

1.1 Prudent prescription of antibiotics (QA3;QA4;QA5)

1.1.1. Documentation sheet

Description	Three indicators and two sub-indicators are used to assess the prudent prescription of antibiotics in the ambulatory care sector: QA-3: Volume in Defined Daily Dose (DDD) of antibiotics prescribed reimbursed in the ambulatory care sector QA-4: Proportion of patients with at least one antibiotic prescribed in the year QA-5: The ratio of second-line antibiotics, compared to the total of DDDs prescribed Sub-indicator 1: The proportion amoxicillin/ amoxicillin+amoxicillin – clavulanate Sub-indicator 2 : Proportion of all antibiotics representing quinolones
Calculation	QA-3: Amount of antibacterials for systemic use (ATC group J01) prescribed within ambulatory care and expressed in DDD per 1000 inhabitants per year (DID). Numerator = Total DDDs per year of J01 reimbursed antibacterials, at national level extrapolated to cover the whole Belgian population. The prescriptions made in nursing homes were not removed, so this represents consumption in the ambulatory sector including residential homes. Denominator = total number of inhabitants (Eurostat). When this indicator is explored at regional level or by age group, the numerator is not extrapolated and the denominator corresponds to the total number of insured persons (so called beneficiaries) and thus expressed in DDD/1000 beneficiaries/day (DBD). QA-4: Proportion of patients with at least one ATC group J01 DDD. Numerator = Number of beneficiaries with a reimbursed treatment in ATC class J01 in ambulatory care (Pharmanet - public pharmacies) between 1 July of the year and 30 June of the following year. Denominator = all insured population. QA-5: Number of DDDs with criteria (criteria = prescription second line antibiotic (i.e. amoxicillin - clavulanate, 3 rd and 4 th generation cephalosporins, quinolones and macrolides)) among all other antibiotic DDDs.
Rationale	Rising rates of antimicrobial resistance, i.e. the ability of microorganisms to resist antimicrobial products, is a growing concern. Antimicrobial resistance is primarily driven by non-prudent use of antimicrobials, including antibiotics, in human health, agriculture and livestock production and by contamination of the environment. In May 2015, the World Health Assembly ^a endorsed a global action plan to tackle antimicrobial resistance, reflected in several national strategies. The European Centre for Disease Prevention and Control (ECDC) monitors antibiotic use in Europe, among others, through the European Surveillance of Antimicrobial Consumption network (ESAC-Net ^b). The Belgian Antibiotic Policy Coordination Committee (BAPCOC) is active since 1999 to approach the problem; it defined several targets for the 2014-2019 period. ^c One of them is to decrease total antibiotic use in the ambulatory sector (from more than 800 prescriptions per 1000 inhabitants per year in 2014 to 600 prescriptions by 2020 and 400 prescriptions by 2025); a second target is the increase of the amoxicillin versus amoxicillin-clavulanate ratio. ¹ The total volume of antibiotics prescribed, and the second line antibiotics used as a proportion of total volume of antibiotic prescribed, have been designated by BAPCOC as markers of quality in the primary care setting. Since 1 May 2018, ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin and ofloxacin (quinolones) are no longer reimbursed

^a World Health Assembly addresses antimicrobial resistance, immunization gaps and malnutrition; available at: <https://www.who.int/publications/i/item/9789241509763> (last access: 10 July 2023)

^b Antimicrobial consumption interactive database (ESAC-Net); available at: <https://www.ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database> (last access: 10 July 2023)

^c Plan stratégique BAPCOC 2014-2019, available at: <https://organesdeconcertation.sante.belgique.be/fr/documents/plan-strategique-bapcoc-2014-2019> (last access: last access: 10 July 2023) 1. Balligand E, Costers M, Van Gastel E. Belgian Antibiotic Policy Coordination Committee. Note de politique pour la législature 2014-2019. 2014.

unless very specific diagnoses are confirmed by the prescribing doctor. The NIDHI has specified seven narrowly defined diagnostic conditions, such as "acute prostatitis".

Implementation of the One Health plan in 2019:

In collaboration with the Federal Expertise Centre for Healthcare², the Belgian Antibiotic Policy Coordination Commission has drawn up a national action plan with an integrated and holistic One Health approach against antimicrobial resistance, to be implemented in the medical, pharmaceutical and veterinary sectors, from the end of 2019.³ This One Health approach aims to coordinate the approach to the irrational use of antibiotics in "human" medicine with that of veterinary medicine and actions linked to the food chain and the environment. The players involved will work together to tackle the problem of antimicrobial resistance, which is difficult to control in Belgium, situate the problem in a wider context than just human medicine (e.g. resistant bacteria in our drinking water), define the objectives for the period 2020-2024, discuss the recommendations for the desired holistic approach and translate these recommendations into more concrete operational proposals, with the critical performance indicators needed for evaluation.

Data source

QA-3: Sciensano analysed RIZIV – INAMI consumption data (Pharmanet), reimbursed prescriptions of J01 antimicrobials from 2010 to 2021; aggregated by molecule, patient age, gender and province. National figures are shared annually with ECDC (ESAC-Net) for international comparison.

QA-4: IMA-AIM atlas. Variable = (STAT_004_004) * 365/1 000. See also https://atlas.aim-ima.be/info/metadataPDF/METADATA_004_004_FR.pdf

QA-5: Sciensano analysed RIZIV – INAMI consumption data (Pharmanet)

Technical definition

QA-3: Amount antibacterials for systemic use (ATC group J01) consumed within ambulatory care extrapolated and expressed in DDD per 1 000 inhabitants and per day (DID). When not extrapolated, the numbers are expressed as DDD per 1 000 beneficiaries and per day (DBD). DDDs are calculated according to the ATC classification and the data source is Pharmanet (ambulatory reimbursement database, including GPs, specialists and dentists) (see data source section).

ATC code	DENOMINATION
J01A	TETRACYCLINES
J01B	AMPHENICOLS
J01C	PENICILLINS
J01D	OTHER BETA-LACTAM ANTIBACTERIALS
J01E	SULFONAMIDES AND TRIMETHOPRIM
J01F	MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS
J01G	AMINOGLYCOSIDE ANTIBACTERIALS
J01M	QUINOLONE ANTIBACTERIALS
J01R	COMBINATIONS OF ANTIBACTERIALS
J01X	OTHER ANTIBACTERIALS

QA-4: Number of patients with at least one prescription of antibiotics (ATC = J01) delivered by a pharmacy open to the public (per year)

QA-5: Number of DDDs with criteria (criteria = prescription second line antibiotic (i.e. amoxicillin - clavulanate, 3rd and 4th generation cephalosporins, quinolones and macrolides)) among all other antibiotic DDDs.

ATC code	DENOMINATION
J01CR	Amoxicillin clavulanate
J01DD and J01DE	3 rd and 4 th generation cephalosporins
J01M	Quinolones
J01FA	Macrolides

Sub-indicator 1 : The proportion amoxicillin (ATC code J01CA04)/ amoxicillin+amoxicillin – clavulanate

Sub-indicator2 : Proportion of all antibiotics (J01) representing quinolones (J01M). To note: To reduce their consumption, the reimbursement criteria for fluoroquinolones (J01MA) were changed on 1 May 2018, so that they are now only reimbursed for the treatment of a small number of well-defined infections. Due to these changes, total sales data are combined with reimbursement data to estimate total consumption of fluoroquinolones in Belgium. Since 2018, an estimate of total consumption of fluoroquinolones has been made on the basis of a comparison between total sales data (IQVIA, reimbursed and non-reimbursed sales) and INAMI data (Farmanet, reimbursed consumption only), with 2017 used as the reference year.

International comparability

ESAC-Net and OECD have data on ambulatory pharmaceutical consumption by daily defined dose, according to the ATC classification and expressed in DDD/1 000 inhabitants/day. Persons residing in nursing homes are included in Belgian results and that can vary between countries.⁴

Limitations

The defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. DDDs are standardized doses provided as part of the Anatomical Therapeutic Chemical drug classification (ATC) system maintained by the WHO Collaborating Centre for Drug Statistics Methodology (www.whocc.no/atcddd).⁵ The DDD is an internationally accepted unit for measuring medicine use and for making comparisons between countries. Yet, it must be realised that the DDD does not necessarily reflect the recommended or Prescribed Daily Dose in the specific country. Only one DDD is assigned per ATC code and route of administration (e.g. oral intake). The DDD is sometimes a 'dose' that is rarely if ever prescribed, because it might be an average of two or more commonly used doses and is based on an adult body weight of 70kg.⁶ Drug utilization data presented in DDDs only give a rough estimate of consumption and not an exact picture of the actual antibiotic use in a specific country. For instance, as DDDs do not take into account the dosage used in children, measures in DDDs should not include children.⁶ However, DDDs provide a fixed unit of measurement independent of price, currencies, package size, strength (i.e. amount of drug per unit) and molecule, as one day of treatment receives approximately equal weight whatever the drug.⁷ This enables the researcher to assess trends in drug use and to perform comparisons between population groups.

Dimension Quality – appropriateness; Safety

Related indicators None

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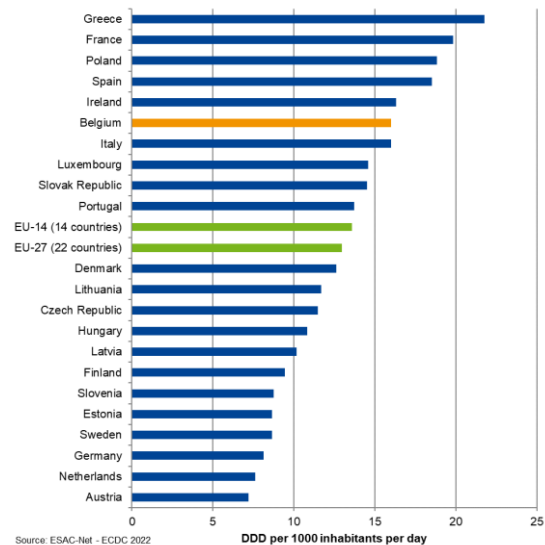
1.1.2. Results

1.1.2.1. QA-3: The volume of antibiotics prescribed in ambulatory care sector (DDD per 1 000 inhabitants per day) (DID)

In 2016, antibiotic consumption in the Belgian ambulatory sector equalled 22.5 Defined Daily Doses (DDD) per 1 000 inhabitants and per day (DID) and decreased to 16.0 DID in 2021.

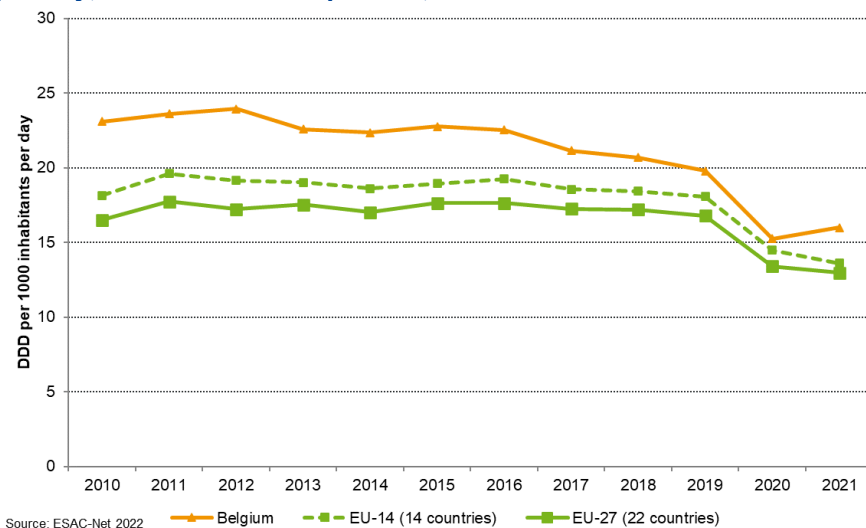
However, the volume of antibiotics remains one of the highest in OECD countries, similar to Ireland and Italy. In comparison, consumption in the Netherlands is much lower: 7.6 DDDs per 1 000 inhabitants per day (Figure 1, Figure 2).

Figure 1 – Consumption of antibacterials for systemic use (J01) in the community sector, expressed as number of DDD per day per 1000 inhabitants, international comparison, 2021



EU-14 countries: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden; EU-27= EU-14 + Poland, Slovak Republic, Lithuania, Czech Republic, Hungary, Latvia, Slovenia, Estonia.

Figure 2 – Consumption of antibacterials for systemic use (J01) in the community sector, expressed as number of DDD per 1000 inhabitants per day, international comparison, 2010-2021

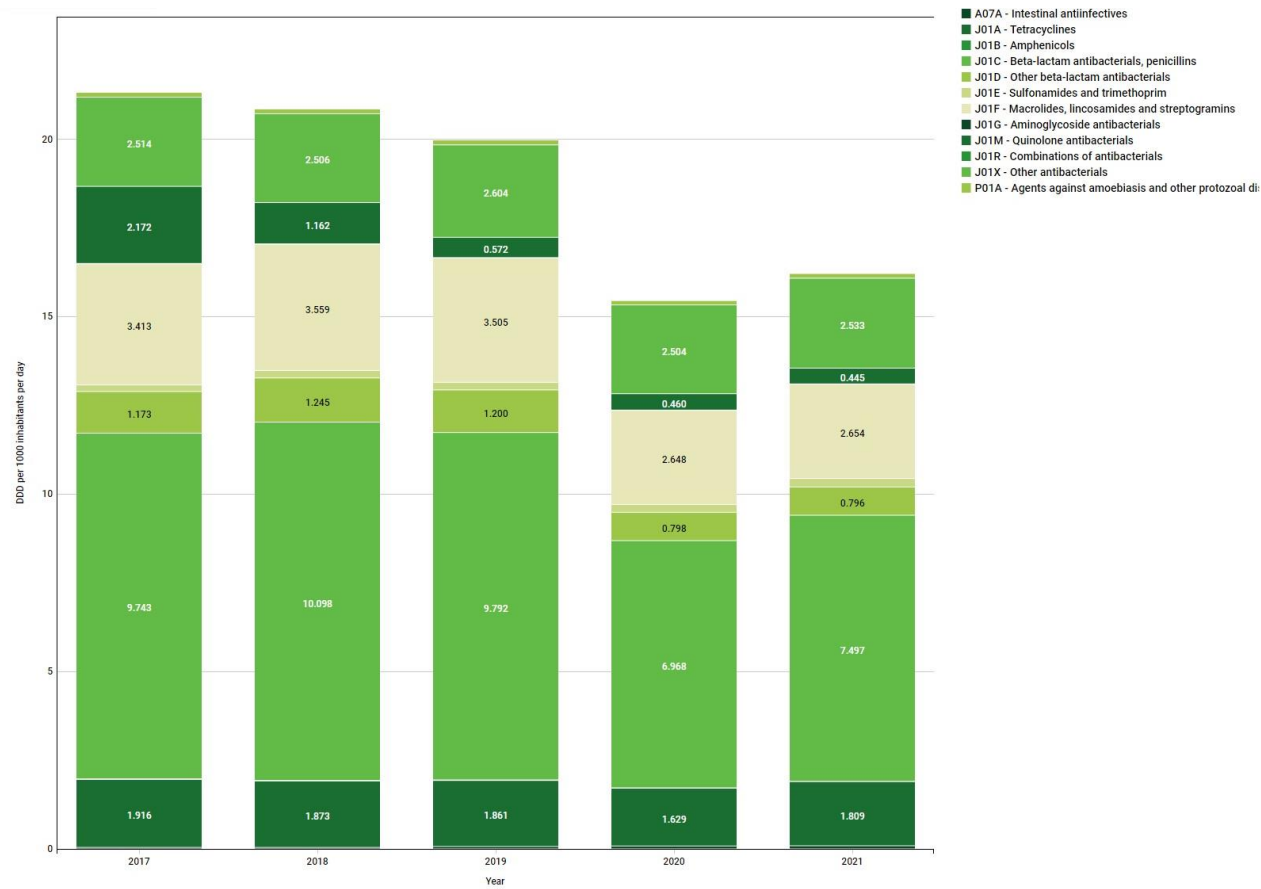


EU-14 countries: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden;
EU-27= EU-14 + Poland, Slovak Republic, Lithuania, Czech Republic, Hungary, Latvia, Slovenia, Estonia.

Between 2016 and 2020, the total use of antibiotics in the ambulatory sector in Belgium expressed as DDD/1 000 inhabitants/day decreased, with a particularly sharp fall in 2020, due to the COVID-19 crisis. The trend then picks up in 2021, and over the next few years consumption is probably likely to return to pre-crisis levels (Figure 2).

When considering the DID by ATC code we see a continued high proportion of J01C (Beta-lactam antibacterials, penicillins) use. The overall decrease in J01 DDD over time is spread quite evenly over the various J01 subgroups. However, it should be noted that the observed significant decrease in quinolones consumption safter 2018 is influenced by a reduction in the reimbursement of quinolones prescriptions since 2018 (Figure 3).

Figure 3 – Trend in the consumption of antibiotics for systemic use (ATC group J01) in ambulatory care (DDD per 1000 inhabitants per day, 2016-2021)

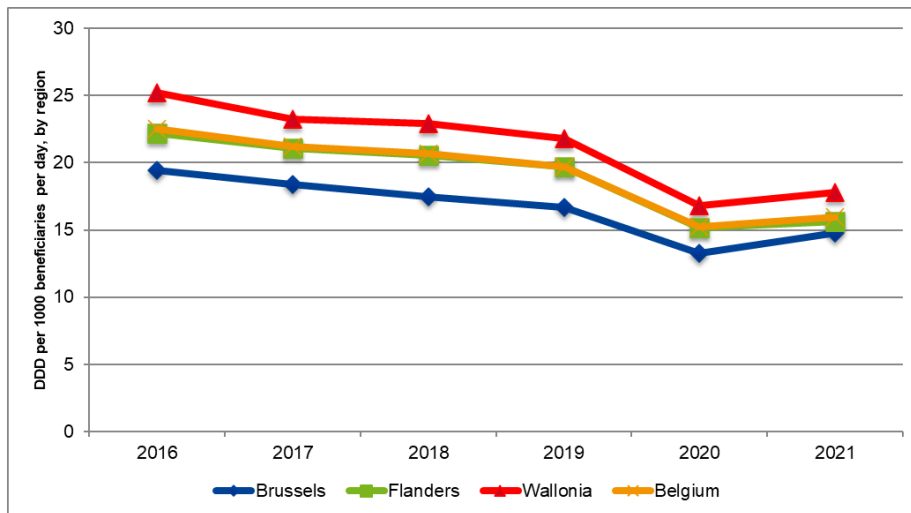


Source: ESAC-Net 2022

Exploring more in depth the national figures, regional and age group comparisons can be done. J01 antimicrobial consumption is expressed in number of DDD/1000 insured persons (beneficiaries)/day (DBD). Differences between regions were important and stable until 2019: Wallonia is continuously above 20 DDDs per 1000 beneficiaries per day (DBD)

(except during the COVID crisis), Brussels under 20 DDDs per 1000 beneficiaries per day and Flanders in between (Figure 4). After a significant reduction in 2020 due to COVID-19, in 2021, Wallonia has a consumption of 17.8 DDDs per 1000 beneficiaries and per day while Brussels is at 14.5 DBDs and Flanders is in between (15.6 DBDs) (Table 1).

Figure 4 – Overall volume of consumed J01 antibacterials for systemic use, DDD per 1000 beneficiaries per day, by region, 2016-2021



Source: Sciensano, Figure: KCE

Table 1 – Number of DDD per 1000 beneficiaries per day, by region, 2016-2021

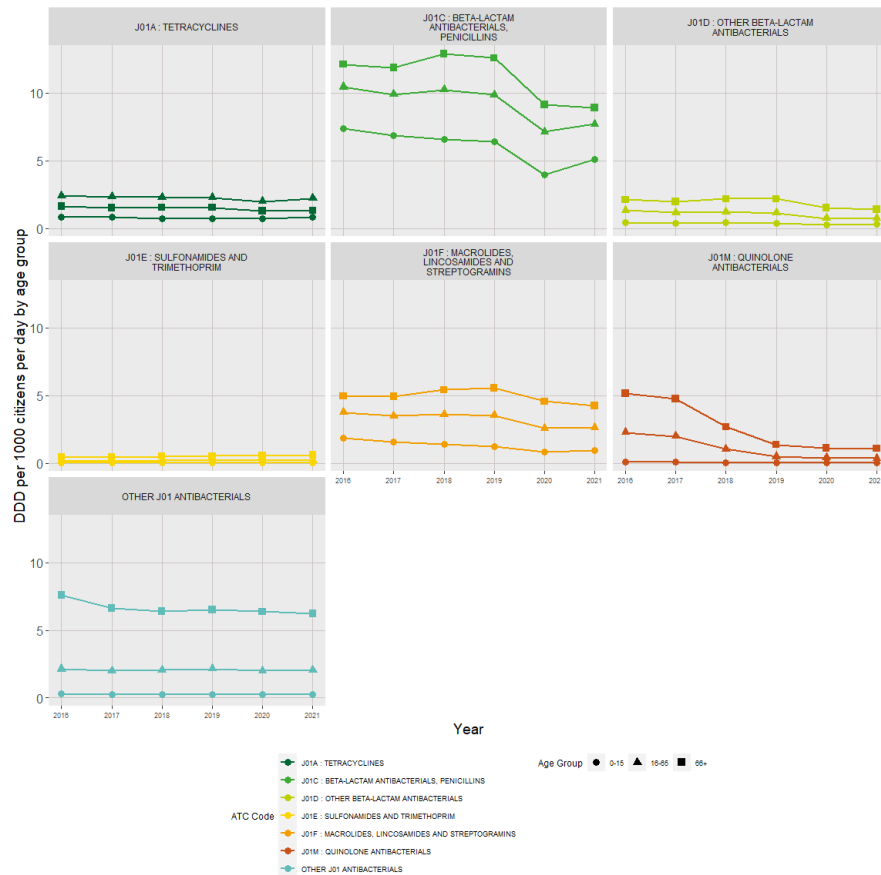
Year	Region	DBD
2016	Brussels	19.44
2016	Flanders	22.20
2016	Wallonia	25.20
2016	Belgium	22.54
2017	Brussels	18.41
2017	Flanders	21.07
2017	Wallonia	23.25
2017	Belgium	21.19
2018	Brussels	17.44
2018	Flanders	20.57
2018	Wallonia	22.90
2018	Belgium	20.66
2019	Brussels	16.65
2019	Flanders	19.67
2019	Wallonia	21.81
2019	Belgium	19.73
2020	Brussels	13.24
2020	Flanders	15.14
2020	Wallonia	16.81
2020	Belgium	15.23
2021	Brussels	14.79
2021	Flanders	15.64
2021	Wallonia	17.82
2021	Belgium	15.96

Source: Sciensano

Considering antimicrobial consumption (AMC) as DDD per 1000 beneficiaries within age groups, we see that while overall consumption is proportionally higher in older age groups, this increase with age is not

proportional across ATC codes. All J01 subgroups show the highest use in the oldest age group (65years +), except for tetracyclines which show the highest use in the 15-65 year age group (Figure 5).

Figure 5 – DDD per 1000 beneficiaries per day stratified by ATC code and patient age, 2016-2021

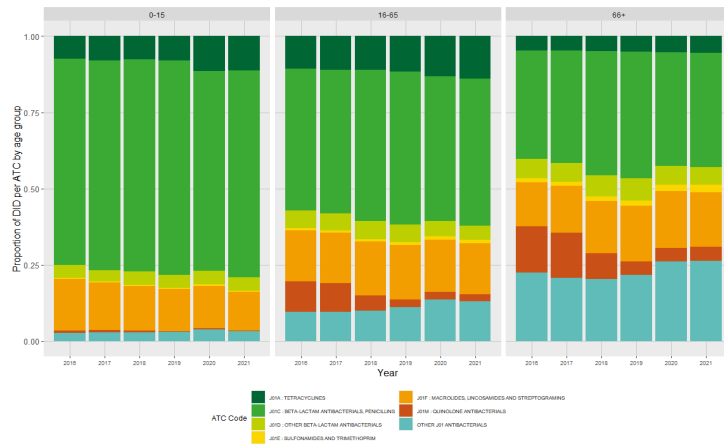


Source: Sciensano

In all J01 antimicrobial classes except tetracyclines we see DID increase with age. But the differences between age groups vary with antimicrobial group, suggesting relative use within age groups varies. Tetracyclines and J01 beta-lactams occupy a lower proportion of AMC in the oldest age group,

with proportionally more “other” J01 antimicrobials prescribed to this age group. Macrolides, lincosamides and streptogramins are the only antibacterial group with similar proportional use across all age groups (Figure 6).

Figure 6 – Proportional antimicrobial use by ATC code per age group, 2016-2021

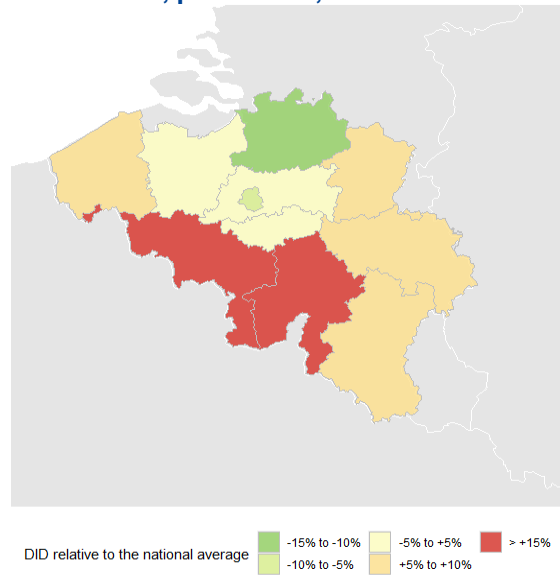


Source: Sciensano

By visualising the DDD in relation to the National average, per province, we observe higher DBD values in Hainaut (18.72) and Namur (18.56), with

below national average consumption in Brussels (14.79) and Antwerp (14.05).

Figure 7 – Total volume of reimbursed J01 antimicrobials for systemic use delivered in the ambulatory sector in Belgium, DDD per 1000 beneficiaries per day, standardised relative variations around the national mean, per district, 2021



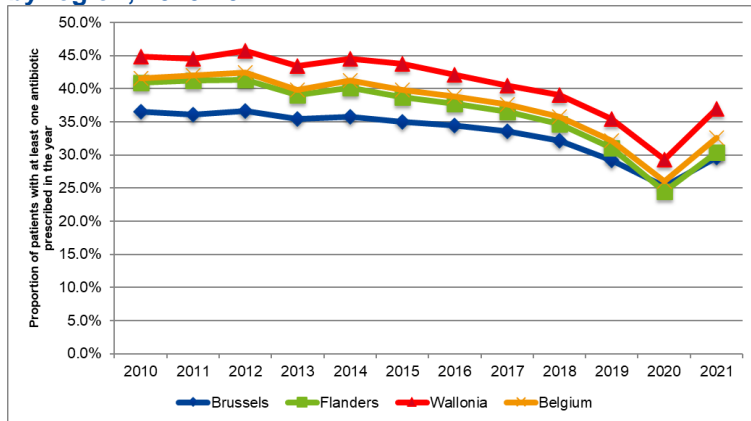
Source: Sciensano

1.1.2.2. QA-4: Proportion of patients with at least one antibiotic prescription a year

In 2021, 32.6 % of patients have received at least one antibiotic prescription. There is a sharp drop in consumption in 2020 (26.0%) following the COVID

crisis. There will then be a marked increase in 2021 to reach a higher pre-COVID consumption levels (2019: 32.1%; 2021: 32.6%) (Figure 8).

Figure 8 – Proportion of patients with a least one AB (J01) prescription, by region, 2010-2021



Source: IMA-AIM atlas, figure: KCE

Table 2 – Proportion of patients with at least one antibiotic prescription (J01), by patient characteristics, 2021*

Variable	Category	Percentage with AB
Age (years)	0-4	43.8%
	5-14	21.5%
	15-24	30.3%
	25-44	31.0%
	45-64	33.2%
	65-74	35.0%
	75 et plus	39.8%

Gender	Female	36.5%
	Male	28.1%
Entitlement to increased reimbursement (18 years or more)	No	31.8%
	Yes	36.1%
Province	Antwerpen (2018)	31.8%
	Brabant Wallon	34.7%
	Brussels	32.1%
	Hainaut	40.2%
	Liège	38.3%
	Limburg	37.6%
	Luxembourg	NA
	Namur	NA
	Oost-Vlaanderen	33.6%
	Vlaams Brabant	33.9%
West-Vlaanderen	37.2%	
Total	Belgium	32.5%

Source: IMA-AIM (atlas), calculation KCE, * 2018 for Province, NA=Not available

Women (43.8%), inhabitants between 0 and 4 years (43.8%) and older than 75 years (39.8%), as citizens from Hainaut (40.2%) were most frequently exposed to at least one antibiotic in 2021. There is no important difference in AB use according to BIM status in 2021 (Table 2). Sciensano, through its

HISLink project, was however able to highlight a significant difference in antibiotic use according to the new socio-economic status of patients (aged 15 and over).⁸

1.1.2.3. QA-5: The ratio of second-line antibiotics, compared to the total of DDDs delivered

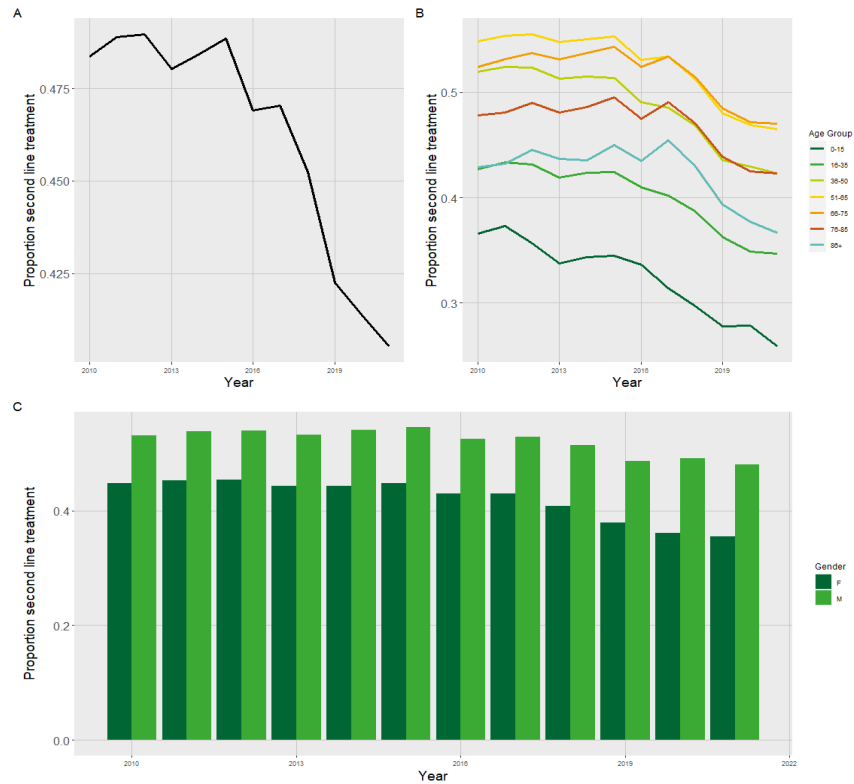
In 2021, 40.5% of antibiotics prescribed were second-line. Wallonia prescribes proportionately more second-line antibiotics than Flanders or Brussels (Table 3). We observe a consistent reduction in second line

treatments as a proportion of total J01 antimicrobials over time. While the use of second line antibacterials is higher in older age groups, this reduction is observed in all age groups. More second line treatments are prescribed to males, as a proportion of total prescriptions per gender, and a greater decrease in second-line treatments is observed in females (t-test = 23.12, $p < 0.001$) (Figure9).

Table 3 – Use of AB of second intention (% total DDD antibiotics), 2021

Region	Use of AB of second intention (% total DDD antibiotics)
Brussels	0.359
Flanders	0.399
Wallonia	0.413
Belgium	0.405

Figure 9 – Proportion of total J01 prescriptions representing second line treatments. A) Nationally, B) stratified by age c) stratified by gender



Source: Sciensano

We observe that while the proportion of second line treatments decreases over time in all provinces, this reduction is slower in some provinces, such as Hainaut, Liege and Luxembourg, than in others.



The ratio amoxicillin to amoxicillin – clavulanate

While we have continued to see improvements in the ratio of amoxicillin:amoxicillin clavulanic acid in the youngest age group, which is approaching the BAPCOC goal of 4:1 ratio, or 80% use. However, we saw decreases in this ratio in the oldest age group in the last two years. Nationally, and in the population above 16 years of age we are still far from the target ratio (Table 4).

Proportion of all antibiotics representing quinolones

It is worth noting that the reimbursement of quinolones was changed in 2018, such that only certain medications are refunded for specific medical conditions. As such, a greater proportion of quinolones may be prescribed without reimbursement and therefore not included in this dataset - this is reflected in the large drop in quinolone reimbursements from 2018 (2017: 100% reimbursed and 2021: 39.6% reimbursed) (Table 5). Reducing the consumption of fluoroquinolones to 5% of total consumption of antimicrobials in ATC group J01 has been a national objective since 2014.

Table 4 – Proportion Amoxicillin of total Amoxicillin and Amoxicillin-Clavulanic acid DDDs reimbursed per age group by year from 2010 to 2021

Age group	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Total	0.448	0.453	0.461	0.469	0.463	0.467	0.504	0.499	0.486	0.506	0.466	0.481
0-15	0.671	0.679	0.700	0.718	0.722	0.735	0.755	0.771	0.780	0.795	0.777	0.799
16-65	0.439	0.443	0.451	0.459	0.454	0.457	0.492	0.489	0.476	0.498	0.463	0.471
66+	0.340	0.338	0.346	0.353	0.346	0.354	0.387	0.382	0.369	0.387	0.345	0.336

Source: Sciensano

Table 5 – Reimbursed and Total (reimbursed and non-reimbursed) quinolones as a proportion of total J01 antimicrobial reimbursements, 2010-2021

Value	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Reimbursed Quinolone (%)	11.51	11.54	11.4	10.91	10.96	10.85	10.65	10.26	5.61	2.89	3.02	2.79
Total Quinolone (%)*	11.51	11.54	11.4	10.91	10.96	10.85	10.65	10.26	7.68	6.67	7.44	7.05

Source: Sciensano; * Since 2018, total sales data are combined with reimbursement data to estimate total consumption of fluoroquinolones in Belgium.



In 2021, the use of quinolones as a proportion of total reimbursements varied across the country with greatest proportional use observed in West

Flanders (4.11%) and Limburg (3.78%), and lower use in Liege (1.68%), Luxembourg and Namur (1.75%) (Table 6).

Table 6 – Proportion of total J01 DDDs representing reimbursed quinolones (as a proportion of total J01 antimicrobial reimbursements) per province in 2021

Province	Quinolone Proportion
Anvers	2.88%
Brabant flamand	3.09%
Brabant wallon	2.12%
Bruxelles-Capitale	2.14%
Flandre occidentale	4.11%
Flandre orientale	3.4%
Hainaut	2.15%
Liege	1.68%
Limbourg	3.78%
Luxembourg	1.78%
Namur	1.75%

Source: Sciensano

**Key points**

- In 2021, antibiotic consumption in the Belgian ambulatory sector equalled 16.0 Defined Daily Doses (DDD) per 1000 inhabitants and per day (DID), compared to other European countries (e.g. the Netherlands with 7.6 DDDs) Belgium ranks poorly.
- Geographical variation within Belgium is also observed: Wallonia has a consumption of 17.8 DDDs per 1000 beneficiaries and per day while Brussels is at 14.8 DBDs and Flanders in between (15.6 DBDs).
- In 2021, 32.6 % of Belgian citizens received at least one antibiotic prescription. Some differences between the regions were observed :37% in Wallonia, 30.4% in Flanders and 29.6% in Brussels. The proportion of citizens with at least one antibiotic prescription was highest among the younger (i.e. 0 to 4 years) and the elderly (i.e. 75+ years old).
- The proportion amoxicillin to amoxicillin – clavulanate improved slightly from 0.46 in 2014 to 0.48 in 2021 but remains far from the BAPCOC goal of 80%.
- In 2021 the quinolone use was still 7.05% of the total DDD for the ambulatory sector.



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