2.2. Prudent prescription of antibiotics in the ambulatory care sector (QA-3, QA-4, QA-5)

2.2.1. Documentation sheet

Description	Three indicators and two sub-indicators are used to assess the prudent prescription of antibiotics in the ambulatory care sector:
	1. **Volume in Defined Daily Dose (DDD) of antibiotics prescribed in the ambulatory care sector**
	2. Proportion of patients with at least one antibiotic prescribed in the year
	3. **The ratio of second line antibiotics, compared to the total of DDDs prescribed**
	    3.1. **The ratio amoxicillin to amoxicillin – clavulanate**
	    3.2. **The proportion of quinolone use**

Calculation	See technical definition section for calculation details.
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[d] endorsed a global action plan to tackle antimicrobial resistance which is also reflected in several national strategies. In Europe, 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[e]). The Belgian Antibiotic Policy Coordination Committee (BAPCOC) is active since 1999 to approach the problem; it defined several targets for the 2014-2019 period.[f] 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 amoxicilline-clavulanate ratio (from about 50/50 in 2014 to 80/20 by 2018); a third objective from the BAPCOC strategic plan is a reduction of the quinolone use by 50% by 2018 (from 10% of the total DDD of antibiotics to 5%)[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.
Data source	RIZIV – INAMI (Pharmanet – Farmanet database, i.e. ambulatory reimbursement database) for indicator 1, IMA – AIM (KCE calculation) for indicators 2 and 3, KCE report entitled "proposals for a more effective *antibiotics policy* in Belgium" (expected publication in April 2019) for subindicators 3.1 and 3.2.

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[d] World Health Assembly addresses antimicrobial resistance, immunization gaps and malnutrition; available at: https://www.who.int/mediacentre/news/releases/2015/wha-25-may-2015/en/ (last access: 31 January 2019)

[e] Antimicrobial consumption interactive database (ESAC-Net); available at: https://ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/esac-net (last access: 31 January 2019)

[f] Plan stratégique BAPCOC 2014-2019, available at: https://organesdeconcertation.sante.belgique.be/fr/documents/plan-strategique-bapcoc-2014-2019 (last access: 9 January 2019) [1]

Technical definitions

1. Amount antibacterials for systemic use (ATC group J01) prescribed within ambulatory care and expressed in DDD per 1000 insured persons and per day. DDDs are calculated according to the ATC classification and the data source is Pharmanet (ambulatory reimbursement database, including GPs, specialists and dentists).

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

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

3. Number of DDDs with criteria (criteria = prescription second line antibiotic (i.e. amoxicillin – clavulanate, cephalosporin, quinolones and macrolides)) among all other antibiotic DDDs.
   3.1 Ratio of amoxicillin (ATC code J01CA04) DDDs vs. amoxicillin – clavulanate (ATC code J01CR02) DDDs.
   3.2 Number of quinolones (ATC code J01M) DDDs on the total number of DDDs.

Limitation

The defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults.[2] DDDs are standardized doses provided as part of the Anatomical Therapeutic Chemical drug classification system maintained by the WHO Collaborating Centre for Drug Statistics Methodology (www.whocc.no/atcddd). [3] 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.[4] 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.[4] 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.[5] This enables the researcher to assess trends in drug use and to perform comparisons between population groups.[2]

Indicator 3 slightly differs from the international indicator. The Dutch HSPA report 2014 [6] includes the following indicator: total DDD beta-lactam antibacterials + total DDD quinolones prescribed divided by the total DDD antibiotics prescribed. Since the range of second line AB prescribed in

	ambulatory setting is large in Belgium, this indicator has been adapted as follows: total DDD of cephalosporin, quinolones, amoxicillin-clavulanate and macrolides prescribed divided by the total DDD antibiotics prescribed.
International comparability	ESAC-Net and OECD have data on the ambulatory pharmaceutical consumption by daily defined dose, according to the ATC classification. Indicator 3 (proportion of second line antibiotic): the Netherlands uses a similar indicator.
Dimension	Quality – appropriateness; Safety
Related indicators	Incidence of MRSA

2.2.2. Results

**Volume of antibiotics prescribed in ambulatory care sector (DDDs per 1000 inhabitants per day)**

Since 2000, the Belgian government information campaigns inform population, pharmacists and practitioners about the correct use of antibiotics and the danger of antibiotic resistance. Antibiotics only need to be prescribed if necessary. Second choice antibiotics (i.e. amoxicillin – clavulanate, cephalosporin, quinolones and macrolides) should not be used in first intention and be kept in reserve. General practitioners (GPs) are in first line to inform the patient about the risk of misuse or overconsumption of antibiotics and to follow the recommendations.

In 2016, antibiotic consumption in the Belgian ambulatory sector equalled 27.7 Defined Daily Doses (DDD) per 1000 inhabitants and per day (DID). However, the volume of antibiotics remains one of the highest in OECD countries, similar to France. In comparison, the consumption in the Netherlands is much lower: 9.7 DDDs per 1000 inhabitants per day.[7] The change in trend observed at the national level in 2015-2017 should be confirmed (Figure 18).

Figure 18 – Overall volume of antibiotics, DDD AB per day per 1000 inhabitants, international comparison, 2016

Source: OECD health data 2018

Source: OECD health data 2018
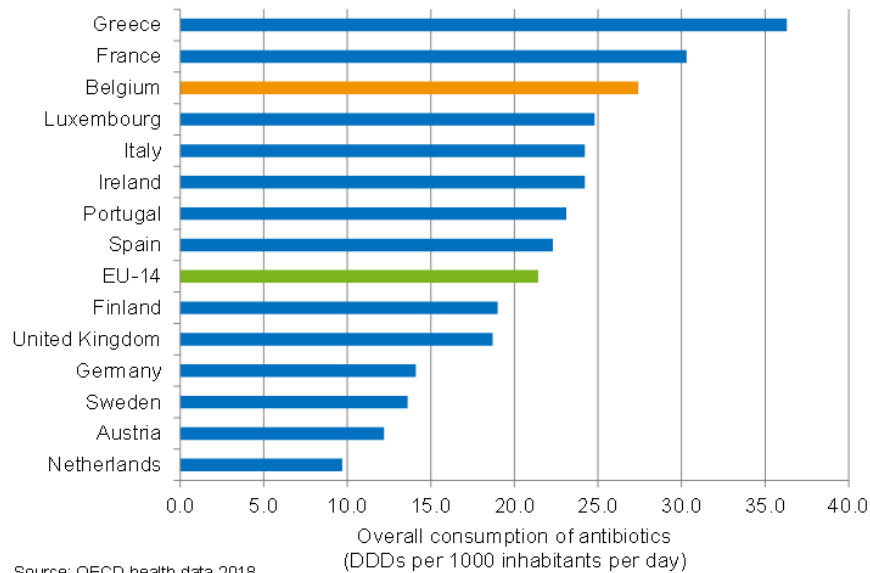
Source: OECD Health Statistics 2018

Between 2007 and 2012, the total use of antibiotics in the ambulatory sector in Belgium expressed as DDD per 1000 inhabitants per day fluctuated, increased and decreased again in 2013-2017. Proportions of tetracyclines (J01A) and other beta-lactam antibacterials (J01D) decreased from 1997 to 2017 (Figure 19).
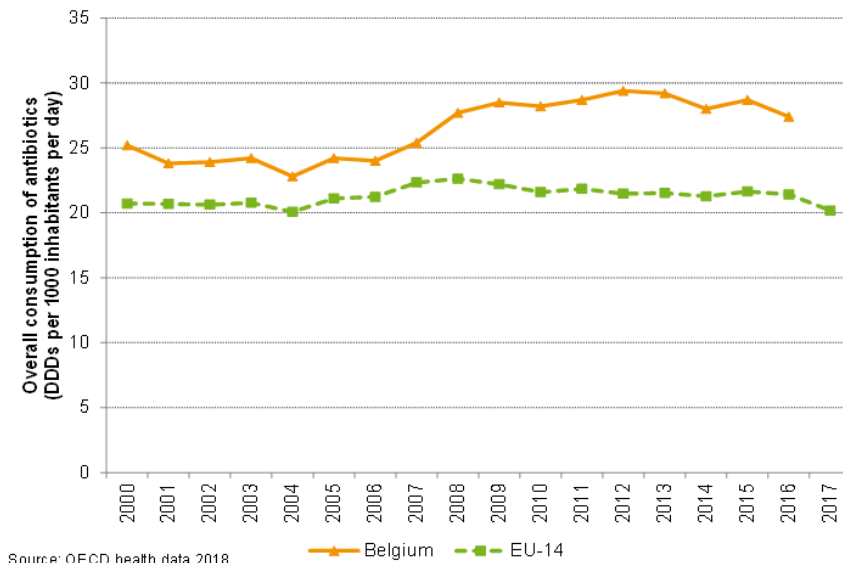
Note: due to a bug in the TESSy data, the data for the period 1997-2006 are presented based on the 2018 ATC/DDD index; at the moment of the editing of this report ECDC was still working on a solution.(ECDC, personal communication) Data for the other years are presented based on the 2019 ATC/DDD index.

Figure 19 – Trend in the consumption of antibiotics for systemic use (ATC group J01) in ambulatory care (DDD per 1000 inhabitants per day, 1997-2017)
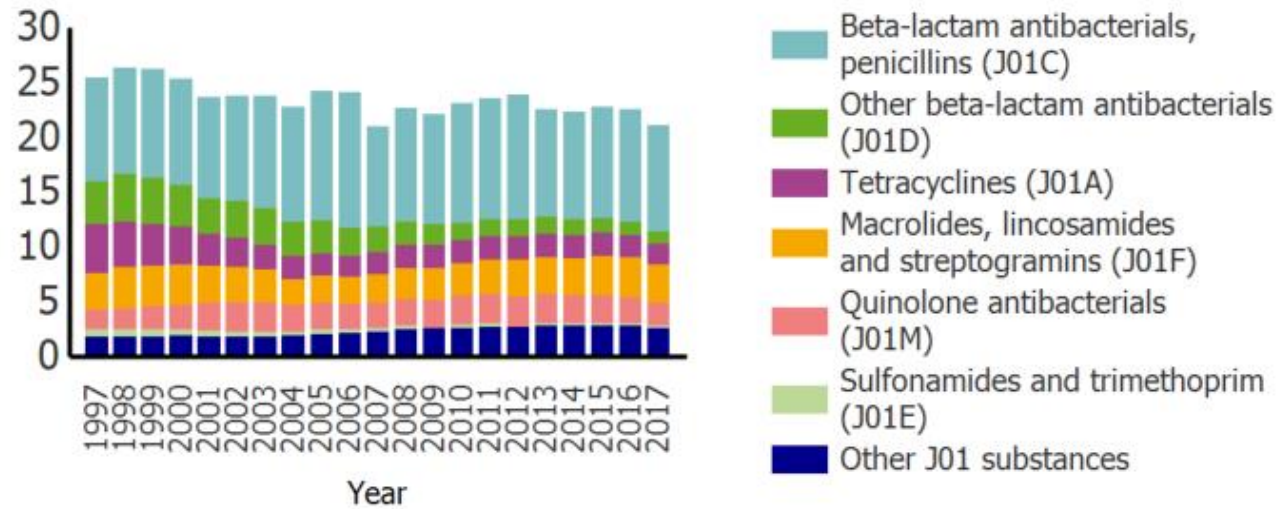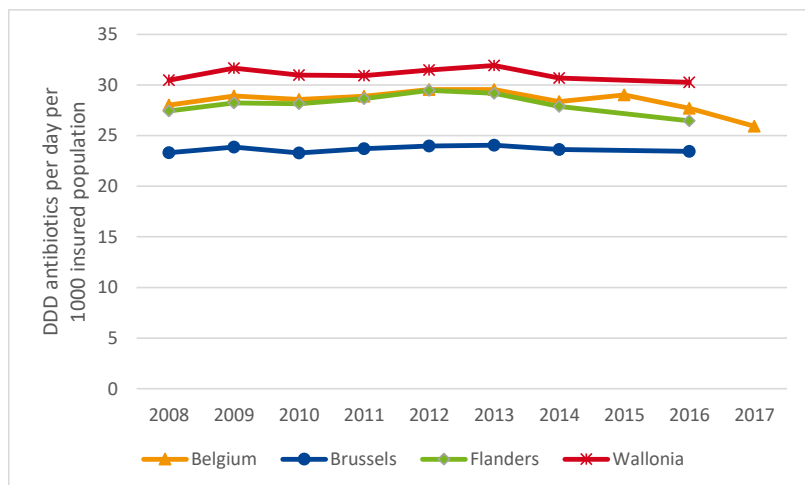

Source: ESAC-Net

Differences between regions are important and stable: Wallonia is continuously above 30 DDDs per 1000 inhabitants per day, Brussels under 25 DDDs per 1000 inhabitants per day and Flanders in between (Figure 20)

Figure 20 – Overall volume of antibiotics delivered, DDD per 1000 inhabitants per day, by region, 2008-2017

Source: RIZIV – INAMI; data are presented based on the 2018 ATC/DDD index

Table 5 – Antibiotic use in the ambulatory sector, by ATC code and by age-group, 2016

| ATC code	0-14 years	15-64 years	65 +
	% total DDD	% total DDD	% total DDD
Tetracyclines (J01A)	4.5%	11.2%	4.9%
Amphenicols (J01B)	0.1%	<0.1%	<0.1%
Penicillins (J01C)	70.4%	46.5%	35.8%
Other beta-lactam antibacterials (J01D)	4.2%	6.0%	6.2%
Sulfonamides and trimethoprim (J01E)	0.4%	0.8%	1.4%
Macrolides, lincosamides and streptogramins (J01F)	17.5%	16.6%	14.7%
Aminoglycoside antibacterials (J01G)	0.2%	0.1%	0.0%
Quinolone antibacterials (J01M)	0.6%	9.9%	15.2%
Other antibacterials (J01X)	2.0%	9.2%	21.8%

DDD: Defined Daily Dose, Data source: KCE report on proposals for a more effective antibiotics policy *in Belgium (expected publication: April 2019)*

In 2016 the highest ratio penicillin to total antibiotic use expressed in DDD, was observed in the age group 0-14 years (Table 5). Most commonly used penicillins in children (0-14 years) were amoxicillin (75% of total penicillin DDD in 0-14 years) and the association amoxicillin and a beta-lactamase inhibitor such as clavulanate (23.6% of total penicillin DDD in 0-14 years). It should be noted that DDD is a metric based on an adult dosage and DDD in children are thus more difficult to interpret.

When looking at the variations per district, once the figures have been standardised (Figure 21), it appears that Brussels, Antwerp and Mechelen districts are below the national mean, and that most of the districts in Wallonia (but not all of them) along with some districts in West-Vlaanderen (Dixmuide, Roeselaere and Ieper) have antibiotic use at least 30% over the national mean.

Figure 21 – DDD antibiotics delivered in the ambulatory sector, DDDs per day per 1000 insured population, standardised relative variations around the national mean, per district, 2016

	< -50%
	-50% – -30%
	-30% – -10%
	-10% 10%
	10% – 30%
	30% – 50%
	> 50%
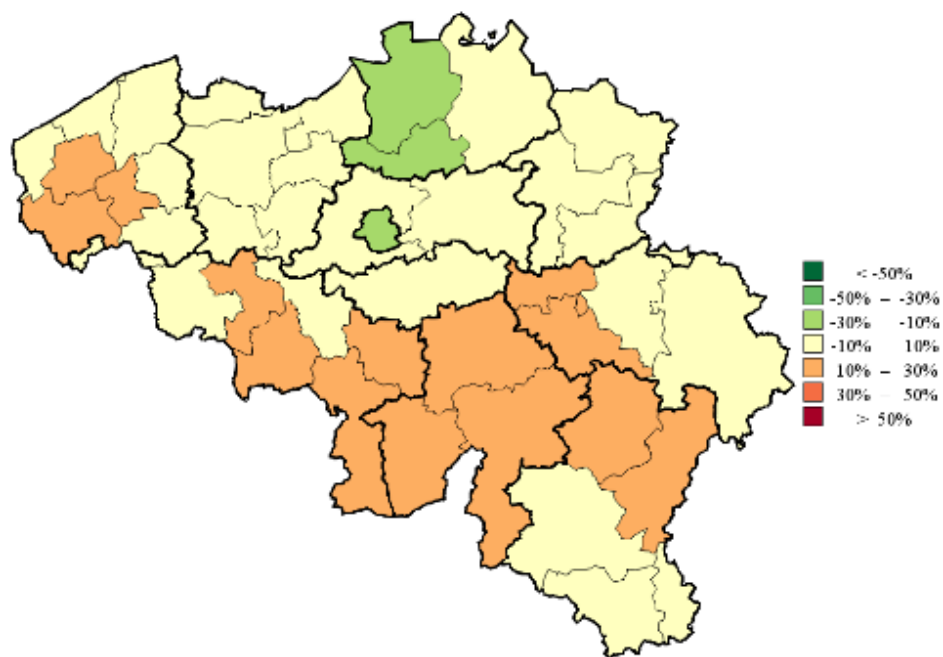
Source: INAMI – RIZIV

The Belgian Antibiotic Policy Coordination Committee (BAPCOC) uses another indicator consisting in the number of antibiotics treatments per 1000 inhabitants per year. In its 2014-2019 policy paper, BAPCOC has set a target of 400 by 2025 (starting from more than 800 in 2014). The current trend will not make it possible to reach the goal for 2025 (Figure 22): after an initial decrease from 1.40 in 1997 to 0.9 in 2004, the evolution has stagnated (0.8 in 2017).

Figure 22 – Number of antibiotic treatments per inhabitant per year
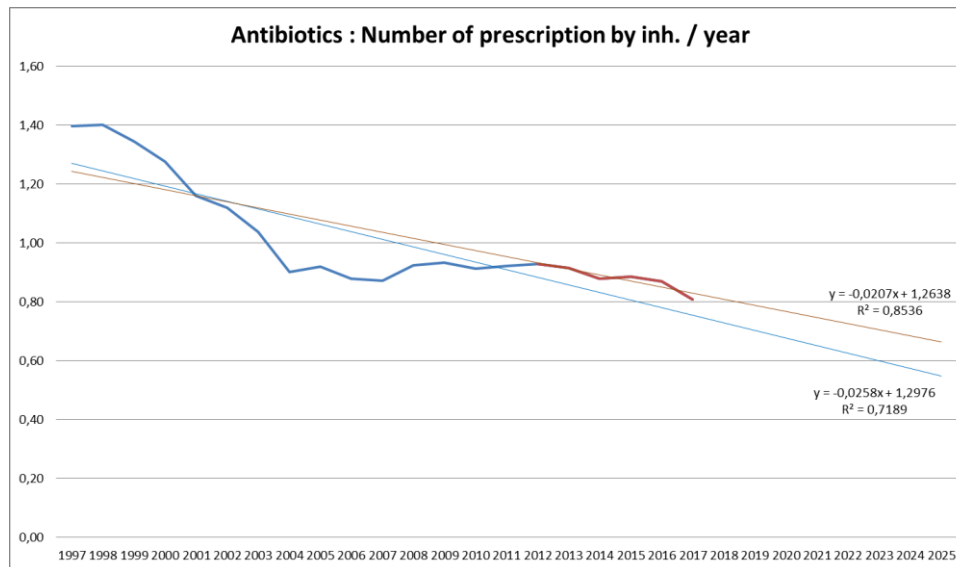
Source: INAMI – RIZIV

Proportion of patients with at least one antibiotic prescription a year
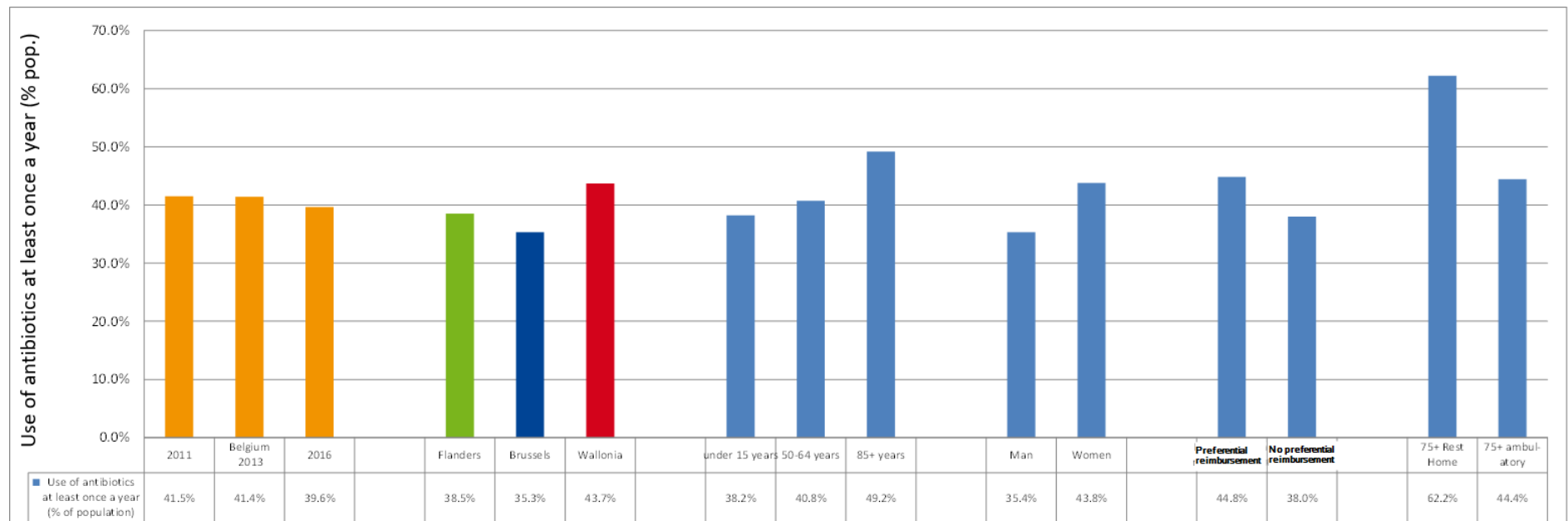
In 2016, 39.6 % of patients have received at least one antibiotic prescription. This is a slight improvement over the period 2010-2013 which had values around 41 to 42%. There are large differences between regions: 43.7% in Wallonia, 38.5% in Flanders and 35.3% in Brussels (Figure 23, Table 6).

Figure 23 – Percentage of patients with antibiotics, by patient region and characteristics

	2011	Belgium 2013	2016		Flanders	Brussels	Wallonia		under 15 years	50-64 years	85+ years		Man	Women		Preferential reimbursement	No preferential reimbursement		75+ Rest Home	75+ ambul-atory
Use of antibiotics at least once a year (% of population)	41.5%	41.4%	39.6%		38.5%	35.3%	43.7%		38.2%	40.8%	49.2%		35.4%	43.8%		44.8%	38.0%		62.2%	44.4%

Source: INAMI – RIZIV (when not specified, data refer to 2016)

Table 6 – Proportion of patients with at least one antibiotic prescription, by patient characteristics, 2016

Variable	Category	Percentage with antibiotics
Age (years)	0-14	38.2%
	15-34	36.7%
	35-49	38.7%
	50-64	40.8%
	65-74	42.9%
	75-84	45.2%
	>=85	49.2%
Gender	Female	43.8%
	Male	35.4%
Entitlement to increased reimbursement	No	38.0%
(18 years or more)	Yes	44.8%
Place of residence	Institutions	62.2%
(75 years old or more)	Not in institutions	44.4%
Province	Antwerpen	36.0%
	Brabant Wallon	39.1%
	Brussels	35.3%
	Hainaut	45.2%
	Liège	43.8%
	Limburg	42.7%
	Luxembourg	42.4%
	Namur	43.9%
	Oost-Vlaanderen	37.5%
	Vlaams Brabant	38.4%
	West-Vlaanderen	40.9%

Source: IMA-AIM (EPS); calculation: INAMI – RIZIV

Women (43.8%), inhabitants older than 65 years (44.6%), and among the elderly (≥ 75 years) those in nursing homes (62.2%) and citizens from Hainaut (45.2%) were most frequently exposed to at least one antibiotic in 2016 (Table 6).

The ratio of second line antibiotics, compared to the total of DDDs prescribed

Even if it is improving slightly over time, the proportion of second line antibiotics is still quite high in Belgium: 52% in 2016 (60% in 2006). In comparison, the same indicator in the Netherlands is 16 % for the same year.[g] This indicator scores badly even by children (35%), and all over the country (Table 7).

Table 7 – Proportion of volume (DDD) antibiotics for amoxicillin clavulanate, cephalosporin, quinolones and macrolides related to total antibiotics by patient characteristics, 2016

Variable	Category	Percentage with 2nd line antibiotics
Age (years)	0-14	35.0%
	15-34	44.7%
	35-49	54.1%
	50-64	58.4%
	65-74	57.8%
	75-84	55.1%
	>=85	51.8%
Gender	Female	43.8%
	Male	35.4%
Entitlement to increased reimbursement (18 years or more)	No	49.2%
	Yes	55.9%
Place of residence (75 years old or more)	Institutions	49.4%
	Not in institutions	55.1%
Province	Antwerpen	50.1%
	Brabant Wallon	52.0%
	Bruxelles-Capitale	47.9%
	Hainaut	58.9%
	Liège	46.3%

g   Dutch performance report [6] p.128, figure 5.11.

Variable	Category	Percentage with 2nd line antibiotics
	Limburg	57.8%
	Luxembourg	56.2%
	Namur	52.7%
	Oost-Vlaanderen	50.9%
	Vlaams Brabant	47.5%
	West-Vlaanderen	50.1%

Source: IMA data, INAMI – RIZIV calculation.

The ratio amoxicillin to amoxicillin – clavulanate

An objective in the BAPCOC 2014-19 plan was to reach an amoxicillin to amoxicillin – clavulanate ratio of 80/20 by 2018, [1] as amoxicillin – clavulanate has a limited role as first-line treatment for ambulatory infections. The analysis of the data indicate a slight improvement of this ratio from 2014

(0.86) to 2016 (1.02), but the ratio in 2016 was still far from the BAPCOC objective. For this indicator important differences exist between age groups: in the 0-14 years old, this ratio has progressively increased to 3.16 in 2016, thus close to BAPCOC's objective (Table 8).

Table 8 – Ratio amoxicillin to amoxicillin – clavulanate in the ambulatory sector, by year and age-group

Age-group	2014	2015	2016
0-14 years	2.65	2.86	3.16
15-64 years	0.84	0.86	0.98
65 + years	0.53	0.55	0.63
Total	**0.86**	**0.88**	**1.02**

Data source: KCE report on proposals for a more effective antibiotics policy *in Belgium (expected publication: April 2019)*

The proportion of quinolone use

An objective in the BAPCOC's 2014-19 plan was to decrease the quinolone use in the ambulatory sector from 10% of the total antibiotic use in 2014 to 5% by 2018.[1] In 2016 the quinolone use was still 10.7% of the total DDD for

the ambulatory sector, hence far away from the BAPCOC objective (Table 9). The highest ratio quinolone to total antibiotic use expressed in DDD was observed in the age group ≥ 65 years (Table 9). Stratification by province of the prescriber indicates that the geographical variation is limited (Table 10).

Table 9 – Antibiotic use in the ambulatory sector, by ATC code, 2016

ATC code	Proportion of total DDD
Tetracyclines (J01A)	8.8%
Amphenicols (J01B)	0.0%
Beta-lactam antibacterials; penicillins (J01C)	45.3%
Other beta-lactam antibacterials (J01D)	5.8%
Sulfonamides and trimethoprim (J01E)	0.9%
Macrolides, lincosamides and streptogramins (J01F)	16.1%
Aminoglycoside antibacterials (J01G)	0.1%
Quinolone antibacterials (J01M)	10.7%
Other antibacterials (J01X)	12.3%

DDD: Defined Daily Dose, Data source: KCE report on proposals for a more effective antibiotics policy *in Belgium (expected press release, April 2019)*

Table 10 – Proportion of quinolone of the total DDD in the ambulatory sector, by province of the prescriber, 2016

Province	Proportion quinolones (ATC code J01M) of total DDD
Antwerpen	11.1%
Brabant Wallon	10.2%
Brussels	9.5%
Hainaut	10.3%
Liège	9.7%
Limburg	11.3%
Luxembourg	9.2%
Namur	9.8%
Oost-Vlaanderen	11.3%
Vlaams Brabant	11.1%
West-Vlaanderen	11.4%

DDD: Defined Daily Dose, Data source: KCE report on proposals for a more effective antibiotics policy *in Belgium (expected press release, April 2019)*

Key points

- **In 2016, antibiotic consumption in the Belgian ambulatory sector equalled 27.7 Defined Daily Doses (DDD) per 1000 inhabitants and per day (DID), compared to other European countries (e.g. the Netherlands with 9.7 DDDs) Belgium ranks poorly.**

- **Geographical variation within Belgium is also observed: Wallonia has a consumption above 30 DDDs per 1000 inhabitants and per day while Brussels is at 23.4 DDDs and Flanders in between.**

- **In 2016 40 % of Belgian citizens received at least one antibiotic prescription. Again, differences between the regions were observed (44% in Wallonia, 39% in Flanders and 35% in Brussels). The proportion of citizens with at least one antibiotic prescription was highest among elderly (i.e. 75+ years old) residing in nursing homes (i.e. 62%).**

- **The amount of second line antiobiotics expressed in DDD, even if improving slightly through the time are quite high in Belgium, about 52 % (60% in 2006). In comparison, the same indicator in the Netherlands is about 15 %. This indicator score badly even by children (> 35%) and all over the country.**

- **The ratio amoxicillin to amoxicillin – clavulanate improved slightly from 0.86 in 2014 to 1.02 in 2016.**

- **In 2016 the quinolone use was still 10.7% of the total DDD for the ambulatory sector, hence far away from the BAPCOC objective. The highest ratio quinolone to total antibiotic use expressed in DDD was observed in the age group ≥ 65 years.**

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