivatives	2.39	2.45	2.48	2.54	2.59	2.57	2.59	2.34	2.33	2.41	3.43			12.17
J01XX	Other antibacterials	0.13	0.14	0.15	0.15	0.16	0.16	0.15	0.16	0.17	0.18	5.88		↑↑	0.91
J01	**Antibiotics for systemic use**	**23.11**	**23.60**	**23.94**	**22.57**	**22.36**	**22.75**	**22.53**	**21.14**	**20.77** 21.23[c]	**19.80** 20.59[c]	**-4.67**		↓↓	100.00
		Packages/1000 inhabitants/day (PID)													
J01	**Antibiotics for systemic use**		**2.53**	**2.54**	**2.51**	**2.42**	**2.45**[b]	**2.36**[b]	**2.17**[b]	**2.10**[b]	**2.01**[b]	**-4.29**[b]		↓↓ *	100.00

Classes with no consumption in 2019 are not shown in the table, blanks: data not available for those years.
2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)
[a] Lineair regression: ↑/↑↑ = positive significant trend; ↓/↓↓ = negative significant trend; ↑/↓ = p<0.05 but ≥0.001; ↑↑/↓↓ = p<0.001
[b] Calculated without the tarification in units in nursing homes (small underestimation starting from 2015).
[c] If the the non-reimbursed consumption of fluoroquinolones (estimated based on sales data) is taken into account.

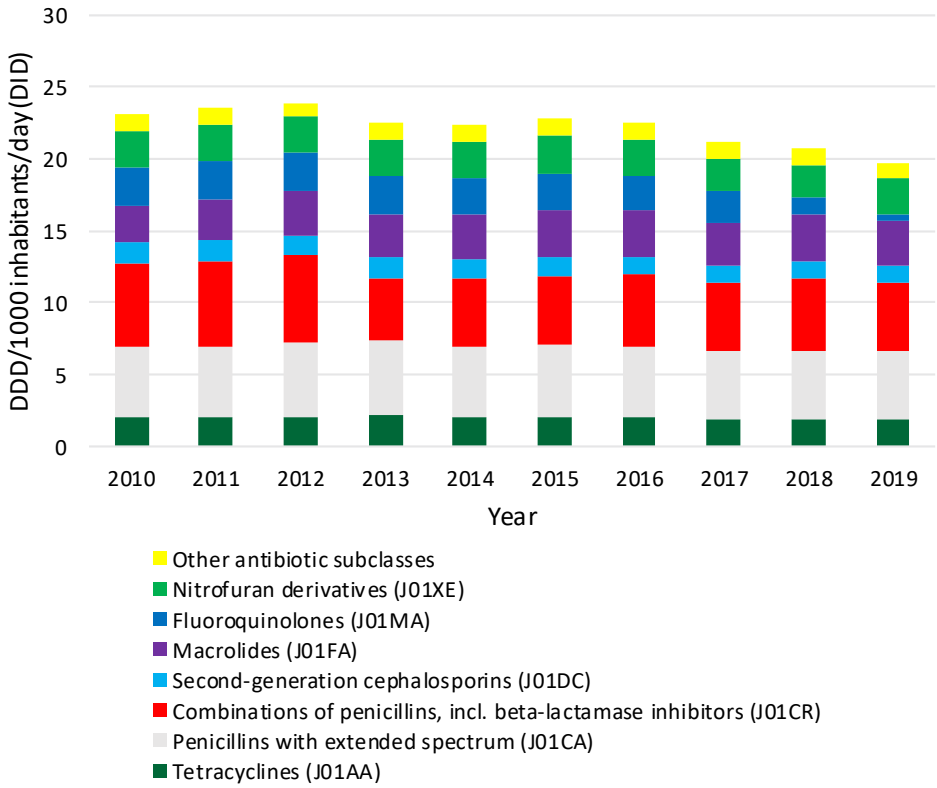
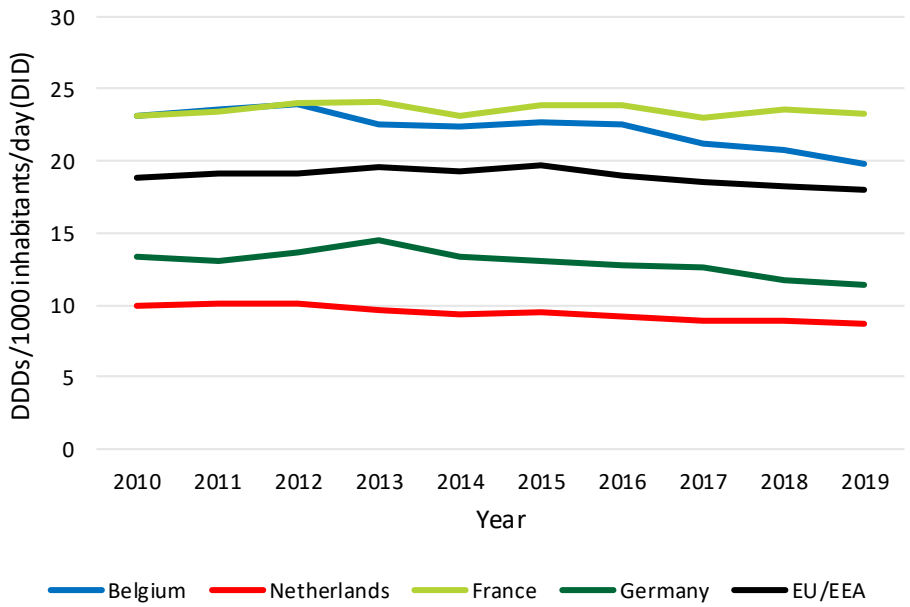


Figure 1: Stacked bar plot with the evolution (2010-2019) of antibiotic consumption in the community (nursing homes included) per antibiotic subclass (ESAC-Net 2019, Belgium)



* EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data in ESAC-Net of all 30 European Union (EU)/European Economic Area (EEA) countries

Figure 2: Evolution (2010-2019) of total antibiotic consumption (J01) in the community in Belgium, the Netherlands, France, Germany and the mean in the EU/EEA countries (ESAC-Net 2019 (25,26))

Table 3: Evolution (2010-2019) of the consumption of other antimicrobial products in the community (nursing homes included) per subclass (ESAC-Net 2019, Belgium)

ATC	Name antibiotic class	DDDs/1000 inhabitants/day (DID)												
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Change (%) 2018-2019	Evolution 2010-2019	10-year trend[a]
A07AA	Intestinal antibiotics							0.04	0.04	0.04	0.07	75.00		
D01BA	Antifungals for systemic use	1.76	1.82	1,88	1,84	1,82	1,83	1,84	1,82	1,82	1,78	-2.20		
J02AC	Antimycotics for systemic use: triazole derivatives	1.41	1.41	1.39	1.34	1.33	1.3	1.27	1.21	1.19	1.18	-0.84		↓↓
P01AB	Nitroimidazole derivatives	0.13	0.13	0.13	0.13	0.14	0.14	0.14	0.14	0.14	0.14	0.00		↑
J04A	Drugs for treatment of tuberculosis	0.23	0.23	0.22	0.05	0.05	0.05	0.20	0.20	0.21	0.21	0.00		
J05	Antivirals for systemic use	1.08	1.45	0.93	1.49	1.33	1.44	1.73	1.81	1.94	1.85	-4.64		↑

Classes with no consumption in 2019 are not shown in the table, blanks: data not available for those years
2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)
[a] Lineair regression: ↑/↑↑ = positive significant trend; ↓/↓↓ = negative significant trend; ↑/↓ = p<0.05 but ≥0.001; ↑↑/↓↓ = p<0.001

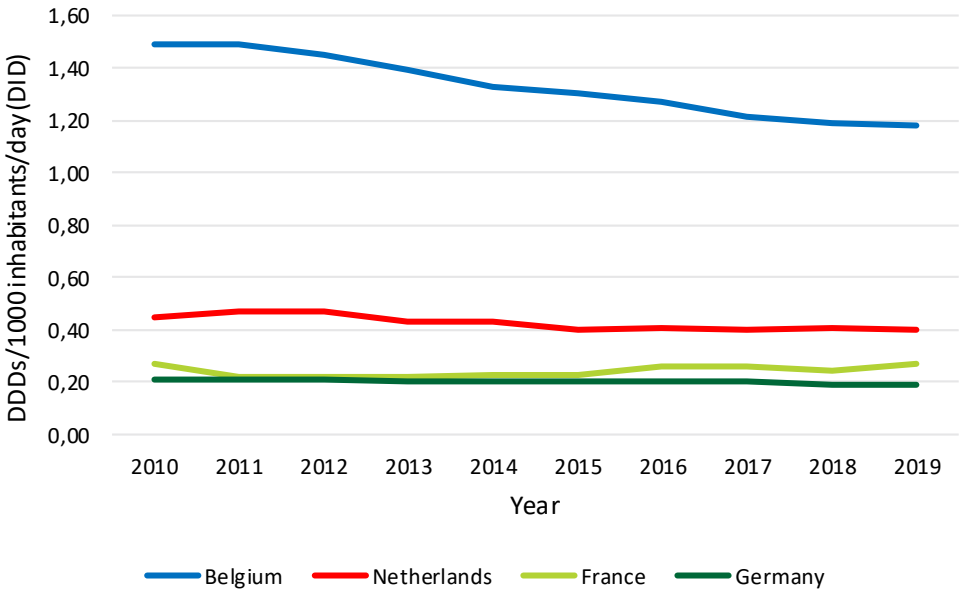


Figure 3: Evolution (2010-2019) of total antimycotic consumption (J02) in the community in Belgium, the Netherlands, France and Germany (ESAC-Net 2019 (25))

More results on antimicrobial consumption in the community in Belgium can be consulted through the following sources:

- The online interactive database of ESAC-Net with the results of all participating EU/EEA countries at the ATC 4 level: website (25) or in the latest report of ESAC-Net (26)
- Analyses of antibiotic consumption by patient and prescriber characteristics (2016) in the report of the Belgian Knowledge Centre (chapter 4.4) (14)
- Individual feedback reports to prescribers, specialists and nursing homes from NIHDI (41)
- Research of Struyf et al. on antimicrobial prescribing by Belgian dentists in ambulatory care (2010 to 2016) (42)
- Research of Colliers et al. on disease-specific antibiotic prescribing quality indicators in out-of-hours primary care (43)
- Research of Bruyndonckx et al. on the impact of two decades of national campaigns on antibiotic consumption and resistance in Belgium (44)
- Research of Bruyndonckx et al. on the trends (1997-2017) of consumption of antibiotics in the community in EU/EAA countries, based on ESAC-Net data (10 manuscripts under revisions in Journal of Antimicrobial Chemotherapy)
- Research of Goemaere et al. on antifungal use in Belgium (2003 to 2016) (45)
- IFEB-IPhEB: newsletters of analyses on the IFSTAT database (https://www.ipheb.be/crbst_29_nl.html)

NURSING HOMES

In 2016, the observed prevalence of residents with at least one antimicrobial prescription on the day of the study in nursing homes was 5.6%. This prevalence increased in comparison with the HALT study in 2010 (4.3%) and 2013 (5.1%). Most prescribed antibiotic subclasses (treatment and prophylaxis) were other antibacterials (J01X, including nitrofuran derivates), penicillins (J01C) and quinolone antibacterials (J01M). One-third (35.8%) of the prescriptions were for prophylactic use. Antimicrobials were most frequently prescribed for urinary tract infections (50.4%). More results are presented in Table 4.

Table 4: Summary table of the main results on antimicrobial consumption of HALT-1 to 3 in Belgian nursing homes and HALT-3 in EU/EEA long-term care facilities

	HALT-1 Belgium (2010) (29)	**HALT-2 Belgium (2013)** (30)	**HALT-3 Belgium (2016)** (28)	**HALT-3 EU/EEA[a] (2016-2017)** (46)
Number of included NHs	107	87	158	1797 (NHs, residential homes and mixed LTCFs included)
Number of eligible residents	11911	8756	16215	102301
Number of residents with at least one AM prescription on one day	514	443	900	5035
Observed prevalence (% and 95%CI)	4.3 (4.0-4.7)	5.1 (4.6-5.5)	5.6[b] (5.2-5.9)	4.9 (4.8-5.1)
Mean prevalence (%)	4.6	5.4	5.5[b]	5.8
Median prevalence (% and IQR)	4.3 (1.9-6.1)	4.7 (2.1-8.2)	5.0 (2.9-7.9)[b]	3.6 (0.0-8.5%)
Number of prescription for AMs	534	455	928	5344
Top 3 most used antibiotics (% of all antibiotic prescriptions)	J01X:38.7% J01C: 27.6% J01M: 21.0%	J01X:48.2% J01C: 24.0% J01M: 15.3%	J01X:40.6% J01C: 26.9% J01M: 15.5%	J01C: 30.2% J01X: 18.6% J01M: 14.9%
Top 3 most common diagnoses (% of all AM prescriptions, treatment or prophylaxis)	UTI: 50.3% RTI: 31.4% Skin or wound infections: 11.3%	UTI: 57.4% RTI: 27.3% Skin or wound infections: 8.4%	UTI: 50.4% RTI: 31.5% Skin or wound infections: 8.8%	UTI: 46.1% RTI: 29.4% Skin or wound infections: 12.6%

Data presented where available in the concerning reports
AM = antimicrobial; IQR = interquartile range; LTCFs = long-term care facilities; NH = nursing home; RTI = respiratory tract infections; UTI = urinary tract infections; 95%CI = 95% confidence intervals
J01C = Penicillins; J01M = Quinolone antibacterials; J01X = Other antibacterials (including nitrofuran derivates)
[a] EU/EEA: 24 European Union (EU)/European Economic Area (EEA) countries
[b] results of the randomized selected subset of Belgian LTCFs (n=79, 8206 residents) used for the EU/EEA results (46):

- Observed prevalence: 5.9% (95%CI 5.4-6.4%)
- Mean prevalence: 5.8%
- Median prevalence: 5.1% (IQR: 2.9-8.1%)

More results on antimicrobial consumption in Belgian and European nursing homes and long-term care facilities can be found in:

- The national HALT-3 report (28)
- The HALT-3 report of ECDC (https://www.ecdc.europa.eu/en/healthcare-associated-infections-long-term-care-facilities)
- Paper of Ricchizzi et al. with the main HALT-3 results regarding antimicrobial use (46)

HOSPITALS

ALL SORTS OF HOSPITALS (ACUTE/CATEGORICAL/PSYCHIATRIC)

Based on the results of ESAC-Net in DID, presented in Table 5 and Figure 4 (stacked bar plot per antibiotic subclass), a significant decrease was detected between 2010 and 2019 in the total (reimbursed) antibiotic consumption across all sorts of Belgian hospitals (acute/categorical/psychiatric). In 2019, the estimated total antibiotic consumption was 1.54 DID (-12.5% in comparison with 2010, -4.9% in comparison with 2018).

In BeH-SAC (see Table 6), results are available per sort of hospital and with the hospital population as denominator. A significant increase (2010-2019) was seen in the total (reimbursed) antibiotic consumption in acute hospitals in DDDs/1000 patient days (+3.4%), and a significant decrease (2010-2018) in DDDs/1000 admissions (-6.0%). This difference can be explained by the evolution towards shorter hospital stays in acute hospitals (a shift towards ambulatory care), with a more intensive antibiotic treatment on less patient days and hence an increase in DDDs/1000 patient days. In 2019, the total (reimbursed) antibiotic consumption in acute hospitals was 457.8 DDDs/1000 patient days (2018: 3275.5 DDDs/1000 admissions). In categorical hospitals (2018: 130.8 DDDs/1000 patient days), there was no significant change in the total (reimbursed) antibiotic consumption in DDDs/1000 patient days between 2010 and 2018. In psychiatric hospitals (2019: 31.5 DDDs/1000 patient days), there was a small significant decrease in the total (reimbursed) antibiotic consumption in DDDs/1000 patient days between 2010 and 2019.

In acute hospitals, the most used antibiotic subclasses in 2019 were penicillins in combination with beta-lactamase inhibitors (J01CR, 34.0% of J01), fluoroquinolones (J01MA, 10.2% of J01) and first-generation cephalosporins (J01DB, 8.1% of J01). Over the 10-year period, the largest absolute increase was detected for beta-lactamase resistant penicillins (J01CF, +9.2 DDDs/1000 patients days) and penicillins with extended spectrum (J01CA, +7.6 DDDs/1000 patient days). The largest absolute decrease was seen for fluoroquinolones (J01MA, -14.7 DDDs/1000 patient days) and penicillins in combination with beta-lactamase inhibitors (J01CR, -7.2 DDDs/1000 patient days).

In Figure 5 (in DID) and in Figure 6 (in DDDs/1000 patient days and DDDs/1000 admissions), the total antibiotic consumption in Belgian hospitals is compared with other European countries. As methodologies/definitions can differ between countries, this comparison has to be carefully interpreted and can only offer a rough estimation. In DID, the antibiotic consumption in Belgian hospitals is higher than the Netherlands (0.80 DID in 2019, change 2010-2019: -14%), but comparable with France (1.74 DID in 2019, change 2010-2019: -4%)/Sweden/Denmark and slightly lower than the EU/EEA mean (1.77 DID in 2019, change 2010-2019: +0%). The antibiotic consumption in acute hospitals in DDDs/1000 patient days is, except for France, lower than the other countries (Sweden/Denmark/Netherlands). In contrary, the antibiotic consumption in DDDs/1000 admissions is higher than in these countries (Sweden/Denmark). These differences underlie the importance of looking at different indicators side by side.

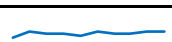
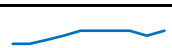
Detailed results on the consumption of other antimicrobial products in all sorts of hospitals can be found in Table 7. The (reimbursed) consumption of antimycotics for systemic use (J02) in the hospitals was 0.09 DID in 2019 (-0.01 DID in comparison with 2018). Between 2010 and 2019, there was a significant decrease (-0.04 DID) in the use of triazole derivates. Looking at the total consumption of antimycotics and antifungals (J02 and D01B), also a significant decrease was seen between 2010 (0.13 DID) and 2019 (0.09 DID, -28%, EU/EEA mean in 2019: 0.12 DID, France 0.21 DID (26)).

The main results of the ECDC- and Global-PPS (2011, 2015, 2017, 2019) in Belgian and European acute hospitals are presented in Table 8. In 2019, the observed prevalence of patients with at least one antimicrobial prescription in Belgian acute hospitals was 27.8% (95%CI 27.1-28.4%, in EU/EEA countries in 2017: 32.9%). Most used antibiotics were amoxicillin in combination with a beta-lactamase inhibitor (J01CR02, 26.0%), cefazolin (J01DB04,

10.3%) and piperacillin in combination with a beta-lactamase inhibitor (J01CR05, 9.1%). The most common diagnosis for treatment was pneumonia (25.3% of all prescriptions). Surgical prophylaxis was registered as indication in 12.3% of the prescriptions, of which 18.9% treatment longer than one day. The reason for prescription and a stop/review data were recorded in the medical file in 85.2% and 49.9% of the prescription, respectively. Of the antibiotic prescriptions (therapeutic use), 83.7% were registered as compliant with local guidelines.

Finally, results of the HALT-PSY study can be found in Table 9. In 2017, the observed prevalence of residents with at least one antimicrobial prescription on the day of the study was 3.8% (95%CI 3.2-4.3%) in psychiatric hospitals and 3.7% (95%CI 2.5-5.3%) on psychiatric wards in acute hospitals.

Table 5: Evolution (2010-2019) of antibiotic consumption in the hospitals (all sorts combined) per antibiotic subclass, expressed in DDDs/1000 inhabitants/day (ESAC-Net 2019, Belgium)

ATC	Name antibiotic class	DDDs/1000 inhabitants/day (DID)												
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019[a]	Change (%) 2018-2019	Evolution 2010-2019	10-year trend[b]	% of total J01 use (2019)
J01AA	Tetracyclines	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	-4.38		↓	0.99
J01BA	Amphenicols	0	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-39.53			0.02
J01CA	Penicillins with extended spectrum	0.07	0.07	0.07	0.07	0.07	0.08	0.08	0.08	0.09	0.08	-12.09		↑↑	5.19
J01CE	Beta-lactamase sensitive penicillins	0.08	0.07	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.04	90.00			2.47
J01CF	Beta-lactamase resistant penicillins	0.09	0.09	0.09	0.09	0.09	0.09	0.10	0.10	0.11	0.10	-7.41		↑↑	6.49
J01CR	Combinations of penicillins incl. beta-lactamase inhibitors	0.62	0.61	0.62	0.57	0.56	0.58	0.56	0.54	0.54	0.51	-6.99		↓↓	32.86
J01DB	First-generation cephalosporins	0.14	0.12	0.13	0.13	0.14	0.14	0.14	0.13	0.14	0.13	-2.90			8.70
J01DC	Second-generation cephalosporins	0.08	0.08	0.08	0.09	0.08	0.08	0.08	0.08	0.08	0.08	-1.28			5.00
J01DD	Third-generation cephalosporins	0.09	0.10	0.10	0.09	0.09	0.10	0.09	0.09	0.10	0.10	-1.01			6.36
J01DE	Fourth-generation cephalosporins	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	25.00		↓↓	0.65
J01DF	Monobactams	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	25.00		↑	0.32
J01DH	Carbapenems	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.04	-14.29			2.73
J01EE	Combinations of sulfonamides and trimethoprim incl. derivatives	0.02	0.03					0.04	0.04	0.04	0.04	13.21		↑	2.73
J01FA	Macrolides	0.06	0.06	0.06	0.06	0.06	0.07	0.07	0.07	0.07	0.07	3.47		↑↑	4.65
J01FF	Lincosamides	0.03	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	-4.52		↑	2.47
J01GB	Aminoglycosides	0.04	0.04	0.04	0.03	0.03	0.03	0.03	0.02	0.02	0.02	-3.98		↓↓	1.41
J01MA	Fluoroquinolones	0.24	0.24	0.23	0.22	0.21	0.21	0.20	0.19	0.17	0.15	-11.11		↓↓	9.87
J01XA	Glycopeptide antibacterials	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	-10.79			2.42
J01XB	Polymyxins	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-3.85			0.16

J01XD	Imidazole derivatives	0.03	0.02	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	3.05		↓	1.32
J01XE	Nitrofuran derivatives	0.04	0.07	0.06	0.06	0.05	0.05	0.05	0.04	0.04	0.03	-7.56		↓	2.14
J01XX	Other antibacterials	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	-1.40		↑↑	1.37
J01	**Antibiotics for systemic use**	**1.76**	**1.76**	**1.70**	**1.64**	**1.62**	**1.64**	**1.64**	**1.62**	**1.62**	**1.54**	**-4.94**		↓↓	**100.00**

Classes with no consumption in 2019 are not shown in the table, blanks: data not available for those years

2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)

[a] 2019 data are an estimation (15% extrapolation), see methods section

[b] Lineair regression: ↑/↑↑ = positive significant trend; ↓/↓↓ = negative significant trend; ↑/↓ = p<0.05 but ≥0.001; ↑↑/↓↓ = p<0.001

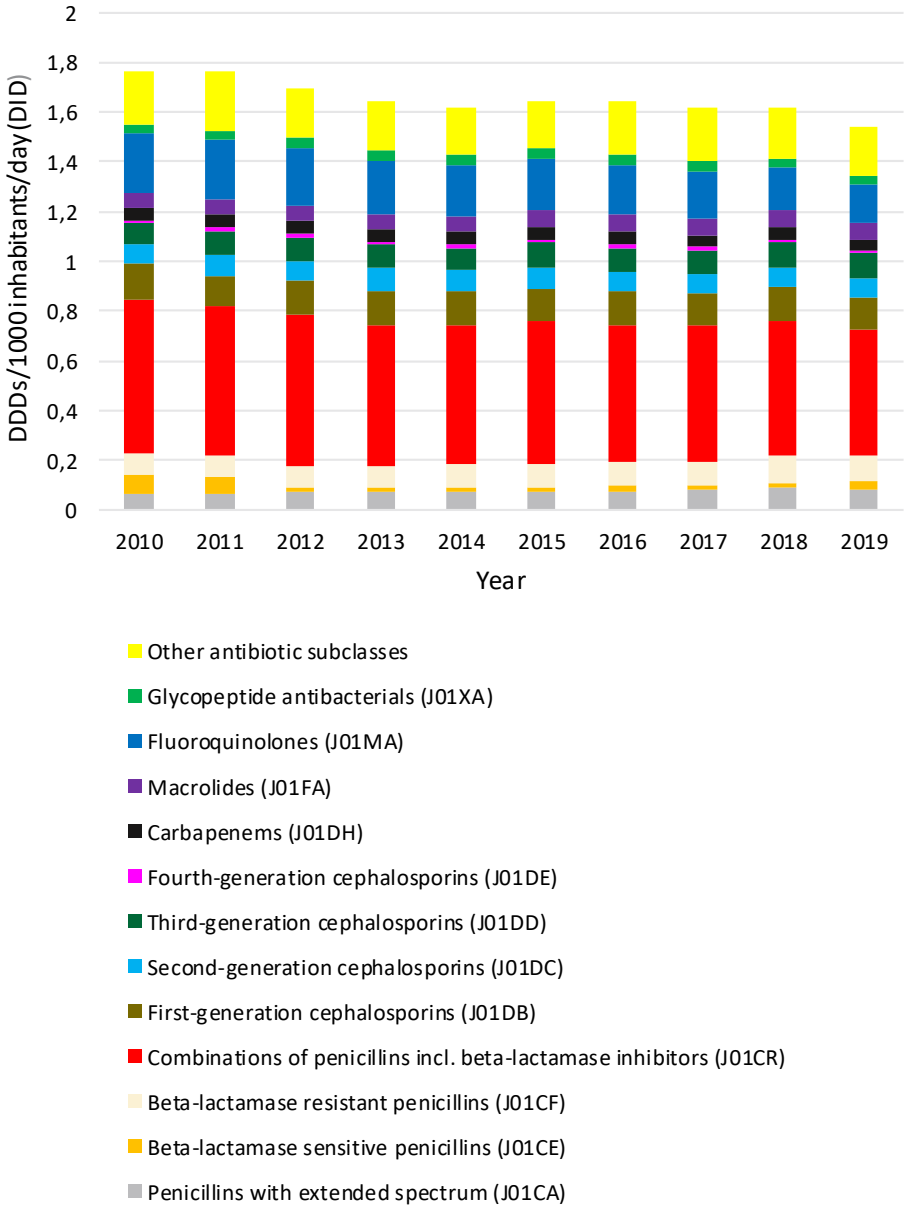
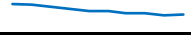


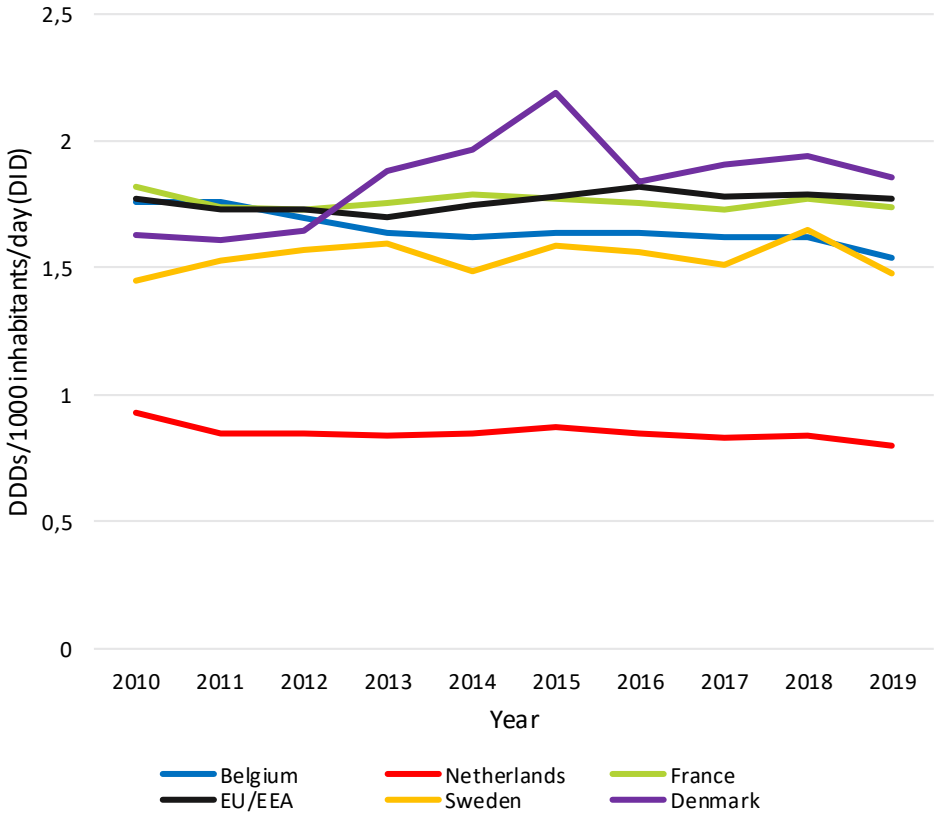
Figure 4: Stacked bar plot with the evolution (2010-2019) of antibiotic consumption in the hospitals (acute/categorical/psychiatric) per antibiotic subclass (ESAC-Net 2019, Belgium)

Table 6: Evolution (2010-2019) of antibiotic consumption in the hospitals per sort of hospital (acute/categorical/psychiatric , inpatient wards[a]) and antibiotic subclass, expressed in DDDs/1000 patient days and DDDs/1000 admissions (BeH-SAC, Belgium)

ATC	Name antibiotic class	DDDs/1000 patient days													
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Change (%) 2018-2019	Evolution 2010-2019	10-year trend[c]	% of total J01 use (2019)
Acute hospitals (n=103[b] in 2019)															
J01AA	Tetracyclines	3.42	3.33	3.26	3.10	3.32	3.37	3.61	3.74	3.55	3.82	7.61		↑	0.83
J01BA	Amphenicols	0.09	0.09	0.21	0.16	0.09	0.09	0.11	0.10	0.10	0.06	-40.00			0.01
J01CA	Penicillins with extended spectrum	14.80	15.33	16.25	16.56	17.51	18.19	19.17	20.39	23.94	22.36	-6.60		↑↑	4.88
J01CE	Beta-lactamase sensitive penicillins	4.71	4.57	4.90	5.00	5.25	5.18	5.36	5.62	5.85	7.25	23.93		↑	1.58
J01CF	Beta-lactamase resistant penicillins	23.30	23.32	23.80	25.78	27.13	26.62	28.71	30.26	32.53	32.51	-0.06		↑↑	7.10
J01CR	Combinations of penicillins. incl. beta-lactamase inhibitors	162.61	163.06	167.79	157.67	157.54	162.69	159.20	159.48	159.40	155.46	-2.47			33.96
J01DB	First-generation cephalosporins	33.14	33.76	34.22	35.18	36.39	36.51	36.95	37.37	38.39	37.29	-2.87		↑↑	8.15
J01DC	Second-generation cephalosporins	20.27	21.26	22.22	25.24	24.21	23.97	23.25	23.40	23.39	23.50	0.47			5.13
J01DD	Third-generation cephalosporins	24.51	26.06	25.35	25.86	25.18	26.99	26.66	27.44	28.60	29.51	3.18		↑↑	6.45
J01DE	Fourth-generation cephalosporins	4.48	4.35	3.87	3.70	3.61	3.63	3.26	3.45	2.51	3.26	29.88		↓↓	0.71
J01DF	Monobactams	0.42	0.52	0.50	0.64	0.67	0.66	0.63	0.66	0.66	0.71	7.58		↑	0.16
J01DH	Carbapenems	14.32	14.89	14.40	14.34	15.26	15.45	15.02	14.85	14.89	14.28	-4.10			3.12
J01DI	Other cephalosporins and penems	0	0	0	<0.01	0.01	0.02	<0.01	0.02	0.02	0.03	50.00		↑↑	0.01
J01EE	Combinations of sulfonamides and trimethoprim	7.72	7.81	7.72	8.01	8.33	7.94	8.16	8.63	8.36	9.52	13.88		↑	2.08
J01FA	Macrolides	15.74	16.02	17.44	17.40	17.98	19.16	19.51	20.61	20.76	21.30	2.60		↑↑	4.65
J01FF	Lincosamides	8.76	9.55	10.16	10.28	10.46	11.13	11.26	11.84	11.59	11.71	1.04		↑↑	2.56
J01GB	Aminoglycosides	10.18	9.73	9.10	8.10	7.74	7.35	6.81	6.40	6.03	5.95	-1.33		↓↓	1.30
J01MA	Fluoroquinolones	61.47	62.93	61.07	58.55	56.87	57.62	56.00	54.21	49.52	46.82	-5.45		↓↓	10.23
J01XA	Glycopeptide antibacterials	10.54	10.68	10.65	10.85	11.19	11.57	11.84	12.07	12.03	11.86	-1.41		↑↑	2.59

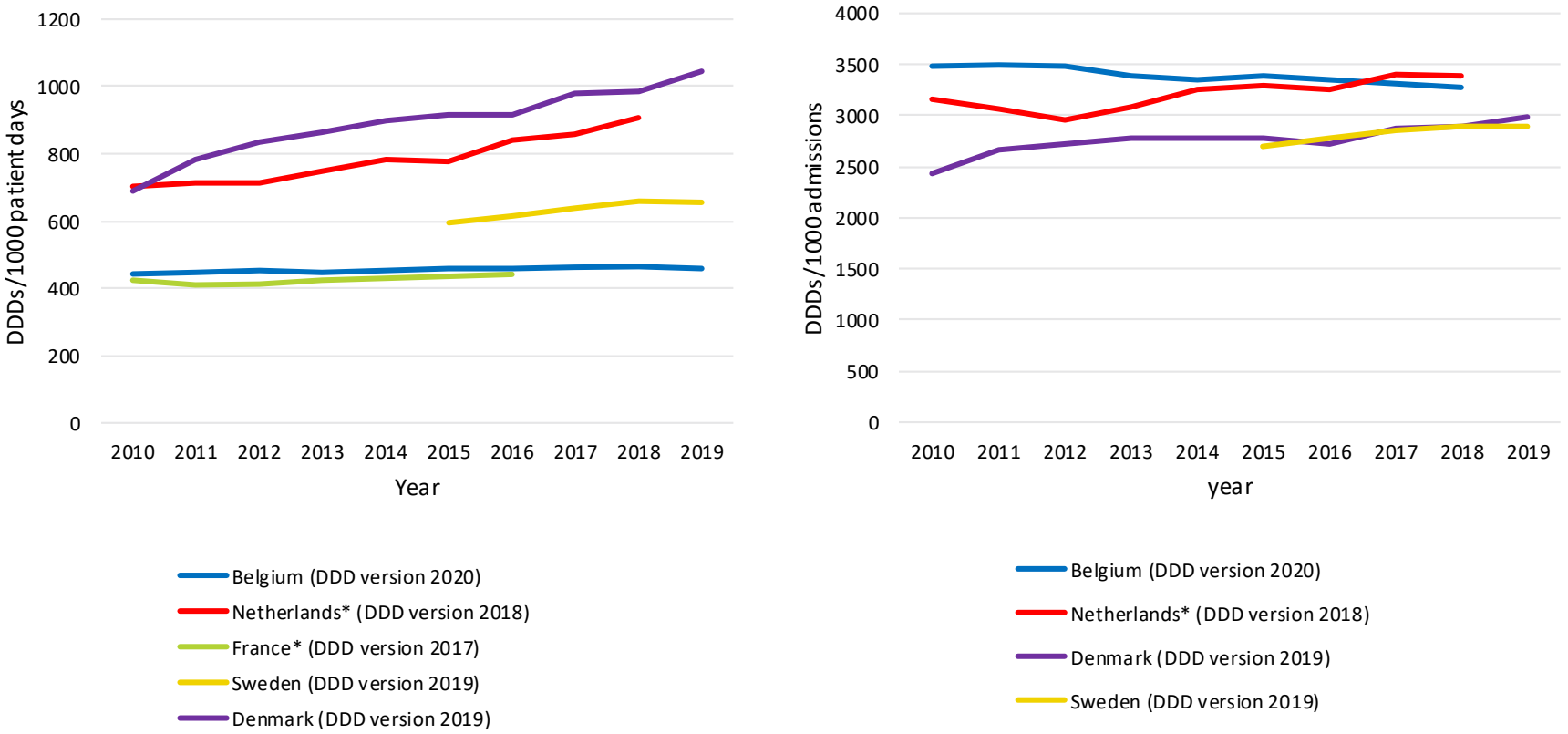
J01XB	Polymyxins	0.62	0.69	0.68	0.78	0.81	0.74	0.90	0.83	0.65	0.59	-9.23			0.13
J01XD	Imidazole derivatives	6.90	7.05	7.39	7.57	7.79	7.97	7.72	7.80	7.50	8.08	7.73		↑	1.77
J01XE	Nitrofuran derivatives	12.03	12.07	11.49	11.38	11.13	11.31	10.99	9.89	8.13	8.08	-0.62		↓↓	1.77
J01XX	Other antibacterials	2.77	2.90	2.93	3.15	3.23	3.37	3.53	3.58	3.72	3.85	3.49		↑↑	0.84
J01	**Antibiotics for systemic use**	**442.79**	**449.99**	**455.40**	**449.32**	**451.71**	**461.53**	**458.67**	**462.64**	**462.14**	**457.77**	**-0.95**		↑	**100.00**
Categorical hospitals (n=8 in 2018)															
J01	**Antibiotics for systemic use**	**154.58**	**149.76**	**139.94**	**131.45**	**147.06**	**148.92**	**139.40**	**136.74**	**130.80**					**100.00**
Psychiatric hospitals (n=59 in 2019)															
J01	**Antibiotics for systemic use**	**36.05**	**34.92**	**36.43**	**36.36**	**35.10**	**36.35**	**34.67**	**33.72**	**33.35**	**31.52**	**-5.49**		↓	**100.00**
		DDDs/1000 admissions													
Acute hospitals (n=103[b] in 2019)															
J01	**Antibiotics for systemic use**	**3486.0**	**3494.8**	**3484.0**	**3389.0**	**3348.5**	**3397.1**	**3350.6**	**3309.9**	**3275.5**				↓↓	**100.00**

Classes with no consumption in 2019 are not shown in the table, blanks: data not available for those years
2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)
[a] inpatient wards include surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care (ICU), specialized care and psychiatry (outpatient wards and day hospitalizations excluded)
[b] exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)
[c] Lineair regression: ↑/↑↑ = positive significant trend; ↓/↓↓ = negative significant trend; ↑/↓ = p<0.05 but ≥0.001; ↑↑/↓↓ = p<0.001



* EU/EEA refers to the corresponding population-weighted mean consumption based on reported antimicrobial consumption data in ESAC-Net of all 30 European Union (EU)/European Economic Area (EEA) countries

Figure 5: Evolution (2010-2019) of total antibiotic consumption (J01) in hospitals, expressed in DDDs/1000 inhabitants/day (DID), in Belgium, the Netherlands, France, Germany, Sweden, Denmark and the mean in the EU/EEA countries (ESAC-Net 2019 (25,26))



* calculated with the WHO DDD version of 2017/2018 in the national reports (leading to an overestimation in comparison with the other countries where WHO DDD version 2019/2020 is used)
As methodologies/definitions can differ between countries, this comparison has to be interpreted carefully and can only offer a rough estimation.

Figure 6: Evolution (2010-2019) of total antibiotic consumption (J01) in acute or general hospitals, expressed in DDDs/1000 patient days (left) and DDDs/1000 admissions (right), in Belgium, the Netherlands, France, Sweden and Denmark (BeH-SAC and national reports (27,47–50))

Table 7: Evolution (2010-2019) of the consumption of other antimicrobial products in hospitals (all sorts combined) per subclass, expressed in DDDs/1000 inhabitants/day (ESAC-Net 2019, Belgium)

ATC	Name antibiotic class	DDDs/1000 inhabitants/day (DID)												
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019[a]	Change (%) 2018-2019	Evolution 2010-2019	10-year trend[b]
A07AA	Intestinal antibiotics							0.02	0.02	0.02	0.03	11.64		
D01BA	Antifungals for systemic use	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-36.36		↓
J02AA	Antimycotics for systemic use: antibiotics	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	-19.66		
J02AB	Antimycotics for systemic use: imidazole derivatives	<0.01	<0.01	<0.01	<0.01	0	0	0	0	0	0	0.00		↓
J02AC	Antimycotics for systemic use: triazole derivatives	0.11	0.11	0.11	0.10	0.09	0.09	0.09	0.09	0.08	0.07	-10.74		↓↓
J02AX	Antimycotics for systemic use: other	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	-12.24		
P01AB	Nitroimidazole derivatives	0.02	<0.01	0.02	0.02	0.01	0.02	0.02	0.02	0.01	0.01	-10.07		
J04A	Drugs for treatment of tuberculosis	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.03	-5.74		↓
J05	Antivirals for systemic use	0.24	0.30	0.21	0.20	0.20	0.25	0.26	0.27	0.24	0.23	-0.85		

Classes with no consumption in 2019 are not shown in the table, blanks: data not available for those years
2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)
[a] 2019 data are an estimation (15% extrapolation), see methods section
[b] Lineair regression: ↑/↑↑ = positive significant trend; ↓/↓↓ = negative significant trend; ↑/↓ = p<0.05 but ≥0.001; ↑↑/↓↓ = p<0.001

Table 8: Summary table of the main results on antimicrobial consumption of the ECDC- and Global-PPS in Belgian acute hospitals and ECDC-PPS 2 in EU/EEA acute hospitals

	ECDC-PPS 1 Belgium (2011) (51)	**Global-PPS (2015)** (52)	**ECDC-PPS 2 and Global-PPS Belgium (2017)** (31,32,53)	**Global-PPS (2019)[a]**	**ECDC PPS 2 EU/EAA[b] (2016-2017)** (54)
Number of included hospital sites	52	100	110	74	1275
Number of eligible patients	13758	26315	28023	19640	325737
Number of patients with at least one AM prescription on the day of the study	3974	7212	7565	5452	102093
Observed prevalence (% and 95%CI) Mean prevalence (% and 95%CI)	28.9 (26.8-31.1)	27.4 (26.9-28.0) 26.3 (24.7-27.9)	27.0 (26.5-27.5) 26.6 (25.1-28.2)	27.8 (27.1-28.4) 27.7 (26.0-29.4)	32.9 (weighted prevalence: 30.5, country range 15.9-55.6)
Number of prescription for AMs	4962	8804	9217	6690	139609
Top 3 most used antibiotics (% of all AB prescriptions)	J01CR02 (±21.5%) J01DB04 (±8.0%) J01CR05 (±6.5%)	J01CR02: 27.5% J01CR05: 8.7% J01DB04: 6.9%	J01CR02: 22.9% J01CR05: 9.5% J01DB04: 8.6%	J01CR02: 26.0% J01DB04: 10.3% J01CR05: 9.1%	J01CR02: 11.9% J01CR05: 8.1% J01DD04: 7.2%
Top 3 most common diagnoses (% of all AM prescriptions) for treatment		Pneumonia: 27.6% UTI: 13.9% SSI: 10.2%	Pneumonia: 23.1% UTI: 15.2% SSI: 11.9%	Pneumonia: 25.3% UTI: 14.1% SSI: 9.9%	RTI: 31.8% Systemic infections: 14.7% UTI: 13.9%
Prescriptions with HAI as indication (% of all AM prescriptions)	20.5%	28.8%	27.9%	24.5%	19.6%
Prescriptions with SP/MP as indication (% of all AM prescriptions)	11.8/9.0%	9.7/5.9%	11.3/5.9%	12.3/8.0%	24.9% (sum)
Prolonged SP > 1 day (% of all SP prescriptions)	33.6%	28.1%	25.3%	18.9%	54.2%
Parenteral use (% of all AM prescriptions)	66.9%	61.7%	64.6%	62.4%	72.8%
Reason for prescription recorded (% of all AM prescriptions)	73.7%	79.9%	81.9%	85.2%	80.2%
Stop/review date recorded (% of all AM prescriptions)		37.5%	40.8%	49.9%	
Compliance with local guideline (therapeutic use: type of AB) (% of all AB prescriptions)		80.7% (SP: 70.8%)	81.7% (SP: 73.8%)	83.7% (SP: 79.8%)	
Median FTE AMS/250 beds (IQR)			0.29 (0.20-0.55)		0.08 (country range 0.0-0.60)

Data presented where available in the concerning reports
Global-PPS results (2015/2017/2019) are based on the latest version of the database (March 2021), which can explain small differences with results previously published in reports
AB = antibiotic; AM = antimicrobial; AMS = antimicrobial stewardship; FTE = full-time equivalent; HAI = healthcare-associated infection; IQR = interquartile range; MP = medical prophylaxis; RTI = respiratory tract infections; SP = surgical prophylaxis; SSI = Skin and soft tissue infections; UTI = urinary tract infections; 95%CI = 95% confidence intervals
J01CR02 = amoxicillin and beta-lactamase inhibitor; J01DB04 = cefazolin; J01CR05 = piperacillin and beta-lactamase inhibitor; J01DD04 = ceftriaxone
[a] 2 hospitals with non-validated data excluded
[b] EU/EEA: 28 European Union (EU)/European Economic Area (EEA) countries

Table 9: Summary table of the main (preliminary) results on antimicrobial consumption of the HALT-PSY study in Belgian psychiatric hospitals and psychiatric wards in acute hospitals

	HALT-PSY (2017) (22)	
	Psychiatric hospitals	**Psychiatric wards in acute hospitals**
Number of included psychiatric hospitals or wards	23	13
Number of eligible residents	4839	762
Number of residents with at least one AM prescription on the survey day	182	28
Observed prevalence (% and 95%CI)	3.8 (3.2-4.3)	3.7 (2.5-5.3)
Mean prevalence (%)	3.5	3.5
Median prevalence (% and IQR)	3.2 (2.1-5.5)	3.7 (2.1-4.5)
Number of prescriptions for AMs	198	30
Top 3 most used antibiotics (% of all antibiotic prescriptions)	J01C: 42.0% J01X: 15.4% J01A: 13.6%	J01C: 41.4% J01M: 13.8% J01D-E-X: 10.3%
Top 3 most common diagnoses (% of AM prescriptions, treatment or prophylactic)	RTI: 30.3% Skin or wound infections: 26.3% UTI: 19.2%	UTI: 30.0% RTI: 26.7% Skin or wound infections: 16.7%

AM = antimicrobial; IQR = interquartile range; RTI = respiratory tract infections; UTI = urinary tract infections; 95%CI = 95% confidence intervals
J01A = tetracyclines; J01C = Penicillins; J01D = Other beta-lactam antibacterials (beside penicillins); J01E = sulfonamides and trimethoprim; J01M = Quinolone antibacterials; J01X = Other antibacterials (including nitrofuran derivates)

ACUTE HOSPITALS - INPATIENT WARDS (PSYCHIATRY EXCLUDED)

The median (reimbursed) antibiotic consumption in Belgian acute hospitals (inpatient wards without psychiatry) in 2019 was 507.4 DDDs/1000 patient days and 401.6 DDAs/1000 patient days (in 2018: 3265.0 DDDs/1000 admissions and 2662.0 DDAs/1000 admissions), which is in comparison with 2010 an increase of 8.2% and 6.5% respectively (in comparison with 2018: -0.3% and -2.7%). Results in DDA are more in line with the actual doses that are used in Belgian acute hospitals. DDDs are internationally comparable with other countries.

Figures 7-10 present the 10-year evolution of the antibiotic consumption per indicator, displayed with boxplots, for all acute hospitals and per type of hospital. The same data are presented in a violin plot in Figure 11. The boxplots show that there is a high variation in the total antibiotic consumption between acute hospitals, also per type of hospitals, which remains high over time (IQR all acute hospitals in 2010: 414.9-528.0 DDDs/1000 patient days, in 2019: 466.4-546.7 DDDs/1000 patient days).

The highest median antibiotic consumption was seen in tertiary/university hospitals with 601.1 DDDs/1000 patient days (503.7 DDAs/1000 patient days) in 2019. The median antibiotic consumption in primary and secondary hospitals in 2019 was 496.3 and 530.7 DDDs/1000 patient days (399.8 and 416.6 DDAs/1000 patient days), respectively. Compared with 2010, this was an increase of 6.8%, 20.0% and 1.6% for primary, secondary and tertiary hospitals for the median in DDDs/1000 patient days, respectively.

Surprisingly, small hospitals (<400 beds, 518.7 DDDs/1000 patient days, 420,9 DDAs/1000 patient days) had a higher median antibiotic consumption in 2019 than medium (400-600 beds, 487.6 DDDs/1000 patient days, 393.0 DDAs/1000 patient days) and large hospitals (>600 beds, 491.5 DDDs/1000 patient days, 383.6 DDAs/1000 patient days). The median consumption in DDDs/1000 patient days, compared with 2010, increased with 5.2%, 8.5% and 5.8% in small, medium and large hospitals, respectively.

The median antibiotic consumption in 2019 in DDDs/1000 patient days was highest in acute hospitals in Flanders (509.0 DDDs/1000 patient days, 420.4 DDAs/1000 patient days), followed by hospitals in Wallonia (508.7 DDDs/1000 patient days, 391.3 DDAs/1000 patient days) and in Brussels (482.2 DDDs/1000 patient days, 373.0 DDAs/1000 patient days). In comparison with the median antibiotic consumption in DDDs/1000 patient days in 2010, this was an increase of 9.8% and 6.9% in Flanders and Wallonia, respectively, and a decrease of -3.3% in Brussels.

Analyses of outliers for the total antibiotic consumption (in DDDs/1000 patient days, compared per type of hospital), indicate that in the period 2010-2019 13 hospitals (8 primary, 2 secondary, 3 secondary) had an antibiotic consumption ≥P95 for one or more years (2 primary hospitals: 7/10 years, 1 secondary hospital: 7/10 years, 2 primary hospitals: 6/10 years, 1 tertiary hospital: 6/10 years, 1 primary hospital: 5/10 years, other hospitals <5/10 years). In the same period, 7 hospitals (4 primary, 2 secondary, 1 tertiary) had an antibiotic consumption ≤P5 for one or more years (4 primary hospitals: 10/10 years, 1 tertiary hospital: 10/10 years, 1 secondary hospital: 8/10 years, other hospitals <3/10 years). Of notice, the 4 primary hospitals who are a low outlier in all years were previously categorized as chronic hospitals due to their low number of beds and high length of stay. However, in accordance with the list of hospitals of the Belgian Ministry of Health, they are currently classified as acute hospital and therefore included in these analyses. Overall, if the total antibiotic consumption per hospital type and per year (2010-2019) is divided in percentiles (≤P5, P5-10, P11-25, P26-50, P51-75, P76-89, P90-94, ≥P95), 67 hospitals remain in the same percentile for more than 5 year (6/10 years: n=22, 7/10 years: n=23, 8/10 years: n=10, 9/10 years: n=3, 10/10 years: n=9). More results on the validation of BeH-SAC for hospitals with outlying data are presented in Appendix 1.

Figure 12 presents the top 10 of most used antibiotic and antimycotic products in 2019. The most used products in Belgian acute hospitals in 2019 were amoxicillin in combination with clavulanic acid (J01CR02, median in 2019:

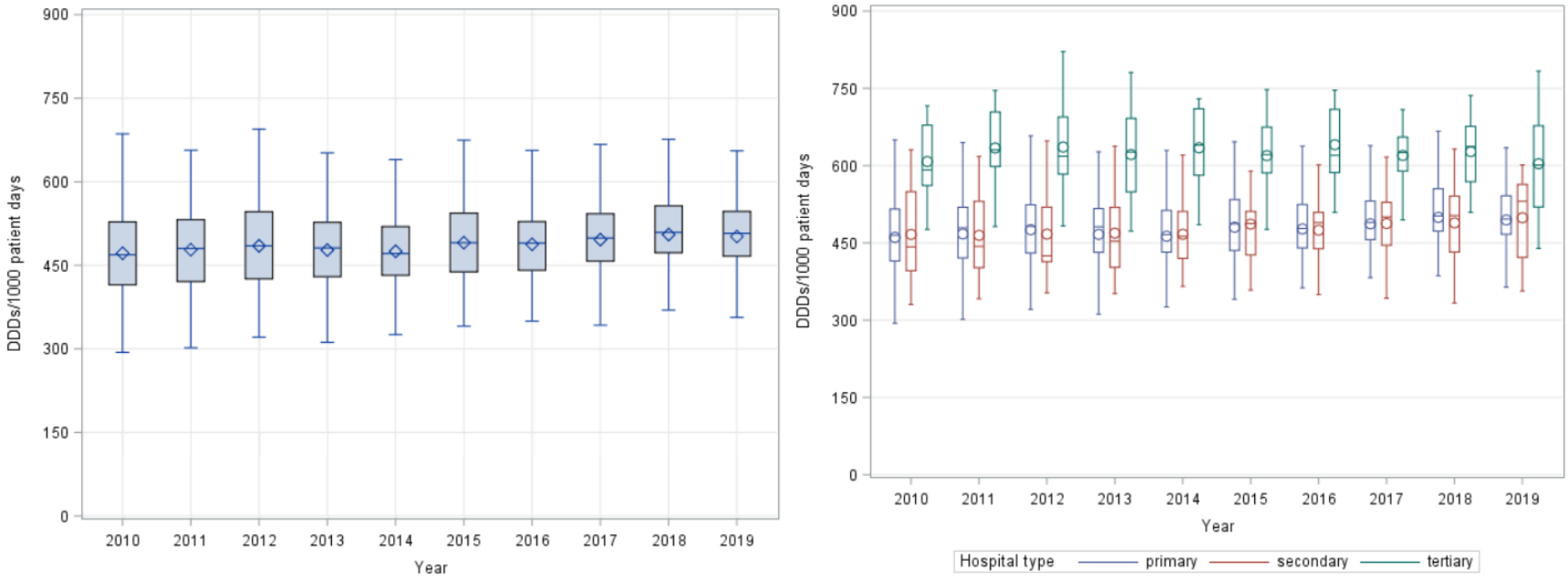
147.4 DDDs/1000 patient days), followed by cefazolin (J01DB04, median in 2019: 39.3 DDDs/1000 patient days) and piperacillin in combination with a beta-lactamase inhibitor (J01CR05, median in 2019: 33.7 DDDs/1000 patient days). Figure 13 displays a stacked bar plot of the evolution (2010-2019) of the consumption per antibiotic subclass and per hospital type. The distribution per subclass and the evolution is similar in primary and secondary hospitals. In tertiary hospitals, the consumption is overall higher for each subclass (especially for third-generation cephalosporins, carbapenems and glycopeptides), except for the second-generation cephalosporins.

The evolution of the broad-spectrum antibiotic use in Belgian acute hospitals per hospital type can be found in Figure 14. In 2019, the median percentage of broad-spectrum use over all antibiotics was 30.6% and this remains stable over time (median in 2010: 29.7%). Again, the boxplots show a high variation between hospitals (IQR in 2019: 25.9-33.6%, range in 2019: 14.2-49.4%). In the 28 EU/EAA countries which participated in the ECDC-PPS 2016-2017, the percentage of broad-spectrum antibiotic use ranged from approximately 20% (Scotland, Lithuania) to more than 60% (Italy, Bulgaria) (54). Details on the consumption of broad-spectrum antibiotics are available in Table 10. Between 2010 and 2019, especially the median consumption of piperacillin in combination with a beta-lactamase inhibitor (J01CR05, +13.8 DDDs/1000 patient days) increased.

The median percentage of intravenous (IV) antibiotic use in 2019 was 63.5% in primary hospitals (IQR 59.9-67.6%), 66.1% in secondary hospitals (IQR 60.3-70.7%) and 69.0% in tertiary hospitals (IQR 67.9-77.6%). Figure 15 presents the evolution (2010-2019) of IV antibiotic use per type of hospital.

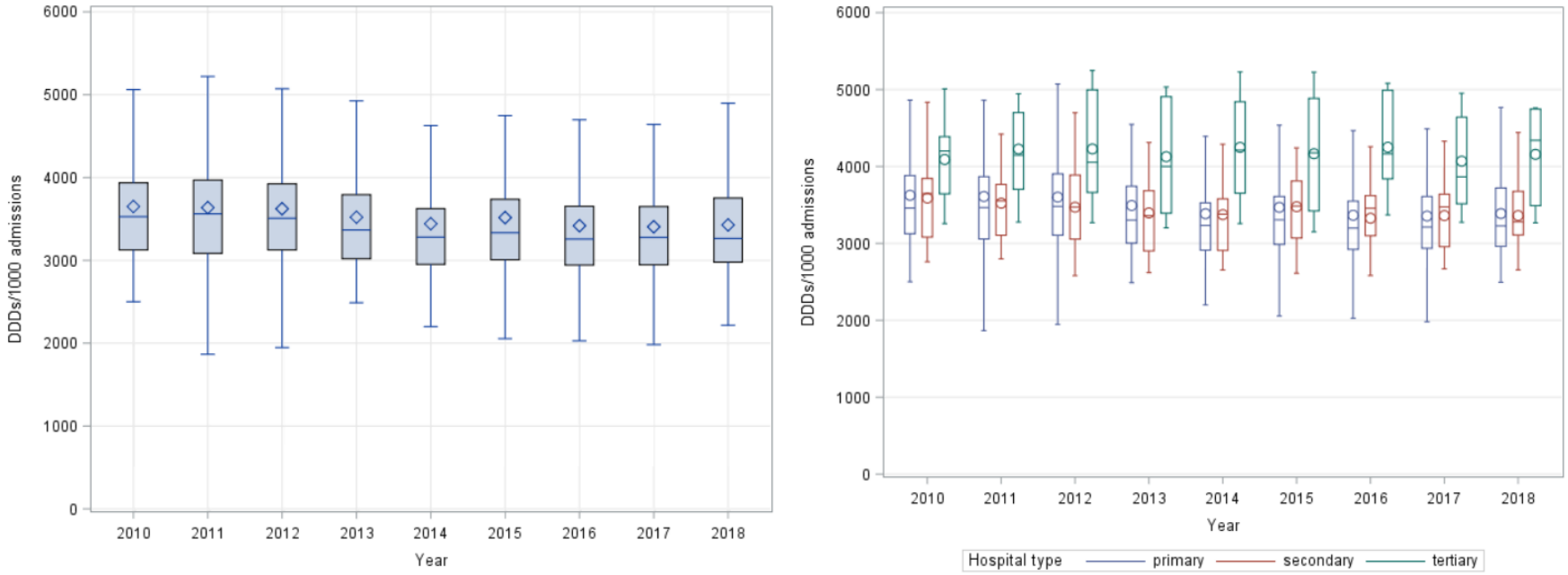
Most antibiotics are consumed on ICU wards as expected. The median antibiotic consumption on ICU in 2019 was 1071.0 DDDs/1000 patient days (IQR 954.2-1258.8) which is a decrease of 3.0% in comparison with the median in 2010. In 2019, the median antibiotic consumption on surgery, internal medicine and geriatrics was 612.4 (IQR 555.0-678.1), 575.4 (534.4-651.7) and 472.4 (IQR 395.1-536.2) DDDs/1000 patient days, respectively. In Figure 16, boxplots with the evolution (2010-2019) of antibiotic consumption per type of ward can be found.

Finally, more details on the evolution (2010-2019) of the (reimbursed) consumption of antimycotics (J02) per type of hospital are available in Figure 17. The median antimycotic consumption in 2019 in all acute hospitals was 16.4 DDDs/1000 patient days (IQR 11.4-24.1). In comparison with 2010 and 2018, this is a decrease of -30.2% and -12.9%. The use of antimycotics is clearly higher in tertiary hospitals (median in 2019: 83.9 DDDs/1000 patient days) compared with primary (median in 2019: 15.6 DDDs/1000 patient days) and secondary hospitals (median in 2019: 21.8 DDDs/1000 patient days).



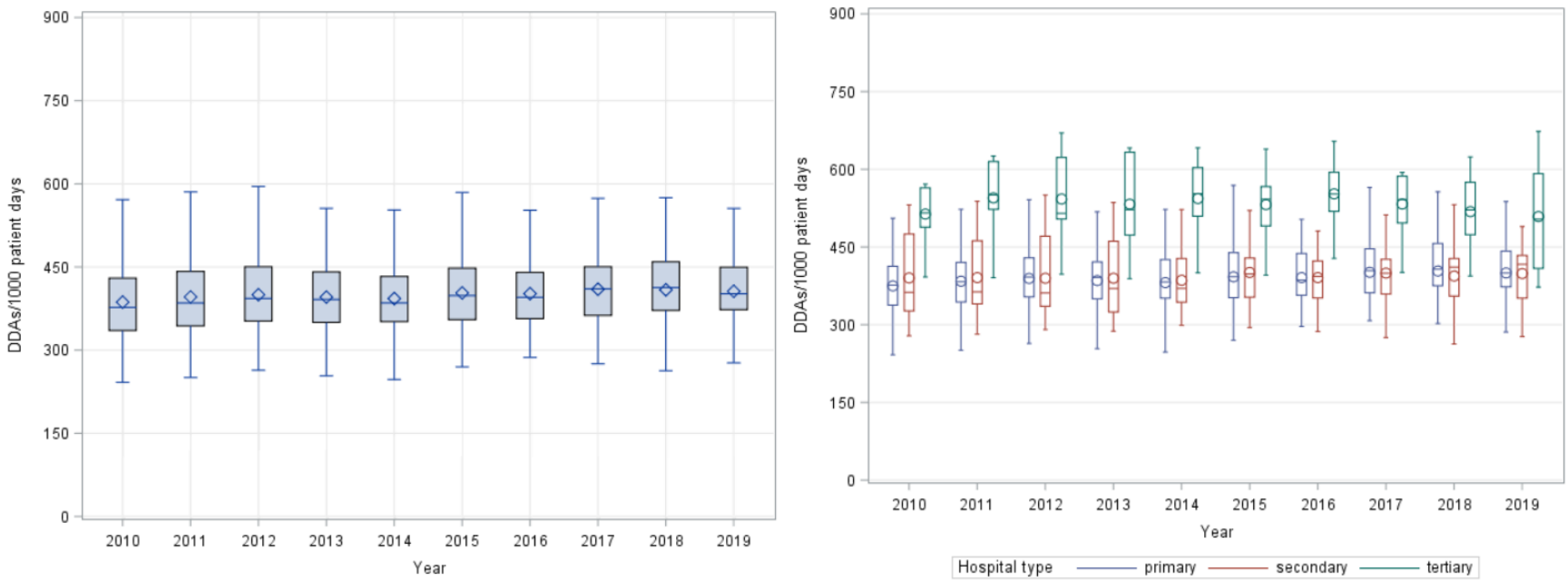
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 7: Boxplots of the evolution (2010-2019) of total antibiotic consumption (J01) in Belgian acute hospitals, expressed in DDDs/1000 patient-days, all hospitals (left) and per type of hospital (right) (BeH-SAC)



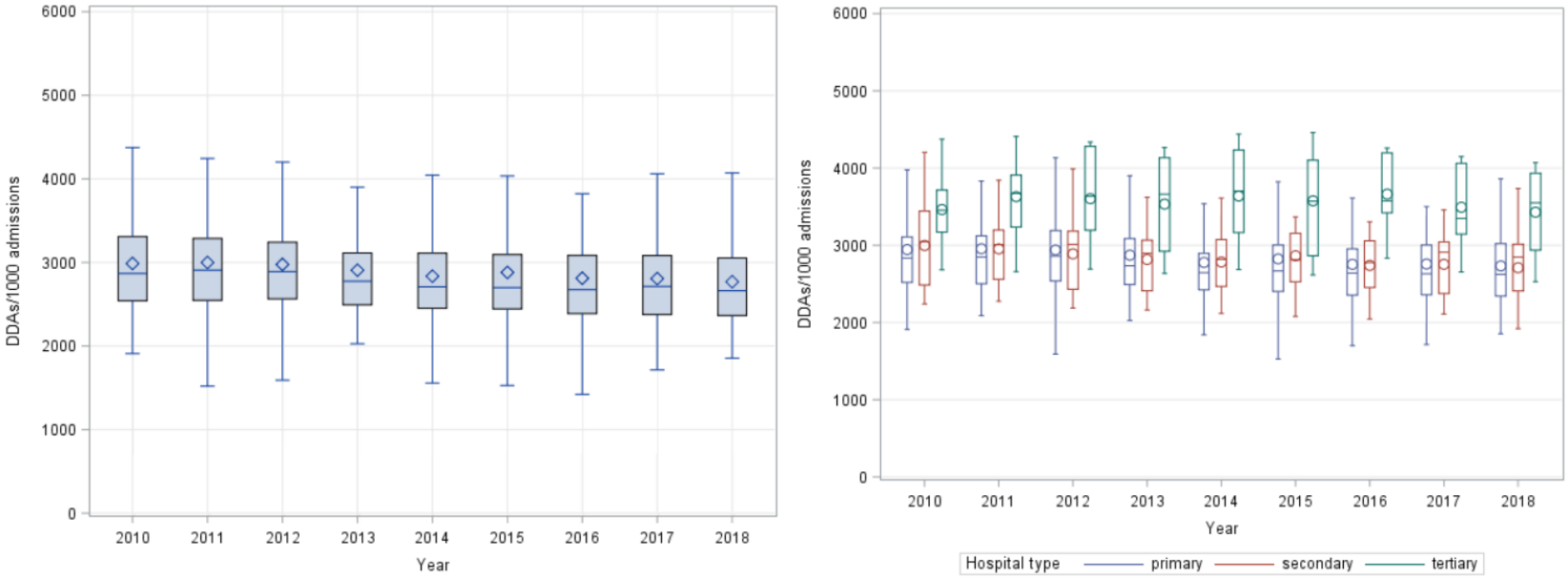
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 8: Boxplots of the evolution (2010-2018) of total antibiotic consumption (J01) in Belgian acute hospitals, expressed in DDDs/1000 admissions, all hospitals (left) and per type of hospital (right) (BeH-SAC)



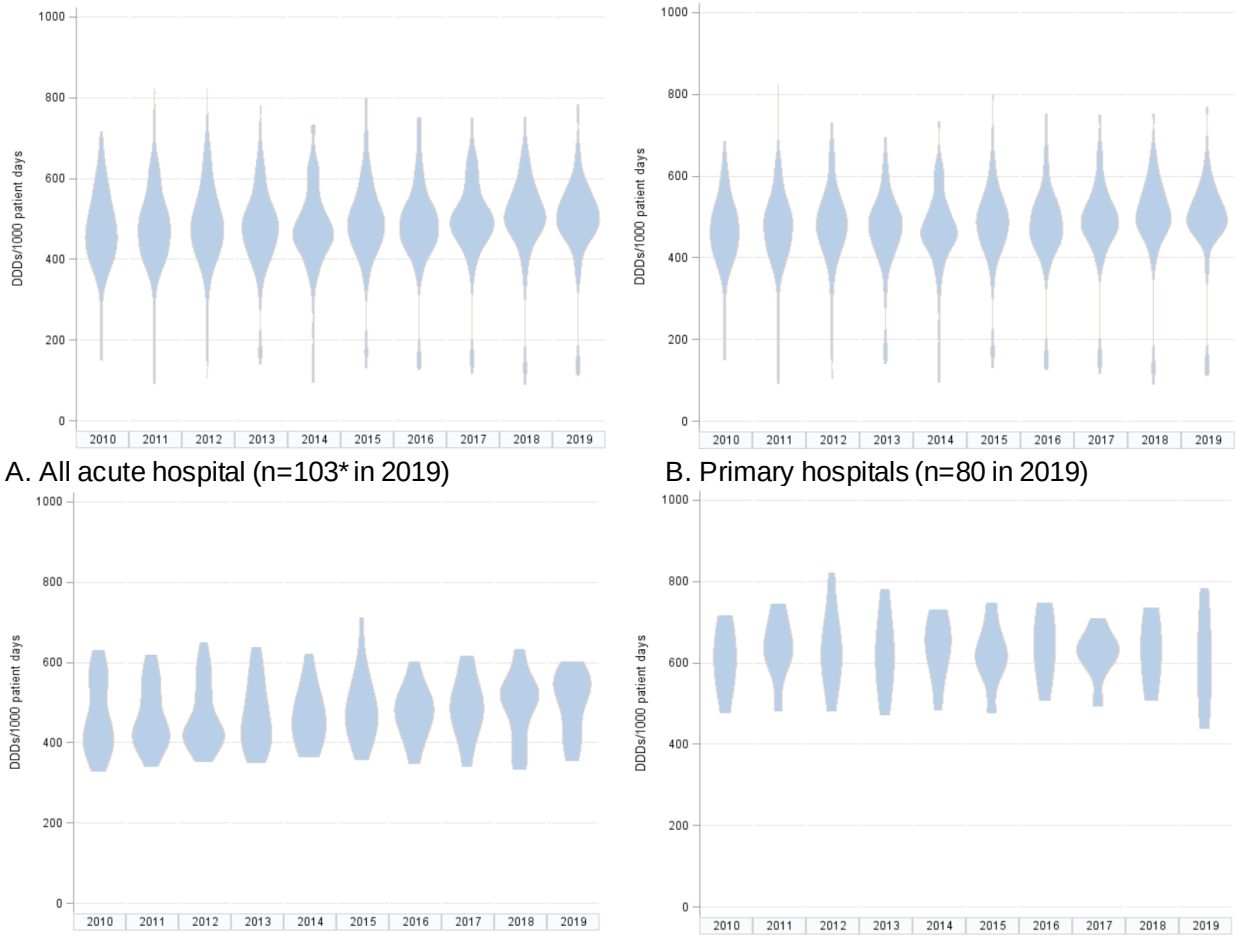
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 9: Boxplots of the evolution (2010-2019) of total antibiotic consumption (J01) in Belgian acute hospitals, expressed in DDAs/1000 patient days, all hospitals (left) and per type of hospital (right) (BeH-SAC)



Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 10: Boxplots of the evolution (2010-2018) of total antibiotic consumption (J01) in Belgian acute hospitals, expressed in DDAs/1000 admissions, all hospitals (left) and per type of hospital (right) (BeH-SAC)



A. All acute hospital (n=103* in 2019)

B. Primary hospitals (n=80 in 2019)

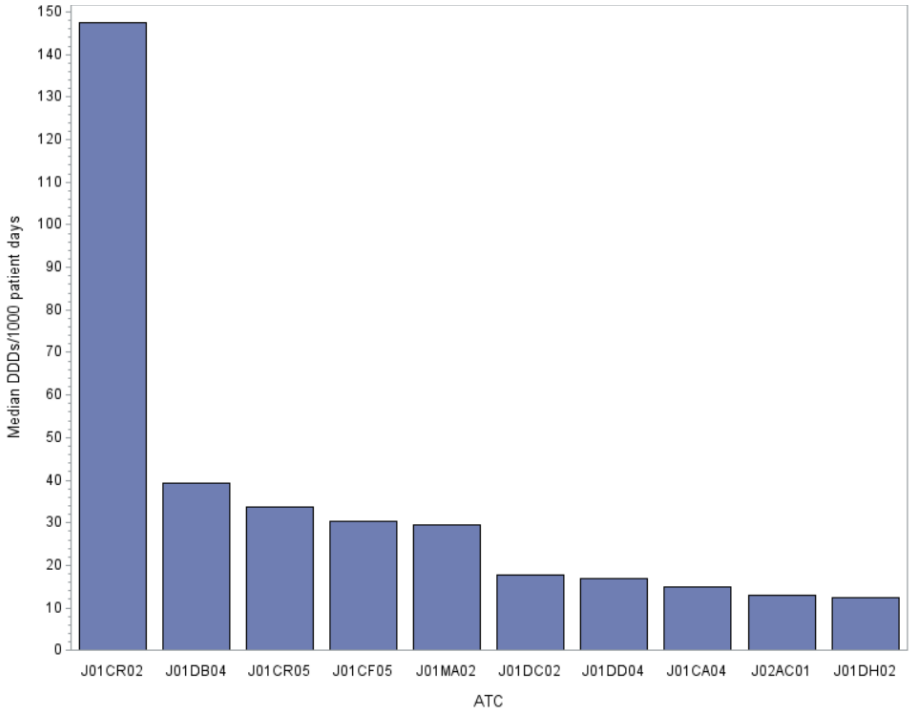
C. Secondary hospitals (n=17 in 2019)

D. Tertiary hospitals (n=6* in 2019)

Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.

* Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

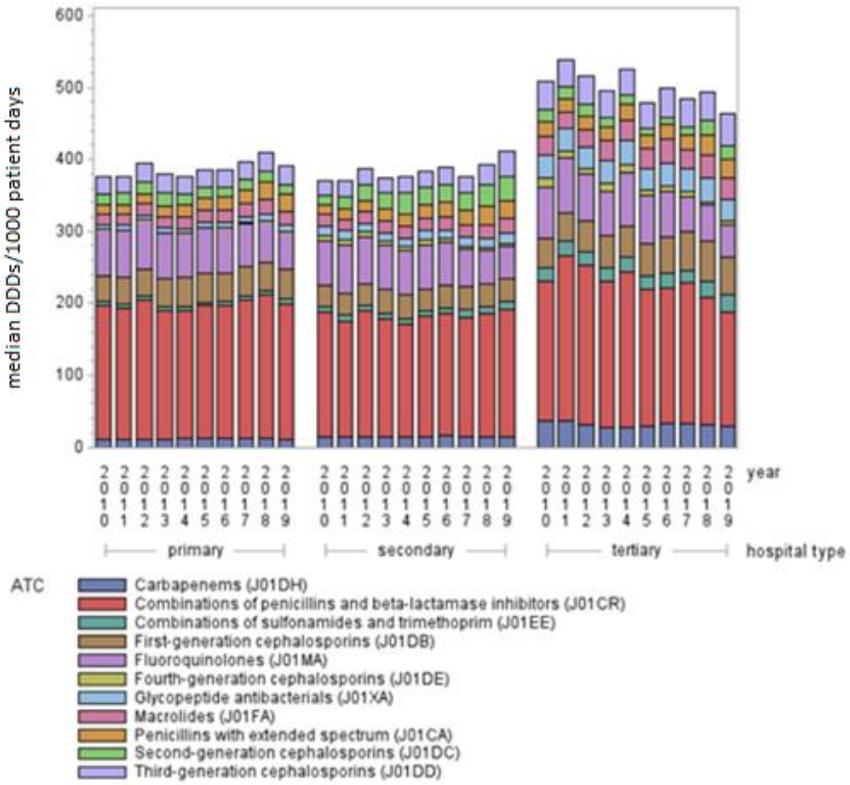
Figure 11: Violin plots of the evolution (2010-2019) of total antibiotic consumption (J01) in Belgian acute hospitals, expressed in DDDs/1000 patient days, all hospitals (A) and per type of hospital (B: primary, C: secondary, D: tertiary) (BeH-SAC)



J01CR02 = amoxicillin in combination with a beta-lactamase inhibitor, J01DB04 = cefazolin, J01CR05 = piperacillin in combination with a beta-lactamase inhibitor, J01CF05 = flucloxacillin, J01MA02 = ciprofloxacin, J01DC02 = cefuroxime, J01DD04 = ceftriaxone, J01CA04 = amoxicillin, J02AC01 = fluconazole, J01DH02 = meropenem

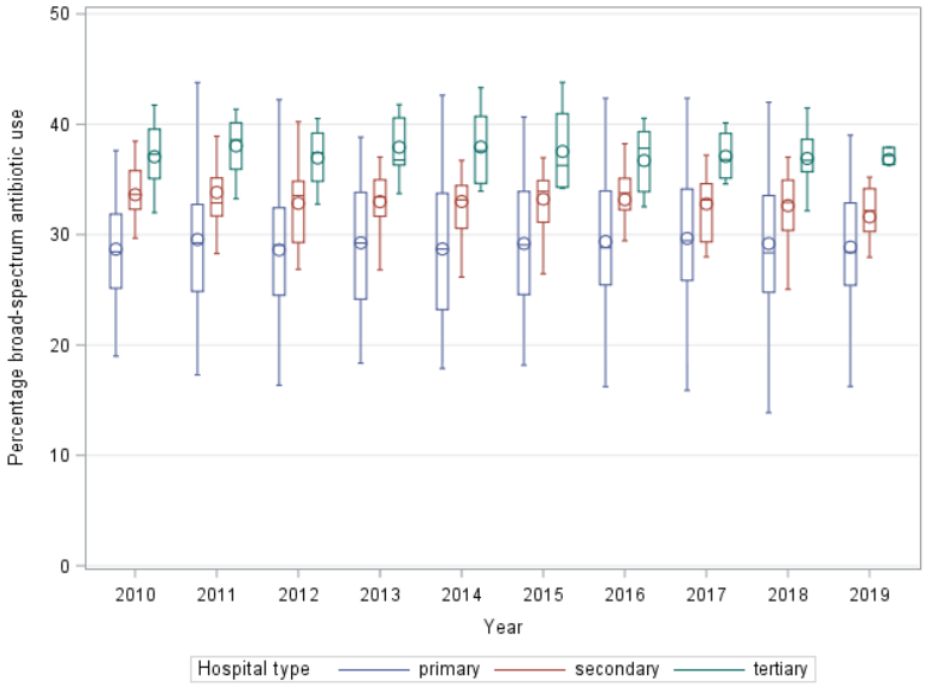
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 12: Top 10 of most used antibiotic (J01) and antimycotic (J02) products in Belgian acute hospitals in 2019, expressed in DDDs/1000 patient days (BeH-SAC)



In this graph, the sum of the median DDDs/1000 patient days per antibiotic subclass is displayed.
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 13: Stacked bar plot with the evolution (2010-2019) of antibiotic consumption in Belgian acute hospitals, per type of hospital and per antibiotic subclass (BeH-SAC)



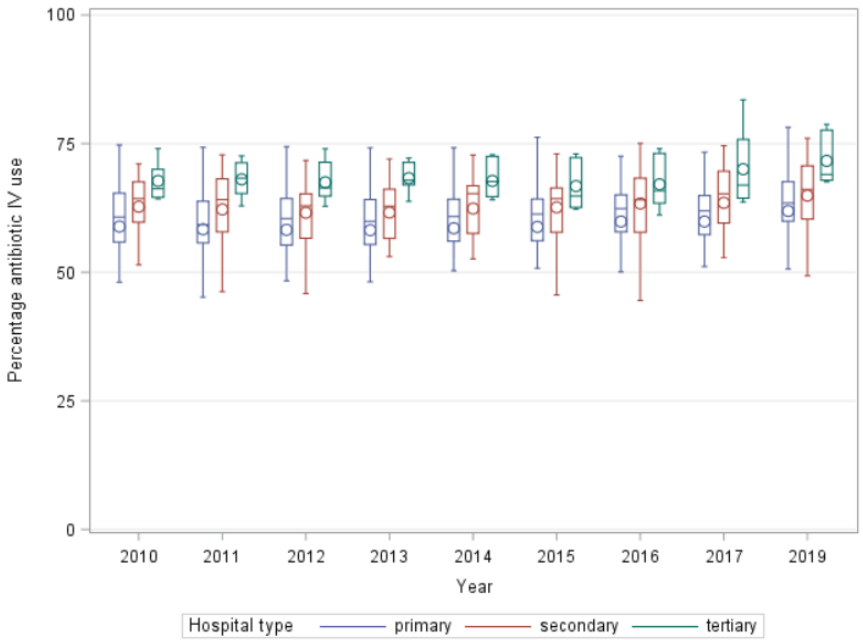
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Calculation broad-spectrum antibiotic use: % DDDs J01(CR05+DD+DE+DF+DH+MA+XA+XB+XX08+XX09+XX11)/J01
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 14: Boxplots with the evolution (2010-2019) of the percentage broad-spectrum antibiotic use of the total antibiotic use in Belgian acute hospitals, per type of hospital (BeH-SAC)

Table 10: Evolution (2010-2019) of the median consumption of broad-spectrum antibiotics in Belgian acute hospitals (2010-2017: n=104, 2018-2019: n=103[a]), expressed in DDDs/1000 patient days (BeH-SAC)

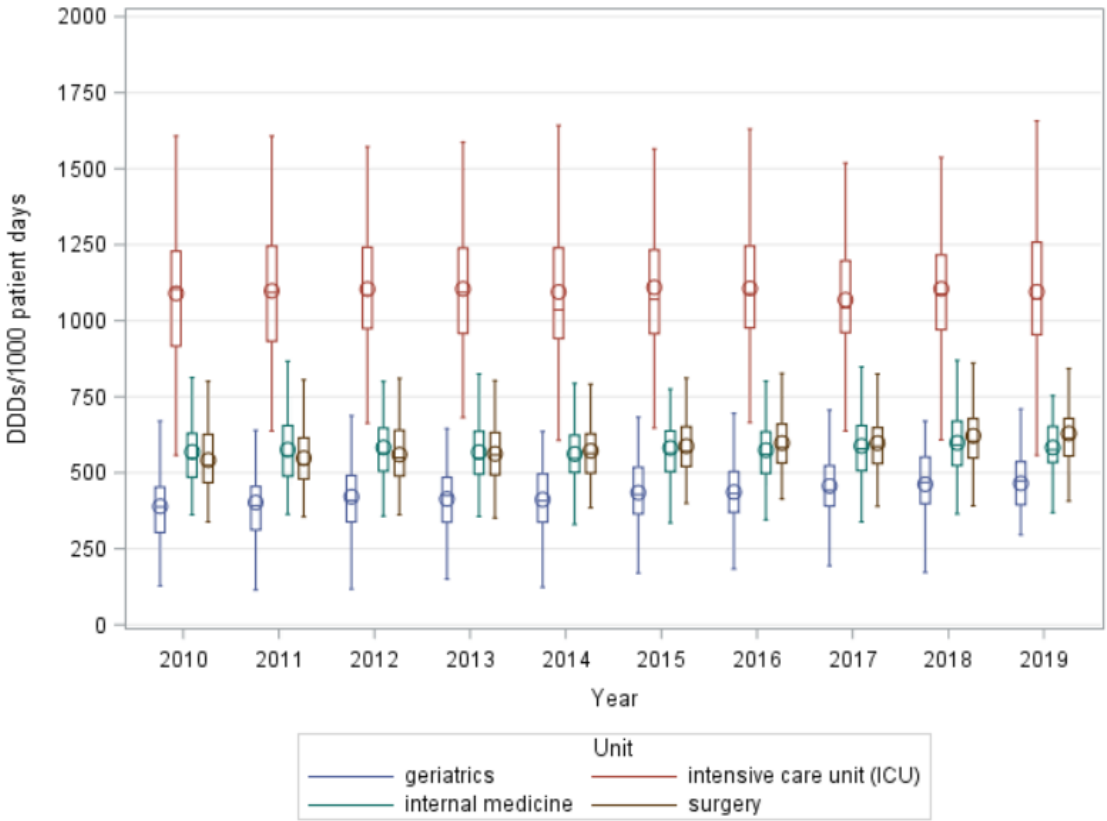
ATC	Name antibiotic class	Median DDDs/1000 patient days										
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Change (%) 2018-2019
J01CR05	Piperacillin and beta-lactamase inhibitor	19.83	20.56	22.81	22.71	23.76	24.54	29.20	31.45	35.36	33.65	-4.84
J01DD01	Cefotaxime	1.49	1.65	1.48	1.12	1.40	1.16	1.40	1.30	1.48	1.34	-9.46
J01DD02	Ceftazidime	6.73	7.33	7.53	7.33	7.26	7.76	6.46	6.92	7.43	7.39	-0.54
J01DD04	Ceftriaxone	10.94	12.45	12.56	13.12	13.04	13.90	13.51	15.55	17.06	16.94	-0.70
J01DE01	Cefepime	2.35	1.67	1.77	2.07	1.60	1.54	1.45	2.04	1.64	2.53	54.27
J01DF01	Aztreonam	0.41	0.47	0.38	0.36	0.45	0.53	0.40	0.49	0.44	0.41	-6.82
J01DH02	Meropenem	11.83	12.25	11.70	12.44	11.97	12.77	13.21	12.75	12.58	12.46	-0.95
J01DH51	Imipenem and cilastatin	0.43	0.17	0.43	0.19	0.20	0.35	0.12	0.23	0.15	0	-100.00
J01MA01	Ofloxacin	0.12	0.09	0.19	0.19	0.20	0.08	0.15	0.21	0.70	0.26	-62.86
J01MA02	Ciprofloxacin	31.52	32.86	33.73	33.16	33.91	34.54	34.99	35.10	30.85	29.56	-4.18
J01MA06	Norfloxacin	1.41	1.10	0.67	0.60	0.31	0.21	0.31	0.17	0.19	0.12	-36.84
J01MA12	Levofloxacin	11.67	9.24	8.17	7.25	4.05	4.86	3.93	4.74	3.55	3.13	-11.83
J01MA14	Moxifloxacin	13.77	15.29	15.47	15.36	13.64	15.09	13.19	13.16	11.64	9.99	-14.18
J01XA01	Vancomycin	6.20	5.92	6.84	6.81	6.91	7.68	7.92	8.49	9.12	9.77	7.13
J01XA02	Teicoplanin	1.03	0.62	0.51	0.45	0.71	0.50	0.47	0.41	0.57	0.37	-35.09
J01XB01	Colistin	0.28	0.31	0.30	0.43	0.27	0.28	0.40	0.40	0.34	0.21	-38.24
J01XX08	Linezolid	1.00	0.94	0.75	0.69	0.80	0.74	0.66	0.75	0.88	0.83	-5.68
J01XX09	Daptomycin[b]	0	0	0	0	0	0	0	0	0	0	0
J01XX11	Tedizolid[b]	0	0	0	0	0	0	0	0	0	0	0

2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
[a] Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)
[b] Not commercialized in Belgium; import from other countries is not reimbursed and hence not included in these data.



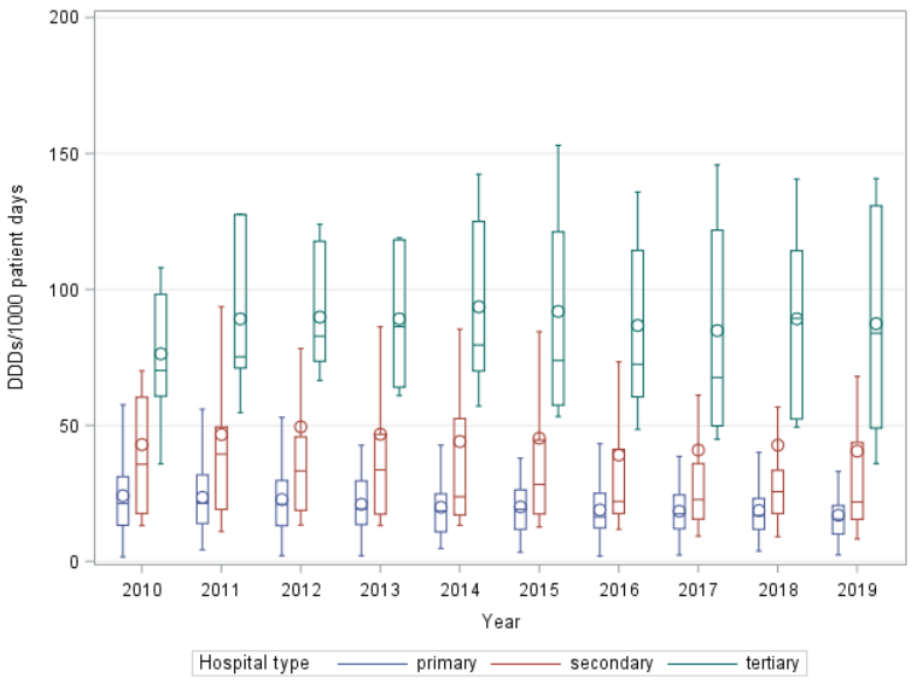
Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 15: Boxplots with the evolution (2010-2019) of the percentage intravenous (IV) use of the total antibiotic use in Belgian acute hospitals, per type of hospital (BeH-SAC)



Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 16: Boxplots with the evolution (2010-2019) of the total antibiotic (J01) use in Belgian acute hospitals, per type of ward (intensive care unit, surgery, internal medicine, geriatrics) (BeH-SAC)



Included inpatient wards: surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care unit (ICU) and specialized care; psychiatry and day hospitalizations excluded.
Outliers not displayed in the graph.
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

Figure 17: Boxplots of the evolution (2010-2019) of total antimycotic consumption (J02) in Belgian acute hospitals, expressed in DDDs/1000 patient days, per type of hospital (BeH-SAC)

ACUTE HOSPITALS - INPATIENT WARDS (PSYCHIATRY AND NEONATOLOGY/PEDIATRICS EXCLUDED)

Specific results for non-pediatric and non-psychiatric inpatient wards in acute hospitals are available in Table 11. These results were suggested as indicators for the hospital setting to follow-up the evolution of antibiotic consumption on a national level. The 10-year evolution of the total antibiotic consumption is similar as presented above (significant increase in DDDs/1000 patient days and significant decrease in DDDs/1000 admissions). Broad-spectrum use slightly decreased in all wards (especially surgery).

The AWaRe classification of WHO aims to emphasize the importance of their optimal uses and potential for antimicrobial resistance. It contains three stewardship categories to be used in the following ascending order of prudence: Access, Watch and Reserve. The ratio of the antibiotic consumption in the Access and Watch groups in all wards changed from 1.41 in 2010 to 1.35 in 2019 (meaning that relatively more Watch antibiotics are used in 2019). Only on surgery wards in Belgium, a positive evolution is seen over the last decade for ratio in the Access and Watch groups (2.20 to 2.33). In 2019, the percentage of consumed DDDs in the Access, Watch and Reserve groups of the total antibiotic use (DDDs J01) was 57.0%, 42.3% and 0.7%, respectively.

Table 11: Evolution (2010-2019) of the total antibiotic consumption, percentage broad-spectrum antibiotic use and ratio antibiotic use in the Access/Watch group (WHO) in non-pediatric and non-psychiatric inpatient wards in acute hospitals (BeH-SAC, Belgium)

Indicator	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Change (%) 2010-2019	10-year trend[c]
Total antibiotic consumption (J01) over all wards												
DDDs/1000 patient days	478.0	485.7	493.8	488.2	491.6	504.6	503.2	509.2	508.2	504.2	+5.48	↑↑
DDAs/1000 patient days	381.6	391.9	396.6	393.9	395.9	407.0	406.6	411.8	402.7	399.7	+4.74	↑
DDDs/1000 admissions	3752.2	3752.8	3743.3	3646.7	3595.7	3651.7	3606.9	3562.8	3525.0		2010-2018: -6.06	↓↓
DDAs/1000 admissions	2995.3	3028.3	3006.7	2942.4	2895.6	2945.6	2914.6	2881.0	2793.2		2010-2018: -6.75	↓
Percentage broad-spectrum antibiotic use over all antibiotic use (in DDDs)[a]												
All wards	32.14	32.80	32.00	32.13	32.03	32.34	32.32	32.25	31.73	31.27	-2.71	
ICU	45.50	46.34	45.45	46.56	46.94	47.17	46.16	45.91	46.11	45.33	-0.37	
Internal medicine	36.61	37.43	36.49	36.66	36.48	36.75	36.68	36.47	35.52	34.94	-4.56	↓
Surgery	23.35	23.45	22.75	22.45	22.45	22.83	22.91	22.97	22.30	22.23	-4.80	↓
Ratio of the antibiotic consumption in the Access and Watch group (in DDDs)[b]												
All wards	1.41	1.36	1.38	1.32	1.33	1.31	1.31	1.30	1.34	1.35	-4.26	
ICU	0.83	0.80	0.82	0.77	0.77	0.75	0.77	0.78	0.76	0.78	-6.02	↓
Internal medicine	1.19	1.13	1.14	1.08	1.10	1.08	1.07	1.07	1.11	1.12	-5.88	
Surgery	2.20	2.19	2.25	2.22	2.24	2.22	2.24	2.24	2.36	2.33	5.91	↑

2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDD) were used (2)
Exclusion of one tertiary hospital from the database for 2018-2019 because of incorrect reimbursement data (total number of tertiary hospitals in 2019: n=7)

[a] The following products were included as broad-spectrum: piperacillin in combination with a beta-lactamase inhibitor (J01CR05), third- and fourth-generation cephalosporins (J01DD and J01DE), monobactams (J01DF), carbapenems (J01DH), fluoroquinolones (J01MA), glycopeptides (J01XA), polymyxins (J01XB), daptomycin (J01XX09) and oxazolidinones: linezolid (J01XX08) and tedizolid (J01XX11) (34)

[b] Access and Watch antibiotic classes defined in accordance with the AWaRe classification of the WHO (version December 2019) (35)

[c] Lineair regression: ↑/↑↑ = positive significant trend; ↓/↓↓ = negative significant trend; ↑/↓ = $p<0.05$ but ≥ 0.001; ↑↑/↓↓ = $p<0.001$

More results on antimicrobial consumption in hospitals in Belgium can be consulted through the following sources:

- National reports (publically available) and individual hospital feedback reports (login with the electronic identity card) on www.healthstat.be. (27)*
- The online interactive database of ESAC-Net with the results of all participating EU/EEA countries of the ATC 4 level: website (25) or in the latest report of ESAC-Net (26)
- Hospital feedback reports from NIHDI per diagnostic groups (55)
- Research of Vandael et al. on BeH-SAC (56)
- Research of Goemaere et al. on the antifungal use in Belgium (2003 to 2016) (45)
- The national ECDC-PPS 2017 report (31) and article with the results of the ECDC/Global-PPS 2017 (32)
- The ECDC-PPS 2017 report of ECDC (https://www.ecdc.europa.eu/en/healthcare-associated-infections-acute-care-hospitals)
- Paper of Plachouras et al. with the main ECDC-PPS 2017 results (54)
- Real-time one-point, longitudinal and merged hospital feedback reports including results on antimicrobial use and resistance, healthcare-associated infections as well as results using the WHO AWaRe classification list, with country and European benchmarking available to Global-PPS participants through https://app.globalpps.uantwerpen.be/globalpps_webpps/
- Interreg project 'i-4-1-Health' in which the Infection Risk Scan (IRIS) was introduced: https://www.grensregio.eu/projecten/i-4-1-health

*The evolution of the use of these reports by Belgian hospitals in presented in Figure 18.

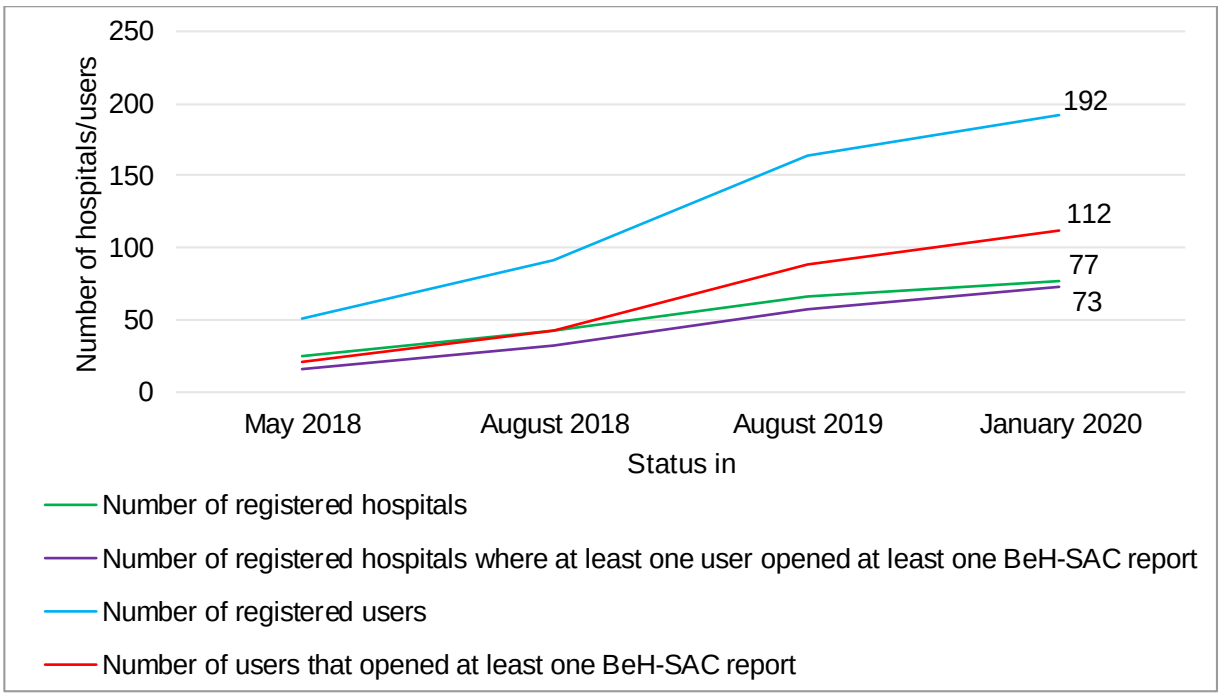


Figure 18: Use of the online reports of BeH-SAC on Healthstat by Belgian hospitals following the introduction (www.healthstat.be)

IMPACT OF SHORTAGES OF ANTIMICROBIAL AGENTS ON CONSUMPTION

In Table 12, an overview is given of antimicrobial agents that were temporally unavailable on the Belgium market in the last five years (January 2015 - January 2020). Where possible, the impact on the consumption of the concerning product is investigated. In total, for the last five years, there were 479 reported shortages for antimicrobial agents/specialties of which 72.7% (n=348) for antibiotics (A07AA: 0.6%, D01BA: 4.4%, J02: 9.4%, J04A: 2.3%, J05: 10.6%, P01BA: 0). Most frequent reasons were delay in the release of the end product (66.0%) and production problems (18.6%). For 44 different antibiotic products/active substances (±38% of all ATC codes for antibiotics that are commercialised in Belgium), one or more shortages were reported. For some products (see indicated in bold in Table 12), the shortage might have had a (small) impact on the consumption (based on ESAC-Net data on product level (ATC level 5), not possible to investigate for specific brands/dosages/pharmaceutical forms). However, with the available information, it is not possible to confirm a straightforward link. In most cases, alternatives were in all likelihood available (other package size/dosage/administration route or other specialty of another firm with the same characteristics).

Besides temporally shortages, there are also many antibiotics (non-exhaustive list) that are or will no longer be commercialized or were never commercialized in Belgium:

- Doxycyclin (J01AA02): IV form not available on the Belgian market
- Ampicillin (J01CA01): no longer commercialized since October 2017
    - Low consumption in the community (<0.0001 DID in 2017, <0.1% of J01CA, <0.1% of J01)
    - Consumption in hospitals in 2017: 0.0102 DID (12.9% of J01CA, 0.7% of J01), replaced by amoxicillin (from 63% of J01CA in 2017 to 73% in 2019)
- Amoxicillin IV (J01CA04): Clamoxyl® will be withdrawn from our market by the end of 2021, consultations with other firms ongoing to ensure that amoxicillin IV remains on the market
    - In acute hospitals in 2019 (BeH-SAC): amoxicillin IV = 49.1% of total amoxicillin use, 1.7% of J01
- Phenoxymethylpenicillin (Penicillin V, J01CE02): no longer commercialized since May 2019
    - Consumption in the community in 2018: 0.022 DID (97.8% of J01CE, 0.1% of J01)
    - Consumption in hospitals in 2018: 0.0001 DID (0.7% of J01CE, <0.01% of J01)
- Oxacillin (J01CF04): no longer commercialized since February 2018
    - No consumption in the community
    - Consumption in hospitals in 2017: 0.005 DID (5.1% of J01CF, 0.3% of J01), replaced by flucloxacillin (from 95% of J01CF in 2017 to 100% in 2019)
- Amoxicillin/clavulanic acid IV (J01CR02): Augmentin® will be withdrawn from our market by the end of 2021, alternatives exists except for the dosage 1000/100 mg
    - In acute hospitals in 2019 (BeH-SAC): amoxicillin/clavulanic acid IV = 58.4% of total amoxicillin/clavulanic acid use, 15.7% of J01
- Ticarcillin/clavulanic acid (J01CR03): no longer commercialized in Belgium (not since 2009)
- Ertapenem (J01DH03): not commercialized in Belgium
- Imipenem + cilastatin (J01DH51): Tienam® no longer commercialized since September 2018
    - Consumption in the community in 2018: <0.0001 DID
    - Consumption in hospitals in 2018: 0.0001 DID (0.3% of J01DH, <0.01% of J01)
- Ceftolozane/tazobactam IV (J01DI54): not commercialized in Belgium
- Fosfomycin IV (J01XX01): not commercialized in Belgium
- Daptomycin (J01XX09): not commercialized in Belgium
- Tedizolid (J01XX11): not commercialized in Belgium

Products for which there is a market authorization in Belgium but no commercialization (e.g. daptomycin) are not reimbursed when imported from other countries and hence not included in the ESAC-Net/BeH-SAC database.

Table 12: Overview of shortages of antimicrobial agents in Belgium in the last five years (January 2015-January 2020, source: PharmaStatus database of the Federal Agency of Medicines and Health Products) and changes in consumption data

Product	ATC	Pharmaceutical form + dose	Period shortage	Reason(s) supply problem[a]	Change in consumption (ESAC-Net data, ATC 5 level)?	
					Community	Hospitals[b]
Nystatin	A07AA02	Oral suspension 100.000 IU/ml	Nov-Dec 2019	Delay in release of end product	**Consumption decreased in 2019** (0.021 DID) compared to 2018 (0.022 DID)	**Consumption decreased in 2019** (0.020 DID) compared to 2018 (0.021 DID)
Paromomycin	A07AA06	Tablets 250 mg	Nov 2018-Jan 2019 May 2019-Sept 2019	Delay in release of end product	**Consumption decreased in 2019** (0.015 DID) compared to 2017 and 2018 (0.019 DID)	**Consumption decreased in 2019** (0.0002 DID) compared to 2017 and 2018 (0.0001 DID)
Terbinafine	D01BA02	Tablets 250 mg (several firms)	Oct-Nov 2016 May 2017-Jan 2020*	Production problems Delay in production Delay in release of end product	Similar consumption in 2015-2016-2017-2018-2019 (1.8 DID)	Similar consumption in 2015-2016-2017-2018 (0.008 DID), **decreased in 2019** (0.005 DID)
Doxycycline	J01AA02	Capsules 40 mg Tablets 100 mg, 200 mg (several firms)	Mar-May 2015 Sep-Oct 2015 Jul 2018-Mar 2019 Jul 2019 – Jan 2020*	Production problems Delay in release of end product FMD Serialization (new barcodes) Increased demand	Similar consumption in 2015-2016-2017-2018-2019 (0.7 DID)	Similar consumption in 2015-2016-2017-2018-2019 (0.009 DID)
Lymecycline	J01AA04	Capsules 300 mg	Apr-Dec 2015	Production problems	Similar consumption in 2015-2016 (0.8 DID)	Similar consumption in 2015-2016 (0.002 DID)
Minocycline	J01AA08	Capsules 100 mg	Nov 2015	Temporary suspension of the commercialisation	Similar consumption in 2015-2016 (0.5 DID)	Similar consumption in 2015-2016 (0.003 DID)
Tigecycline	J01AA12	Powder for infusion (vials) 50 mg	June 2015	Production problems	No consumption	Similar consumption in 2015-2016 (0.002 DID)
Thiamphenicol	J01BA02	Powder for injection (vials) 500 mg	Jan-Feb 2016	Delay in release of end product	Similar consumption in 2016-2017 (0.02 DID)	Similar consumption in 2015-2016 (0.0005 DID)
Thiamphenicol combinations	J01BA52	Powder for (nebulization) solution (vials) 405 mg	Oct-Nov 2015	Delay in release of end product	No consumption	No consumption
Amoxicillin	J01CA04	Tablets 1000 mg Capsules 500 mg Oral suspension 250 mg/5 ml Powder for injection/infusion (vials) 1000 mg (several firms)	Jan-Feb 2016 Nov 2017-Jan 2018 Jul-Aug 2018 Mar 2019-Jan 2020	Temporary suspension of the commercialisation Production problems Delay in release of end product	Same consumption in 2015 and 2016 (5.0 DID), **decreased in 2017** (4.7 DID), increased in 2018 and 2019 (4.8 DID)	Same consumption in 2015 and 2016 (0.045 DID), increased in 2017 (0.050 DID) and 2018 (0.068 DID), **decreased in 2019** (0.058 DID)
Temocillin	J01CA17	Powder for injection (vials) 1000 mg, 2000 mg	Feb-Mar 2017	Delay in release of end product	No consumption	Similar consumption in 2016 and 2017 (0.019 DID)

Benzylpenicillin	J01CE01	Powder for injection (vials) 2 MU, 5 MU	Mar-Jun 2019 Nov 2019 - Jan 2020*	Delay in release of end product Delay in production	No consumption	Consumption increased in 2019 (0.02 DID) compared to 2018 (0.04 DID)
Phenoxymethylpenicillin	J01CE02	Tablets 1 MU	May-Jun 2017	Production problems	**Decreased consumption in 2017** (0.017 DID) compared to 2016 (0.026 DID) and 2018 (0.023 DID)	Similar consumption in 2016 and 2017 (0.0002 DID)
Benzathine Benzylpenicillin	J01CE08	Powder for injection (vials) 1.2 MU	Aug-Nov 2015 Dec 2016 - Feb 2017 Jan-Nov 2018 Jul-Aug 2019	Temporary suspension of the commercialisation Delay in release of end product Unknown reason Production problems	Very low consumption (<0.001 DID)	Similar consumption in 2014-2019 (0.0002 DID)
Oxacillin	J01CF04	Powder for injection (ampoules) 1000 mg	Jul-Sep 2015	Delay in release of end product	No consumption	Similar consumption in 2015 and 2016 (0.009 DID)
Flucloxacillin	J01CF05	Powder for injection (vials) 250 mg, 500 mg, 1000 mg (several firms)	May-Sep 2015 Jan-Apr 2016 Oct-Dec 2018 Aug-Sept 2019	Production problems Other reason	Similar consumption in 2015-2017 (0.25 DID), increased in 2018 (0.26 DID) and 2019 (0.27 DID)	Increased consumption over time (from 0.08 DID in 2015 to 0.10 DID in 2019)
Amoxicillin + clavulanic acid	J01CR02	Tablets 500/125 mg, 875/125 mg, 1000/62.5 mg Oral suspension 125/31.25 mg/5 ml, 250/62.5 mg/5 ml Powder for injection/infusion (vials) 500/50 mg, 1000/100 mg, 1000/200 mg (several firms)	Jan 2015 - Aug 2017 Nov 2017 - Feb 2019 Apr 2019 – Jan 2020*	Production problems Delay in release of end product Temporary suspension of the commercialisation	Increased consumption between 2014 (4.76 DID) and 2018 (5.06 DID), **decrease in 2017 (4.74 DID) and 2019 (4.70 DID)**	**Decreased consumption over time** (from 0.473 DID in 2014 to 0.412 DID in 2018)
Piperacillin + tazobactam	J01CR05	Powder for injection/infusion (vials) 2000/250 mg, 4000/500 mg (several firms)	Nov-Dec 2015 Oct 2017 - Jul 2019 Nov-Dec 2019	Delay in release of end product	Very low consumption (<0.0001 DID)	Increased consumption over time (from 0.090 DID in 2014 to 0.106 in 2018), **decreased in 2019** (0.094 DID)
Cefalexin	J01DB01	Tablets 500 mg	Jul-Aug 2019	FMD Serialization (new barcodes)	Increased consumption in 2019 (0.004 DID) compared to 2018 (0.003 DID)	Increased consumption in 2019 (0.0004 DID) compared to 2018 (0.0002 DID)
Cefazolin	J01DB04	Powder for injection (vials) 1000 mg	Jan-May 2018	Other reason	**Decreased consumption over time** (0.006 DID in 2017 and 0.005 DID in 2018)	Increased consumption (0.132 DID in 2017 and 0.142 DID in 2018)
Cefadroxil	J01DB05	Capsules 500 mg Oral suspension 250 mg/5 ml, 500 mg/5 ml (several firms)	Mar-Aug 2015 Mar 2016 - Aug 2017 May 2018 - Jan 2020*	Production problems Delay in release of end product Other reason	**Decreased consumption over time** (0.093 DID in 2014 to 0.024 DID in 2019)	**Decreased consumption over time** (0.0031 DID in 2014 to 0.0012 DID in 2019)

Cefuroxime	J01DC02	Tablets 250 mg, 500 mg Oral suspension 250 mg/5 ml Powder for injection (vials) 750 mg, 1500 mg (several firms)	May-Jul 2015 June 2016 - Feb 2017 Nov 2017 - Mar 2018 Aug 2018 - Jan 2019 Mar 2019 - Jan 2020*	Production problems Delay in release of end product Reason unknown	**Decreased consumption over time** (1.32 DID in 2014 to 1.17 DID in 2019)	**Decreased consumption over time** (0.084 DID in 2014 to 0.077 DID in 2019)
Cefotaxime	J01DD01	Powder for injection/infusion (vials) 1000 mg, 2000 mg (several firms)	Oct 2015 Aug 2018 - Jan 2019 Nov 2019 - Jan 2020	Temporary suspension of the commercialisation Delay in release of end product Production problems	Very low consumption (<0.001 DID)	Similar consumption between 2014 and 2019 (0.007 DID)
Ceftazidime	J01DD02	Powder for injection/infusion (vials) 500mg, 1000 mg, 2000 mg (several firms)	Aug 2018 - Jan 2020*	Delay in release of end product	**Decreased consumption in 2018-2019** (2016-2017: 0.004 DID, 2018-2019: 0.003 DID)	**Increased consumption over time** (2016: 0.032 DID, 2019: 0.029 DID)
Ceftriaxone	J01DD04	Powder for infusion (vials) 1000 mg, 2000 mg (several firms)	Feb-Mar 2015 Jan 2017 - Feb 2018 Jan-Mar 2019	Delay in release of end product Packaging problems	Similar consumption in 2016-2019 (0.001 DID)	Increased consumption over time (from 0.056 DID in 2015 to 0.062 DID in 2019)
Cefepim	J01DE01	Powder for infusion/injection (vials) 1000 mg, 2000 mg (several firms)	Dec 2017 - May 2018 Oct-Dec 2018	Delay in release of end product Reason unknown Other reason	Very low consumption (<0.001 DID)	**Decreased consumption in 2018** (0.008 DID, 2017: 0.011 DID, 2019: 0.010 DID)
Aztreonam	J01DF01	Powder for injection (vials) 1000 mg	Sep-Oct 2018	Delay in release of end product	No consumption	Similar consumption in 2017, 2018, 2019 (0.0045 DID)
Meropenem	J01DH02	Powder for infusion/injection (vials) 500 mg, 1000 mg (several firms)	Jun 2015 - Jan 2019	Delay in release of end product Logistic problems (transport, customs, ...)	Very low consumption (<0.001 DID)	**Decreased consumption over time** (2014: 0.053 DID, 2019: 0.042 DID)
Imipenem + enzyme inhibitor	J01DH51	Powder for infusion (vials) 500 mg	Sep-Dec 2015 Apr-June 2016 Feb-Mar 2017	Production problems	No consumption	Very low consumption, similar in 2014-2018 (0.0001 DID)

Sulfamethoxazole and Trimethoprim	J01EE01	Tablets 400/80 mg, 800/160 mg Oral suspension 200/40mg/5 ml Concentrate for solution for infusion (ampoules) 400/80 mg/5 ml (several firms)	Jan-Apr 2015 Sep 2015 - Jun 2016 Aug-Sep 2016 Mar-Dec 2017 Mar 2018 - Jan 2020	Temporary suspension of the commercialisation Production problems Delay in release of end product Reason unknown	**Decreased in 2016 and 2017** (2015: 0.209 DID, 2016: 0.203 DID, 2017: 0.185 DID), increased in 2018 and 2019 (2018: 0.210 DID, 2019: 0.214 DID)	Increased consumption in 2016-2019 (2016: 0.038 DID, 2019: 0.042 DID)
Erythromycin	J01FA01	Oral solution 250 mg/5 ml	Aug 2015 - Mar 2016 May 2018 - Dec 2018 May 2019	Production problems Other reason	**Decreased over time** (2015 0.028 DID, and 2019: 0.003 DID)	Similar consumption in 2015-2019 (0.009 DID)
Spiramycin	J01FA02	Tablets 1.5 MU	Mar-Jun 2015	Production problems	Decreased consumption over time (from 0.022 DID in 2014 to 0.014 DID in 2019)	Very low consumption, similar in 2014-2019 (<0.0001 DID)
Clarithromycin	J01FA09	Tablets 250 mg, 500 mg Oral suspension 125 mg/5 ml, 250 mg/5 ml Powder for infusion (vials) 500 mg (several firms)	Feb 2015 - Jan 2016 May 2016 - Mar 2017 Jun 2017 - Aug 2017 Oct 2017 - Jul 2018 Nov 2018 - Jan 2020*	Production problems Packaging problems Delay in release of end product Temporary suspension of the commercialisation FMD Serialization (new barcodes) Other reason	**Decreased consumption over time** (2014: 1.50 DID, 2019: 1.09 DID)	**Decreased consumption over time** (2014: 0.037 DID, 2019: 0.031 DID)
Azithromycin	J01FA10	Tablets 250 mg, 500 mg Oral suspension 200 mg/5 ml (several firms)	Jan-Aug 2015 Apr 2016 Jan 2019 - Jan 2020*	Delay in release of end product Production problems Other reason	Increased consumption over time (2014: 1.44 DID, 2019: 1.98 DID)	Increased consumption over time (2014: 0.017 DID, 2019: 0.031 DID)
Clindamycin	J01FF01	Vaginal cream 100 mg/5000 mg Capsules 150 mg, 300 mg, 600 mg Oral suspension 75 mg/5 ml Solution for injection (ampoules) 600 mg, 900 mg (several firms)	Jan-Apr 2015 Sep-Oct 2015 Dec 2015 - Oct 2016 Jan 2017 - Feb 2017 Jun 2017 Aug 2017 - Mar 2018 Jun 2018 - Jan 2019 Jul 2019 Sept 2019 - Jan 2020*	Delay in release of end product FMD Serialization (new barcodes)	Increased consumption over time (2014: 0.35 DID, 2019: 0.41 DID)	Similar consumption in 2015-2017 (0.040 DID), **decreased in 2018 and 2019** (2018: 0.039 DID, 2019: 0.038 DID)

Lincomycin	J01FF02	Capsules 500 mg Solution for injection (syringe) 600 mg	Nov-Dec 2015 Apr-Aug 2016 Sep-Oct 2018 Feb-Apr 2019	Delay in release of end product	**Decreased consumption over time** (from 0.007 DID in 2014 to 0.003 DID in 2019)	Similar consumption between 2014 and 2019 (0.0001 DID)
Tobramycin	J01GB01	Nebuliser solution (ampoules) 300 mg/5 ml Inhalation powder capsules 28 mg	Nov-Dec 2015 Jan 2020*	Delay in release of end product Increased demand	Decreased consumption between 2015 and 2018 (from 0.013 DID in 2015 to 0.009 DID in 2018), increased in 2019 (0.011 DID)	Decreased consumption between 2015 and 2018 (from 0.005 DID in 2015 to 0.004 DID in 2018), increased in 2019 (0.005 DID)
Ofloxacin	J01MA01	Tablets 400 mg (several firms)	Jul 2017 - Apr 2019 Jan 2020*	Delay in release of end product Production problems FMD Serialization (new barcodes)	**Decreased consumption** between 2016 (0.135 DID) and 2019 (0.022 DID), **probably related to change in reimbursement criteria**	Similar consumption between 2015 and 2019 (0.001 DID)
Ciprofloxacin	J01MA02	Tablets 250 mg, 500 mg, 750 mg Oral suspension 50 mg/ml Solution for infusion (bag/bottle) 200 mg/100 ml, 400 mg/ 200 ml (several firms)	Jul 2015 Jun-Aug 2016 Feb 2017 - Jan 2020*	Delay in release of end product Production problems Reason unknown Other reason FMD Serialization (new barcodes)	**Decreased consumption** between 2014 (1.05 DID) and 2019 (0.29 DID), **probably related to change in reimbursement criteria**	**Decreased consumption over time** (from 0.10 DID in 2014 to 0.08 DID in 2019)
Levofloxacin	J01MA12	Tablets 250 mg, 500 mg Solution for infusion (vials) 5 mg/ml (several firms)	Jul-Nov 2015 Sept 2017 - April 2018 Oct 2018 Feb 2019 - Jan 2020*	Delay in release of end product Delay in production Reason unknown	**Decreased consumption** between 2015 (0.29 DID) and 2019 (0.10 DID), **probably related to change in reimbursement criteria**	**Decreased consumption** between 2015 (0.052 DID) and 2019 (0.042 DID)
Moxifloxacin	J01MA14	Tablets 400 mg Solution for infusion (bottle) 400 mg/250 ml (several firms)	Mar-Aug 2015 Jan-Oct 2016 Jan-May 2017 Sep-Oct 2017 Nov 2017 - Sep 2018 May 2019 - Jan 2020*	Delay in release of end product Production problems Reason unknown Packaging problems Delay in production	**Decreased consumption** between 2015 (0.96 DID) and 2019 (0.15 DID), **probably related to change in reimbursement criteria**	**Decreased consumption** between 2015 (0.050 DID) and 2019 (0.030 DID)
Vancomycin	J01XA01	Solution for infusion (vials) 500 mg, 1000 mg (several firms)	Oct 2019 - Jan 2020*	Delay in release of end product	Very low consumption (<0.001 DID)	Similar consumption in 2016-2018 (0.038 DID), **decreased in 2019** (0.035 DID)
Metronidazole	J01XD01	Solution for infusion (bag) 500 mg/100 ml	May-Jul 2019	Logistic problems (transport, customs, ...)	No consumption	Increased consumption in 2019 (0.017 DID) compared to 2018 (0.016 DID)
Tinidazole	J01XD02	Tablets 500 mg	Jan-Oct 2017 Jan-Sep 2019	Delay in release of end product	No consumption	No consumption
Ornidazole	J01XD03	Tablets 500 mg	Nov 2019 - Jan 2020*	Logistic problems (transport, customs, ...)	No consumption	Similar consumption in 2017-2019 (0.003 DID)

Nitrofurantoin	J01XE01	Capsules 100 mg	Jun-Jul 2019	Packaging problems	Increased consumption in 2019 (2.41 DID) compared to 2018 (2.32 DID)	**Decreased consumption** in 2019 (0.033 DID) compared to 2018 (0.035 DID)
Linezolid	J01XX08	Tablets 600 mg Solution for infusion (bag) 2 mg/ml (several firms)	Oct 2017 - Mar 2018	Production problems Delay in release of end product	No consumption	Similar consumption in 2016-2018 (0.006 DID)
Amphotericin B	J02AA01	Concentrate for dispersion for infusion (vials) 5 mg/ml	Aug-Sep 2019	Delay in release of end product	No consumption	**Decreased consumption** in 2019 (0.009 DID) compared to 2018 (0.012 DID)
Fluconazole	J02AC01	Capsules 50 mg, 150 mg, 200 mg Solution for injection (vials), 2 mg/ml (several firms)	Jul-Oct 2015 Feb-Mar 2016 Nov-Dec 2016 Jul 2017 - Aug 2018 Jun 2019 - Jan 2020*	Delay in release of end product Delay in production FMD Serialization (new barcodes)	**Decreased consumption over time** (from 0.73 DID in 2014 to 0.67 DID in 2019)	**Decreased consumption over time** (from 0.077 DID in 2014 to 0.055 DID in 2019)
Itraconazole	J02AC02	Capsules 100 mg (several firms)	Jul 2015 Jun 2017 - Jan 2019 Jul 2019 - Jan 2020*	Delay in release of end product FMD Serialization (new barcodes)	**Decreased consumption over time** (from 0.60 DID in 2014 to 0.49 DID in 2019)	**Decreased consumption over time** (from 0.005 DID in 2014 to 0.003 DID in 2019)
Voriconazole	J02AC03	Tablets 50 mg, 200 mg (several firms)	Feb-Mar 2016 Oct 2017 - Feb 2019 Apr 2019 - Jan 2020*	Delay in release of end product Reason Unknown Delay in production Delay in release of end product	**Decreased consumption over time** (from 0.014 DID in 2015 to 0.010 DID in 2019)	**Decrease between 2017** (0.010 DID) **and 2019** (0.009 DID)
Posaconazole	J02AC04	Oral suspension 40 mg/ml	Jul-Sep 2017	Production problems	Similar consumption in 2016 and 2017 (0.005 DID)	Similar consumption in 2016 and 2017 (0.008 DID)
Caspofungin	J02AX04	Powder for infusion (vials) 50 mg, 70 mg	Oct 2019 - Jan 2020	Delay in release of end product Increased demand	No consumption	Compared consumption in 2018 and 2019 (0.003 DID)
Rifampicin	J04AB02	Capsules 150 mg, 300 mg	Mar-Apr 2015 Jun-Nov 2016 Jun-Mar 2018 Mar 2019 - Jan 2020*	Logistic problems (transport, customs, ...) Production problems Delay in release of end product	Decrease in 2013-2015 (0.003 DID), similar consumption in 2016-2018 (0.045 DID), **decreased in 2019** (0.042 DID)	Similar consumption in 2014-2017 (0.017 DID), **decreased in 2018 and 2019** (0.016 DID)
Rifabutin	J04AB04	Capsules 150 mg	Mar-Jun 2019	Delay in release of end product	Increased in 2019 (0.006 DID) compared to 2018 (0.007 DID)	Increased in 2019 (0.0012 DID) compared to 2018 (0.0009 DID)
Pyrazinamide	J04AK01	Tablets 500 mg	Feb-Mar 2017	Delay in release of end product	Similar consumption in 2016 and 2018 (0.018 DID), **decreased in 2017** (0.017 DID)	Similar consumption in 2016 and 2018 (0.0037 DID), **decreased in 2017** (0.0033 DID)
Ethambutol	J04AK02	Tablets 400 mg	Aug-Oct 2016 May-Jul 2018	Delay in release of end product Other reason	Similar consumption in 2015 and 2018 (0.023 DID), **decreased in 2016-2017 (0.021 DID)**	Similar consumption in 2015-2016 (0.0038 DID), decreased in 2017 (0.0033 DID), increased in 2018 (0.0041 DID)

Aciclovir	J05AB01	Tablets 200 mg, 800 mg Powder for injection/infusion (vials) 250 mg, 25 mg/ml (several firms)	Dec 2015 - Feb 2016 May 2016 - Jan 2020	Delay in release of end product Production problems FMD Serialization (new barcodes)	Increased consumption over time (from 0.09 DID in 2016 to 0.11 DID in 2019)	Increased consumption over time (from 0.012 DID in 2014 to 0.013 DID in 2019)
Valganciclovir	J05AB14	Tablets 450 mg	Oct 2016 - May 2017 Mar-May 2019	Other reason Delay in release of end product	Increased consumption between 2015 and 2018 (from 0.004 DID in 2015 to 0.015 DID in 2018), **decreased in 2019** (0.012 DID)	Increased consumption over time (from 0.002 DID in 2015 to 0.004 DID in 2019)
Ritonavir	J05AE03	Oral suspension 100 mg	Jun-Jul 2019	Delay in release of end product	**Decreased consumption over time** (from 0.011 in 2017 to 0.006 in 2019)	**Decreased consumption over time** (from 0.002 in 2017 to 0.0005 in 2019)
Tipranavir	J05AE09	Capsules 250 mg	Oct-Nov 2018	Logistic problems (transport, customs, ...)	Very low consumption (<0.001 DID)	Very low consumption (<0.0001 DID)
Didanosine	J05AF02	Oral powder 2000 mg	Jan 2017 - May 2018	Temporary suspension of the commercialisation	Very low consumption (<0.001 DID)	Very low consumption (<0.0001 DID)
Lamivudine	J05AF05	Oral solution 5 mg/ml	Jun-Jul 2015 Dec 2016 - Jan 2017	Delay in release of end product Production problems	Similar consumption in 2015-2018 (0.028 DID)	Similar consumption in 2015-2018 (0.003 DID)
Tenofovir Disoproxil	J05AF07	Tablets 245 mg	Jan-Jul 2018	Reason unknown	Similar consumption in 2017-2019 (0.09 DID)	**Decreased consumption** between 2017 (0.0018 DID) and 2018 (0.0014 DID)
Neviparine	J05AG01	Tablets 200 mg, 400 mg	Apr 2016 Apr 2019 - Aug 2019	Delay in release of end product	**Decreased consumption over time** (from 0.12 DID in 2015 to 0.08 DID in 2019)	**Decreased consumption over time** (from 0.017 DID in 2015 to 0.003 DID in 2019)
Efavirenz	J05AG03	Tablets 200 mg, 600 mg (several firms)	Jul-Aug 2018 Jan-Mar 2019 Jan 2020*	Delay in release of end product Production problems	**Decreased consumption over time** (from 0.017 DID in 2017 to 0.010 DID in 2019)	**Decreased consumption over time** (from 0.002 DID in 2017 to 0.001 DID in 2019)
Ribavirin	J05AP01	Capsules 200 mg	Jul 2016 - Jul 2017	Delay in release of end product	Very low consumption (<0.001 DID)	**Decreased consumption over time** (from 0.014 DID in 2015 to 0.001 DID in 2018)
Zidovudine and Lamivudine	J05AR01	Tablets 300/150 mg	Jan-Aug 2017	Delay in release of end product	**Decreased consumption over time** (0.016 DID in 2016, 0.012 DID in 2017, 0.008 DID in 2018)	**Decreased consumption over time** (0.002 DID in 2016, 0.001 DID in 2017 and 2018)
Lamivudine and Abacavir	J05AR02	Tablets 300/600 mg	Mar 2019 - Jan 2020	Delay in release of end product	**Decreased consumption over time** (from 0.084 DID in 2017 to 0.057 DID in 2019)	**Decreased consumption over time** (from 0.012 DID in 2017 to 0.007 DID in 2019)
Tenofovir Disoproxil and Emtricitabine	J05AR03	Tablets 245/200 mg	Aug 2017- Feb 2019	Other reason	**Decrease in 2017** (0.17 DID), increase in 2018 (0.21 DID) and 2019 (0.25 DID)	**Decrease in 2017** (0.017 DID), increase in 2018 (0.023 DID) and 2019 (0.029 DID)

Emtricitabine, Tenofovir Disoproxil and Efavirenz	J05AR06	Tablets 200/245/600 mg	Jun-Sep 2018 Jan 2020*	Delay in release of end product Delay in production	**Decreased consumption over time** (from 0.077 DID in 2017 to 0.055 DID in 2019)	**Decreased consumption over time** (from 0.006 DID in 2017 to 0.003 DID in 2019)
Inosine pranobex	J05AX05	Tablets 500 mg	Feb-Mar 2015	Production problems	Very low consumption (<0.001 DID)	Very low consumption (<0.0001 DID)

* no end date yet for one or more firms at the time of the analyses
[a] based on the classification in PharmaStatus
[b] ESAC-Net 2019 data in hospitals are an estimation (15% extrapolation), see methods section
ATC = Anatomical Therapeutic Chemical classification; DID = Defined daily doses (DDDs)/1000 inhabitants/day; FMD = Falsified Medicines Directive; IU = international units; mg = milligrams; ml = milliliters; MU = million international units
Jan = January; Feb = February; Mar = March, Apr = April, Jun = June; Jul = July, Aug = August; Sep = September; Oct = October; Nov = November; Dec = December
Possible impact indicated in bold

DISCUSSION

MAIN RESULTS

The main results per sector are summarized below in Table 13 together with an overview of the quality indicators that were set up by BAPCOC in their 2014-2019 action plan (1). Encouragingly, a significant decrease is seen in the (reimbursed) antibiotic consumption in the community, but this overall consumption is still high in comparison with other EU/EEA countries. The ratio amoxicillin/amoxicillin+clavulanic acid only slightly improved over time. Coinciding with a change in reimbursement criteria for fluoroquinolones in May 2018 (39), a large decrease in the reimbursed consumption of fluoroquinoles was detected. In response, a large (undesired) increase was also noted in non-reimbursed consumption of fluoroquinolones. Overall, the use of fluoroquinolones did decrease (-16% in comparison with 2018 and -37% in comparison with 2017), but less than one would conclude only based on reimbursement data. Fluoroquinolones are still responsible for 6.7% of the total antibiotic consumption. Although overall improvement is seen over the last few years, none of the targets of the three indicators set up by BAPCOC (1) were reached based on 2019 data, indicating that the efforts need to be pursued. Further actions are planned to sensitize prescribers to use antibiotics in a prudent way, with special attention for the use of broad-spectrum antibiotics. Moreover, the high use of antimycotics and antifungals in the community in Belgium in striking (among the highest users of all participating EU/EEA countries in ESAC-Net). The reasons for this high use should be further investigated. The possibility to link antimicrobial consumption with indications would help to evaluate this consumption in a more thorough way and to provide more detailed feedback to prescribers.

In Belgian hospitals, the antibiotic and antimycotic/antifungal consumption is in line with EU/EEA mean if expressed in DID. However, it is preferable to use the hospital population as denominator instead of the total country population and express the consumption in DDDs/1000 patient days and DDDs/1000 admissions. Overall, a significant increase in antibiotic consumption in acute hospitals was detected in DDDs/1000 patient days and a significant decrease in DDDs/1000 admissions. The increase in DDDs/1000 patient days can probably be explained by the evolution towards shorter hospital stays in acute hospitals with a more intensive antibiotic treatment on less patient days. In addition, more patients are being discharged with OPAT (Outpatient parenteral antimicrobial therapy). The percentage of broad-spectrum use (±31%) did only slightly (but not significant) improve over time. While the use of fluoroquinolones decreased, the use of piperacillin in combination with tazobactam increased over time. For several indicators (total antibiotic consumption, antibiotic consumption on ICU, % broad-spectrum use, % IV use), boxplots indicated a high variation between acute hospitals, also when compared per type of hospital (primary, secondary, tertiary). High outliers, especially when present over consecutive years, should be further targeted to understand the reasons behind these outlying results and identify possible points for improvement. Again, information on the indications for antimicrobial prescribing would facilitate this process. The results of the Global-PPS 2019 indicate that compliance with the guidelines and registration of the indication in the medical file improved over time, but the targets were not yet reached. Strikingly, only half of antimicrobial prescriptions in 2019 had a stop/review date documented in the medical record. It is advised that a legal framework is provided requiring prescribers to document a stop/review date. Preferably, this would be integrated in the hospital's electronic systems to enable information exchange with the hospital pharmacy.

Table 13: Summary of the main results and strategic target evaluation on antimicrobial consumption per sector (community versus hospitals, Belgium, 2010-2019)

Community (including nursing homes)	Hospitals
Overall (reimbursed) antibiotic consumption: • 2010-2019: significant **decrease** in DID[a] **(-14%)** • 23.1 DID in 2010 to 19.8 DID in 2019 (20.6 DID in 2019 if non-reimbursed consumption of fluoroquinolones (estimation) is taken into account) • Comparison with neighboring countries: - EU/EEA mean in 2019: 18.0 DID (2010-2019: -5%) - The Netherlands in 2019: 8.7 DID (2010-2019: -13%) - France in 2019: 23.3 DID (2010-2019: +0.4%)	**Overall (reimbursed) antibiotic consumption:** *All hospitals* • 2010-2019: significant **decrease** in DID **(-13%)** • 1.76 DID in 2010 to 1.54 DID in 2019 • Comparison with neighboring countries: - EU/EEA mean in 2019: 1.77 DID (2010-2019: +0%) - The Netherlands in 2019: 0.80 DID (2010-2019: -14%) - France in 2019: 1.74 DID (2010-2019: -4%) *Acute hospitals (inpatients wards[$])* • 2010-2019: significant **increase** in DDDs/1000 patient days **(+3%)**, 442.8 in 2010 to 457.8 in 2019 • 2010-2018: significant **decrease** in DDDs/1000 admissions **(-6%)**, 3486 in 2010 to 3276 in 2018
Most increased consumption (% of all antibiotics)**:** • Macrolides (11.3% in 2010 to 15.6% in 2019) • Penicillins with extended spectrum (21.0% in 2010 to 24.3% in 2019)	**Most increased consumption** (% of all antibiotics)**:** *All hospitals* • Beta-lactamase resistant penicillins (4.9% in 2010 to 6.5% in 2019) • Penicillins with extended spectrum (3.7% in 2010 to 5.2% in 2019)
Most decreased consumption (% of all antibiotics)**:** • Fluoroquinolones (11.6% in 2010 to 6.7% in 2019, non-reimbursed consumption included) • Penicillins in combination with beta-lactamase inhibitors (24.9% in 2010 to 23.7% in 2019)	**Most decreased consumption** (% of all antibiotics)**:** *All hospitals* • Fluoroquinolones (13.6% in 2010 to 9.9% in 2019) • Penicillins in combination with beta-lactamase inhibitors (35.0% in 2010 to 32.9% in 2019)
Top 5 most used products in 2019: amoxicillin, amoxicillin + clavulanic acid, nitrofurantoin, azithromycin, cefuroxime	**Top 5 most used products in 2019:** *Acute hospitals (non-psychiatric inpatient wards)* amoxicillin + clavulanic acid, cefazolin, piperacillin + tazobactam, flucloxacillin, ciprofloxacin
Ratio amoxicillin/amoxicillin + clavulanic acid: From 0.85 (46/54) in 2010 to 1.04 (51/49) in 2019	**Ratio amoxicillin/amoxicillin + clavulanic acid:** *All hospitals* From 0.08 (7/93) in 2010 to 0.14 (12/88) in 2019
Indicator broad-spectrum antibiotic use[b]: 2.38 in 2010 to 1.94 in 2019 (% of all antibiotics: 54.3% in 2010 to 48.1% in 2019)	**Indicator broad-spectrum antibiotic use[c]:** *Acute hospitals (non-pediatric, non-psychiatric inpatient wards)* 32.1% in 2010 to 31.3% in 2019 (not significant)
Overall antimycotic and antifungal consumption: • 2010-2019: significant **decrease** in DID **(-9%)** • 3.3 DID in 2010 to 3.0 DID in 2019 • Among the highest consumers of antimycotics and antifungals in EU/EAA countries (2019: EU/EEA mean 1.0 DID, the Netherlands 1.3 DID, France 1.3 DID)	**Overall antimycotic and antifungal consumption:** *All hospitals* • 2010-2019: significant **decrease** in DID **(-28%)** • 0.13 DID in 2010 to 0.09 DID in 2019 • Comparison with neighboring countries in 2019: EU/EEA mean 0.12 DID, France 0.21 DID
Observed prevalence of residents with at least one antimicrobial prescription on one day: *Nursing homes:* 4.3% in 2010, 5.1% in 2013, 5.6% in 2016	**Observed prevalence of patients with at least one antimicrobial prescription on one day:** *Acute hospitals (inpatients wards):* 28.9% in 2011, 27.4% in 2015, 27.0% in 2017, 27.8% in 2019 *Psychiatric hospitals:* 3.8% in 2017
BAPCOC quality indicators policy plan 2014-2019 (1)	
From 800 prescriptions/1000 inhabitants/year in 2014 to 600 in 2020 and 400 in 2025 Not possible to assess with the ESAC-Net data, based on packages/1000 inhabitants in 2019 (734) estimated at ±700 prescriptions/1000 inhabitants/year → target not yet reached	**Choice of the antibiotic in line with the local guidelines in ≥90% of the cases (therapeutic use)** Global PPS: 80.7% in 2015, 81.7% in 2017, 83.7% in 2019 → steady improvement, but target not yet reached
Reduction in % fluoroquinolones from 10% in 2014 to 5% in 2018 Estimated at 6.7% in 2019 (taking non-reimbursed consumption (estimation) into account) → improvement, but target not yet reached	**Indication of the antibiotic noted in the medical file in ≥90% of the cases** Global-PPS 2015: 79.9%, ECDC/Global-PPS 2017: 81.9%, Global-PPS 2019: 85.2% → steady improvement, but target not yet reached
Ratio amoxicillin/amoxicillin + clavulanic acid from 1 (50/50) in 2014 to 4 (80/20) in 2018 Still 1.04 (51/49) in 2019 → target not yet reached	**Choice of the antibiotic for surgical prophylaxis (SP) in line with the local guidelines in ≥90% of the cases** Global PPS: 70.8% in 2015, 73.8% in 2017, 79.8% in 2019 → steady improvement, but target not yet reached
	Duration of the surgical prophylaxis (SP) treatment in line with the local guidelines in ≥90% of the cases Global PPS: 28.1% of SP >1 day in 2015, 25.3% in 2017, 18.9% in 2019 → steady improvement

a. DID: Defined daily doses (DDDs)/1000 inhabitants/day; 2020 edition of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Doses (DDDs) were used (2)
b. total DDDs J01(CR+DC+DD+(F-FA01)+MA)/J01(CA+CE+CF+DB+FA01); c. % DDDs J01(CR05+DD+DE+DF+DH+MA+XA+XB+XX08+XX09+XX11)/J01
$ inpatient wards include surgery, internal medicine, geriatrics, pediatrics, intensive and non-intensive neonatology, maternity, infectious disease, burn unit, intensive care (ICU), specialized care and psychiatry (outpatient wards and day hospitalizations excluded)

*** Values underlined & in bold: significant trend as obtained by linear regression (p-values <0.05)**

Certain agents have been shown to be (temporary) unavailable from the Belgian market, and often this is the case for older small-spectrum agents (out of patent). This scenario promotes the irrational use of more last line agents and should be avoided to decrease the resistance selection for these newer compounds. The results on shortages of antimicrobial agents indicate that this is a growing problem (44 antibiotic products/ATC codes were implicated in the last five years). It is getting more and more challenging to find alternatives for products that are (temporary) unavailable or withdrawn from the market. Especially in case only one alternative exists, a shortage can have an important impact. FAMHP is consulting several companies to find sustainable solutions to bring unavailable antimicrobial agents on the Belgian market again.

CURRENT SITUATION IN THE VETERINARY SECTOR

For the veterinary sector, antibiotic consumption data are yearly published in the BelVet-SAC report (17). These results are based on sales data (collected at the level of the wholesalers distributors and the compound feed producers) and usage data (collected at herd level, Sanitel-Med). The consumption is expressed in milligrams active substance per kilogram produced biomass (based on data of Eurostat (19)).

Clear progress is made in the veterinary sector over the last years. In 2019, there was a decrease of 7.6% mg antibiotic/kg biomass in comparison to 2018 (-40.3% since 2011). Both the consumption of pharmaceuticals (-7.8%) and antibiotic premixes (-5.1%) decreased. The most used class of antibiotics in 2019 was the penicillins (68.6 tons, 38.9%), followed by the tetracyclines (37.1 tons, 21.0%) and the sulphonamides and trimethoprim (33.8 tons; 19.1%). A worrisome evolution in 2019 was the increase of the use of fluoroquinolones for the second year in a row (+10% in comparison with 2018). Fluoroquinolones are part of the red group of antibiotics, meaning products of the highest importance for human medicine that should be avoided in veterinary medicine as much as possible. In 2019, an increase of 8% was seen in the red group while the consumption in the yellow (lowest importance in human medicine) and the orange group (higher importance in human medicine, restricted use) decreased with 7% and 8% respectively (17).

In the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report, the Belgian results on antibiotic consumption (quantified by means of the Population Correction Unit (PCU)) can be compared with the other 30 EU/EEA countries. Based on 2017 data, Belgium (131.3 mg/PCU) is ranked at the 8th place (from high to low, in 2015 still the 5th place). The consumption is still higher than the European median (61.9 mg/PCU) and our neighboring countries (Netherlands: 56.3 mg/PCU) (57).

Two of the three targets of AMCRA were already reached in 2017 (https://amcra.be/nl/visie-2020/): the antibiotic premixes are decreased with more than 50% in comparison with reference year 2011 (in 2019: -71.1%) and the red antibiotics with more than 75% (in 2019: -77.3%). Only the target on total antibiotic consumption, -50% by 2020 in comparison with 2011, still has to be reached (in 2019: -40.3%). Several activities are currently ongoing or planned to further improve (e.g. benchmarking tool, herd health plans, continuous education) in the coming years (17). The clear targets and motivation to reach these targets in the veterinary sector can inspire the human sector to achieve similar progress. Meanwhile, new targets for the veterinary sector were defined by AMCRA to further improve and move towards the median consumption in EU/EEA countries (https://amcra.be/nl/visie-2024/).

In the new Sanitel-Med register (secured online data collection system in which veterinarians are obliged, since February 2017, to register all antibiotic prescriptions, administrations and deliveries), data are also available per herd level. Most recent results can be consulted in the Sanitel-Med barometer: https://www.amcra.be/nl/analyse-antibioticagebruik/.

STRENGTHS AND WEAKNESSES

The main strengths and weaknesses per database are listed in Table 14.

Table 14: Overview of the strengths and weaknesses of the national and international antimicrobial consumption databases used in this report

Database	Strengths	Weaknesses
ESAC-Net	- Data on community and hospitals - Extrapolation to correct for the inhabitants without a health insurance (99% to 100%) - European surveillance (ECDC) which make comparison with the EU mean and other countries possible	- Reimbursement data, so underestimation for certain products (e.g. fluoroquinolones) - Aggregated data, no details per type of prescriber, region, hospitals - Total population as denominator for hospitals (instead of the hospital population), future plan to add hospital-specific indicators in ESAC-Net - Delay in reimbursement data - Whole packages considered as consumed - Limitations of DDDs as indicator (e.g. not appropriate for children, difference with actual doses used in practice) - No link with indication
BeH-SAC	- Reuse of existing data, no registration load for hospitals - Uniform data collection for all hospitals - Detailed data on different levels (national, regional, hospital, ward) - Interactive reports on Healthstat.be - Hospital-specific indicators (DDDs/1000 patient days, DDDs/1000 admissions)	- Reimbursement data, so underestimation for certain products, import from other countries not included (no extrapolations to correct for this) - Delay in reimbursement data (±1 year) - Whole units considered as consumed which may lead to an overestimation (e.g. ampoules used for individual dosing) - Limitations of DDDs as indicator (e.g. not appropriate for children, difference with actual doses used in practice) - Classification of the wards not detailed enough for feedback to specific prescribers - Errors can occur in reimbursement data, so validation/correction of outlying results is needed - No link with indication
Global/ECDC-PPS	- Detailed data on antimicrobial prescribing (per indication, diagnosis), including quality indicators - Large subset of hospitals (±80% of all acute hospitals in 2017) by combining Global- and ECDC-PPS data - Supports antimicrobial stewardship interventions, enhances setting targets and evaluates outcomes through repeated PPS	- Cross-sectional, only prevalence data - No correction for patient case-mix or institutional factors - Voluntary participation (only for the ECDC-PPS random sampling) - Self-collected data by hospital staff (different types of data collectors)
HALT/HALT-PSY	- Specific data for the nursing home and psychiatry setting - Detailed data on antimicrobial prescribing (per indication, diagnosis)	- Cross-sectional, only prevalence data - No correction for patient case-mix or institutional factors - Voluntary participation of institutions, no random sample, so the results cannot be considered as representative for all Belgian institutions - Self-collected data by staff (different types of data collectors), possible variation in data collection (despite provided training) - Different time periods for the 3 HALT studies (HALT 1: May-September 2010, HALT 2: April-May 2013, HALT 3: September-November 2016) which may have an influence on the results

BeH-SAC = Belgian Hospitals - Surveillance of Antimicrobial Consumption; DDD = Defined Daily Dose; ECDC = European Center for Disease Prevention and Control; ESAC-Net = European Surveillance of Antimicrobial Consumption Network; Global/ECDC-PPS = Point Prevalence Study of antimicrobial consumption, resistance and healthcare-associated infections in acute hospitals; HALT = Point prevalence survey of healthcare-associated infections and antimicrobial use in long-term care facilities (HALT-PSY: in psychiatric institutions)

FUTURE PERSPECTIVES

- As mentioned in the introduction of this report, a new national One Health action plan (NAP) against AMR (2020-2024) is currently being finalized. This action plan contains different approaches to improve the prudent use of antimicrobial consumption and new indicators to follow-up the impact of these approaches on antimicrobial consumption and resistance.
- To investigate antimicrobial consumption more in-depth (quality besides quantity) and to be able to provide more detailed feedback to prescribers, a linkage of consumption data with indications is needed. For acute hospitals, a pilot study (AM-DIA: AntiMicrobial consumption data of Belgian hospitals linked with DIAgnoses) is set-up in which reimbursement data coupled with diagnoses from the minimal hospital data are being analyzed to identify reliable indicators on quality of prescribing (project currently on hold due to the COVID-19 crisis). For the community, in the prescribing software of general practitioners, automated feedback based on indication and an optimized integration of the BAPCOC guidelines are two of the planned actions in the coming years.
- The reasons for the increase in the non-reimbursed consumption of fluoroquinolones in the community and the impact on the costs for the patients need to be investigated (58).
- A clear view on the antimicrobial consumption in emergency and outpatient wards is currently lacking and should be studied further. This includes the evolution and the impact of OPAT (Outpatient parenteral antimicrobial therapy).
- In Appendix 1, preliminary results of a validation of BeH-SAC are presented with a focus on low and high outliers in antibiotic consumption. Further analyses of hospitals with outlying results are planned. In addition, new BeH-SAC hospital reports will be added in Healthstat so hospitals can easily identify outlying results and validate them. DDA will also be added in the reports as second indicator besides DDD.
- A new European ECDC-PPS and HALT study are planned in 2022 and 2023, respectively. Additionally, an extra HALT study in Belgian nursing homes will most probably be organized in 2021. The Global-PPS opens three surveys a year. Any hospital is free to join at any time. Regular webinars will be organized focusing on different aspects (data collection and management, data reporting and analysis) (https://www.global-pps.com/).
- Since December 2019, the impact of a shortage of medicines is also registered in the Pharmastatus database (e.g. if alternatives are available, if import from other countries is possible, if the shortage is critical). Based on this new information, further analyses of the impact of shortages of antimicrobial agents are planned in the future.
- So far, consumption and resistance data in humans (AMR surveillance in Belgian hospitals, EARS-Net) and animals (consumption in BelVet-SAC, resistance surveillances in animals) have been published separately (17,59–61). It is planned to publish a One Health national report over all sectors in the coming years.
- When 2020 consumption data become available, the impact of the COVID-19 crisis on antimicrobial consumption will be investigated in detail. Results of a clinical COVID-19 surveillance in Belgian acute hospitals indicate that 18% of all hospitalized COVID-19 patients developed a bacterial or fungal superinfection. Looking at COVID-19 patients on ICU wards, this was 42% (62).

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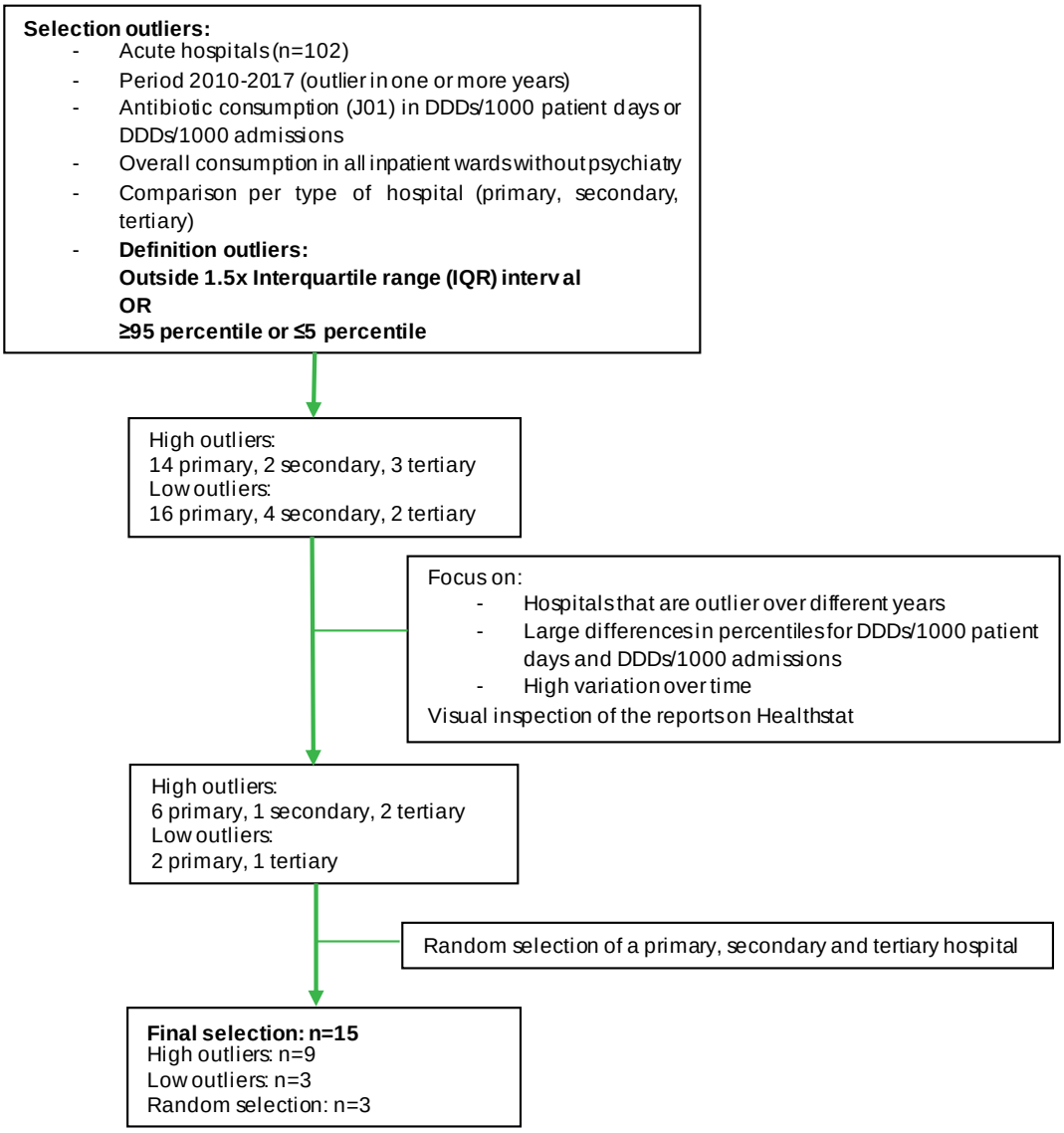
APPENDIX 1: METHODS AND RESULTS OF A VALIDATION STUDY OF BEH-SAC

OBJECTIVE

The objective of this validation study was to compare the results of BeH-SAC with the results of local surveillances in hospitals, with a focus on hospitals with outlying (high or low) results in BeH-SAC, to check for possible errors in BeH-SAC and (where possible) to calculate the percentage difference in results. This validation is one of the action points in the new national One Health action plan (NAP) against AMR (2020-2024).

METHODS

The flow diagram below indicates how hospitals were selected for the validation study. The focus was put on acute hospitals and outliers in total antibiotic consumption (DDDs/1000 patient days or DDDs/1000 admissions) compared with hospitals of the same type (primary, secondary, tertiary). In addition, three extra hospitals (one of each type) were randomly selected for the validation. The analyses were performed on the BeH-SAC database of November 2019 (data until 2017).



In the beginning of January 2020, each of the selected hospitals received a summary report of their results in BeH-SAC (2010-2017, number of patient days/admissions (denominators) and consumption data), where possible compared with results of the old methodology (ABUH, own data uploaded on NSIHweb). This was sent to the contact person of the antibiotic management team of the hospital. They were asked to take a close look at the results and to validate them (if possible by comparing the numbers/trends with own hospital data) by the end of February 2020. A checklist (see below) was provided to guide the validation.

Checklist	**Validation:** **Data RIZIV/INAMI in line with own hospital data? Same trends?**	**Comments**
Evolution total number of patient days, all wards		
Evolution total number of admissions, all wards		
Total antibiotic consumption (J01) in DDDs/1000 patient days, all wards		
Total antibiotic consumption (J01) in DDDs/1000 admissions, all wards		
Total antibiotic consumption (J01) in DDDs/1000 patient days, intensive care unit (ICU)		
Consumption of the specific antibiotic products/classes in DDDs/1000 patient days, all wards Special attention for: *(list of antibiotic classes/products with outlying results in the specific hospital)*		
Total antimycotic consumption (J02) in DDDs/1000 patient days, all wards		
Is there a local surveillance of antimicrobial consumption in your hospital? Please explain.		
Which elements might have influenced the results of antimicrobial consumption for your hospital in last 5 years (e.g. shortages of certain products, non-reimbursed consumption, specific guidelines not in line with the DDDs)?		
Other suggestions for improvement, comments or feedback concerning BeH-SAC:		

RESULTS

The (preliminary) results are presented in the table below.

Hospital	Type	How validated	Results	% difference between BeH-SAC and hospital data
1	Primary LO	Check denominator data No internal consumption data available, limited validation by checking the trends in the graphs	Change of hospital sites, not yet applied in reimbursement data (only from 2018 onwards) Based on the old composition of hospital sites: Trends in denominator data the same Trends in consumption in line with what expected	NA Denominator data: in BeH-SAC 5-10% lower than ABUH data (2010-2013)
2	Primary LO	*No response received from the hospital (validation coincided with the start of the COVID-19 crisis)*		
3	Tertiary LO	Check denominator data Comparison consumption data with own surveillance Same methodology used as BeH-SAC (same DDD-version, billed patient days, same wards, only patients with a hospital insurance) 2012-2017	Trends in denominator data and consumption data the same (also for specific antibiotic subclasses and antimycotics) Lower consumption data expected (total versus reimbursement data)	Denominator data: in BeH-SAC <1-2% lower than own hospital data (on ICU: 2%) Total antibiotic consumption in DDDs/1000 patient days: in BeH-SAC 3-5% lower than own hospital data (ICU: 1-7%) Total antibiotic consumption in DDDs/1000 admission: in BeH-SAC 1-4% lower than own hospital data
4	Primary HO	Check denominator data No internal consumption data available, limited validation by checking the trends in the graphs	Denominator data correct Trends in consumption in line with what expected No data per hospital site makes the interpretation of the results difficult	NA No data in ABUH
5	Primary HO	Check denominator data Comparison consumption data with pharmacy data (units converted in DDDs with the DDD list of BeH-SAC), focus on 4 products with high consumption: amoxicillin + clavulanic acid, piperacillin + tazobactam, ciprofloxacin, fluconazole 2014-2017	Trends in denominator data and consumption data the same Lower consumption data in BeH-SAC as expected (total versus reimbursement data)	Denominator data: in BeH-SAC 1-5% lower than own hospital data (on ICU: 5-10%) Number of DDDs for the 4 products: in BeH-SAC 1-7% lower than own hospital data
6	Primary HO	Check patient days for 2017 Comparison consumption data with pharmacy data (in DDDs/1000 patient days) for 2017, focus on 3 products:	Trends in denominator data and consumption data the same First a high difference for the consumption of	Patient days: in BeH-SAC 4% lower than own hospital data DDDs/1000 patient days for the 3 products: in BeH-SAC 1-5% lower than own hospital data

		amoxicillin + clavulanic acid, piperacillin + tazobactam, fluconazole	amoxicillin + clavulanic acid, explained by different DDD-versions used (DDD for amoxicillin + clavulanic acid changed in 2019) Lower consumption data expected (total versus reimbursement data)	
7	Primary HO	Check denominator data Comparison consumption data with pharmacy data (in units not DDDs), high outlier for levofloxacin so focus on that product Further validation planned for other products	Denominator data correct Error discovered in one TUC code (753947, levofloxacin ampoules), counted as 10 units instead of 1 unit in BeH-SAC → corrected* → Still a high consumption for levofloxacin (± around P75), but no outlier anymore (and ciprofloxacin consumption lower than P50) →High variation (factor 10) of levofloxacin consumption between primary hospitals	NA Denominator data: in BeH-SAC 1-2% lower than ABUH (2010-2013)
8	Primary HO	Check denominator data Consumption data: limited validation by checking the trends in the graphs	Denominator data correct Trends in consumption in line with what expected	NA Denominator data: in BeH-SAC 5-10% lower than ABUH (2012-2017)
9	Primary HO	*No response received from the hospital (validation coincided with the start of the COVID-19 crisis)*		
10	Secondary HO	Check denominator data Comparison of the trends with own surveillance data (based on graphs of ABUH) 2012-2017	Trends in denominator data and consumption data the same High outlying results can be explained by specific patient population (benchmarking not specific enough)	Denominator data: in BeH-SAC 5-10% lower than own hospital data
11	Tertiary HO	Check denominator data (2014-2016) Comparison of the trends with own surveillance data, comparison difficult due to differences in methodology (other definition of wards, patients from abroad not included in BeH-SAC, syrups not included in own surveillance) Visual inspection trends for different antibiotic subgroups (2017-2018) +	Overall trends in denominator data and consumption data the same Comparison of exact numbers: lower consumption in BeH-SAC as expected (total versus reimbursed consumption)	Denominator data: in BeH-SAC 8-12% lower than own hospital data Total consumption J01/J02/J04 in DDDs/1000 patient days: in BeH-SAC 13-20% lower than own hospital data Number of units for the 3 products: in BeH-SAC ±15% lower than own hospital data

		Comparison total consumption J01/J02/J04 in DDDs/1000 patient days (2017-2018) + Comparison consumption data with pharmacy data (in units not DDDs) for 2015-2016, focus on 3 products: amoxicillin + clavulanic acid, piperacillin + tazobactam, ciprofloxacin		
12	Tertiary HO	*No response received from the hospital (validation coincided with the start of the COVID-19 crisis)*		
13	Primary RS	Check denominator data No internal consumption data available, limited validation by checking the trends in the graphs	Denominator data correct Trends in consumption in line with what expected	NA Denominator data: in BeH-SAC 1-4% lower than ABUH (2013-2015)
14	Secondary RS	Check denominator data Comparison of the trends with own surveillance data	Trends in denominator data and consumption data the same	NA Denominator data: in BeH-SAC 5-10% lower than ABUH (2010-2014)
15	Tertiary RS	Check denominator data Comparison of the trends with own surveillance data, comparison difficult due to differences in methodology (other DDD version, other definition of wards, other way of calculating DDDs)	Overall trends in denominator data and consumption data the same Differences could be explained: - 20% lower consumption in BeH-SAC of carbapenems and amoxicillin+clavulanic acid (due to different DDD-version) - 50% higher consumption in BeH-SAC of fluconazole (due to another factor used for the calculation of DDDs)	NA Denominator data: in BeH-SAC 3-5% lower than ABUH data (2010-2013)

DDD = defined daily dose; HO = high outliers; ICU = intensive care unit; LO = low outlier; RS = random selection
ABUH = Antibiotic Use in Hospitals, old methodology of the surveillance based on data delivered by hospitals
NA = not possible to assess
* corrected in the results of this national report (only an impact on the results of two hospitals)

PRELIMINARY CONCLUSION

Only a limited number of the selected hospitals (1 secondary and 3 tertiary hospitals) had a detailed own surveillance system for antimicrobial consumption in place. Where possible, the data of BeH-SAC were compared with pharmacy data. The validation was limited by differences in methodology (e.g. other definition of wards, non-reimbursed consumption included in hospital data, other DDD version). Nevertheless, in most hospitals, the trends in patient days/admissions and antibiotic consumption in BeH-SAC were confirmed with own hospital data.

During the validation, in one hospital, an error in the DDD calculation for one specific product (levofloxacin IV) was discovered in BeH-SAC (10 units calculated instead of 1). Meanwhile, this error had been corrected in the BeH-SAC database (also in the results of this national report).

Overall, differences in denominators between BeH-SAC and hospital data (n=10) varied from <1% to 12%. For the hospitals (n=4) who could compare own consumption data with BeH-SAC (in units, DDDs or DDDs/1000 patient days), differences between 1 and 7% were found, with one tertiary hospital with differences of 15-20%.

Outside this validation, it happens that, while inspecting their BeH-SAC reports on Healthstat, hospitals discover mistakes in their reimbursement data. By informing the insurance companies of these mistakes, the data of NIHDI are automatically retrospectively corrected and included in BeH-SAC. However, due to the delay of these corrections, hospitals can ask for a temporary correction in BeH-SAC (until the official corrections of NIHDI are included). In the near future, extra BeH-SAC reports will be added on Healthstat which will help hospitals to identify outlying results (in comparison with own retrospective data and with data of other hospitals) and which can encourage them to validate these data.

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MORE INFORMATION

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