

Medication use in public pharmacies

Antihistamines for systemic use

Analysis of the distribution and evolution of medication consumption in Belgium, in terms of volume and expenditure per insured (analysis and trends by region, province and district), for the year **2022**



NIHDI – Healthcare Service – Directorate for Research, Development and Quality promotion

Appropriate care unit

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CONTENTS

CONTENTS	2
1. INTRODUCTION	4
2. METHODOLOGY	5
A. ATC CODES (ANATOMICAL THERAPEUTIC CHEMICAL CLASSIFICATION SYSTEM) SELECTED FOR THIS ANALYSIS.....	5
B. SOURCE OF DATA AND ANALYSIS PERIOD.....	6
C. SPECIFIC SELECTION CRITERIA	7
D. STANDARDISATION.....	7
3. RESULTS	8
3.1. PROFILE OF INSURED CONSUMERS	8
A. VOLUME OF INSURED CONSUMERS	8
B. INSURED CONSUMERS BY SEX AND AGE GROUP	9
C. INSURED CONSUMERS BY REIMBURSEMENT SCHEME	13
D. GEOGRAPHICAL VARIATIONS OF INSURED CONSUMERS	14
E. EVOLUTION OF INSURED CONSUMERS	18
3.2. CONSUMPTION PER INSURED CONSUMER.....	19
A. QUANTITY OF MEDICATION CONSUMED PER INSURED CONSUMER.....	19
B. DISTRIBUTION OF INSURED CONSUMERS IN CONSUMPTION CLASSES AND BY ANNUAL AVERAGE	19
C. AVERAGE QUANTITY OF MEDICATION CONSUMED BY SEX AND AGE PER INSURED CONSUMER.....	21
D. AVERAGE QUANTITY OF MEDICATION CONSUMED PER INSURED CONSUMER BY PROVINCE.....	22
E. AVERAGE QUANTITY OF MEDICATION CONSUMED PER INSURED CONSUMER BY REIMBURSEMENT SCHEME AND BY PROVINCE	23
3.3. VOLUME OF PRESCRIBED MEDICATION	24
A. CONSUMPTION OF DDD PER 100.000 INSURED	24
B. VOLUME DISTRIBUTION (DDD) OF ATC CODES DELIVERED	25
C. SPECIALISATION OF PRESCRIBERS.....	26
D. EVOLUTION OF DDD CONSUMPTION PER 100.000 INSURED PERSONS	27

3.4.	EXPENDITURE BORNE BY THE HEALTH INSURANCE AND BY THE INSURED	31
A.	EXPENDITURE BORNE BY THE HEALTH INSURANCE	31
B.	EVOLUTION OF EXPENDITURE PER INSURED	33
C.	EVOLUTION OF EXPENDITURE PER ATC CODE AND PER DDD	35
D.	EXPENDITURE BORNE BY THE INSURED CONSUMER (PATIENT SHARE)	36
4.	KEY DATA SUMMARY	37
5.	APPENDICES	38
A.	ANALYSIS OF VARIANCE (ANOVA), EXCEPT BRUSSELS (BASED ON INSURED-CONSUMERS).....	38
B.	PERCENTAGE OF LOW-COST MEDICATION	39
C.	VARIATIONS IN THE TYPE OF MEDICATION DELIVERED (BASED ON DDD).....	42
D.	SALES VOLUMES OUTSIDE THE HEALTH INSURANCE	44

1. INTRODUCTION

The Appropriate Care Unit was set up within the NIHDI's Directorate for Research, Development and Quality under NIHDI's Administration Contract for 2016-2018¹. Article 35 of this contract refers to 'the setting up of an Appropriate Care Unit, aiming specifically to promote an integrated approach to the rational use of resources'. The Appropriate Care Unit has been up and running since the second quarter of 2017.

The tasks of the Unit were set out formally in the '2016-2017 Healthcare monitoring Action plan', published by NIHDI on 18 July 2016². This plan lists around thirty measures designed to make healthcare provision more efficient, by encouraging appropriate practice and tackling unnecessary or inappropriate care.

The plan states that one of the tasks of the Appropriate Care Unit is to analyse the 'appropriateness of care', in order to identify unexplained variations in consumption patterns, identified after standardisation. Such variations can potentially point to non-optimal use of resources.

"Medication use" documents report on the analyses carried out in this framework. Each report focuses on a particular topic. In this document, we present the figures and graphs relating to analyses³ of insured consumers of Antihistamines for systemic use and of the volumes dispensed within the framework of the health insurance (assimilated to their consumption), and give the explanations necessary to understand these.

We have deliberately chosen not to attempt to interpret the figures, preferring to present the results to experts who are in a better position to do so. This document has nevertheless been made available to the public in order to provide objective, open input to discussions on this issue.

¹ (National Institute for Health and Disability Insurance, 2016)

² (National Institute for Health and Disability Insurance, 2016)

³ Readers interested in the methodology used in these quantitative analyses should consult the document entitled 'Variations in consumption – Methodology'.

2. METHODOLOGY

A. ATC codes (Anatomical Therapeutic Chemical Classification System) selected for this analysis

The ATC codes selected for the analysis are listed below:

Code_atc	Description	Rates	Expenses	CodeGroup
R06AE01	BUCLIZINE	yes	yes	1_PIPERAZINE_DERIVATIVES
R06AE03	CYCLIZINE	yes	yes	
R06AE05	MECLOZINE	yes	yes	
R06AE06	OXATOMIDE	yes	yes	
R06AE07	CETIRIZINE	yes	yes	
R06AE09	LEVOCETIRIZINE	yes	yes	
R06AE55	MECLOZINE, COMBINATIONS	yes	yes	



This (simplified) table shows the ATC codes selected for the analysis, stating whether or not they were included in the analysis of prescriptions and expenditure, with their label. The ATC code groupings used in this report are indicated in the CodeGroups columns (if applicable). Medications considered "low-cost" are listed [on the NIHD website](#).

B. Source of data and analysis period

The data used in the analyses have been taken from the following databases:

Pharmanet document	For the percentage of insured consumers, the volume of medicines dispensed (equivalent to the consumption of medicines consumed and converted into DDD per 100,000 insured) and the amount of expenses of insured persons (who meet the selection criteria) whose age, sex, preferential regime and district are known in 2013-2022. The data are collected per accounting period.
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Analysis period	2013-2022
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Pharmanet documents: Pharmanet documents are data from public pharmacies communicated by the invoice offices within the framework of the health care insurance. These data show the information of the prescriptions issued, namely the identifier of the substance issued, the number of packages, the date of sale, an encrypted patient code and the prescriber code. **These data mainly concern medicines reimbursed under the health insurance scheme** Packaging is converted into DDD (Defined Daily Dose) according to the references of the World Health Organization. The IPhEB (Institute for Pharmacology-Epidemiology in Belgium) explains that this daily dose corresponds to the assumed average maintenance dose per day for a drug used for its main indication in adults. It takes into account the route of administration: for example, that the DDD of morphine is 100 mg orally and 30 mg parenterally or rectally. Cheap drugs are identified on the basis of their CNK code (The CNK code is a unique identification number per package, assigned to all drugs and para-pharmaceuticals (medical devices, food supplements, cosmetics ...) delivered in pharmacies). Pharmanet also provides the following information on patients: can be retrieved: age, gender, social category and district of residence. Cross-referencing the prescriber code with NIHDI data allows the prescriber's specialty to be retrieved. Finally, the comparison of Pharmanet with the database "LMPB - IQVIA" (which are the sales of wholesalers to public pharmacies) converted into DDD allows to estimate the approximate share of medicines delivered outside insurance.

C. Specific selection criteria

Several filters may have been applied to the data, so that only one section of the population or prescribers is considered in the analyses. If so, the filters used are shown in the table below:

FILTERS APPLIED TO DATA	
Sex	women and men
Age	all
-	-

D. Standardisation

Data presented by geographical subset* or population category are standardised per year, based on age, sex and preferential regime of the national population in 2022.

*Note: Districts with fewer than 100,000 insured persons are associated with a neighbouring district from the same province. The following districts are therefore considered together: Oostende/Veurne, Ieper/Diksmuide, Roeselare/Tielt, Gent/Eeklo, Charleroi/Thuin, Huy/Waremme, Namur/Philippeville, Neufchâteau/Marche-en-Famenne, Virton/Bastogne/Arlon. These regroupings and labels apply to all measurements, maps and graphs produced by district. Throughout the document, the concept of regrouped district is reflected in the use of the term "district"



Standardisation renders populations comparable in relation to one or several criteria. If a difference is observed between these populations, we can therefore assume that it is not due to the criteria covered by the standardisation process.

3. RESULTS

3.1. Profile of insured consumers

A. Volume of insured consumers

	TOTAL
<i>Number of consumers</i>	<i>510.305</i>
Percentage of insured consumers	4,43%

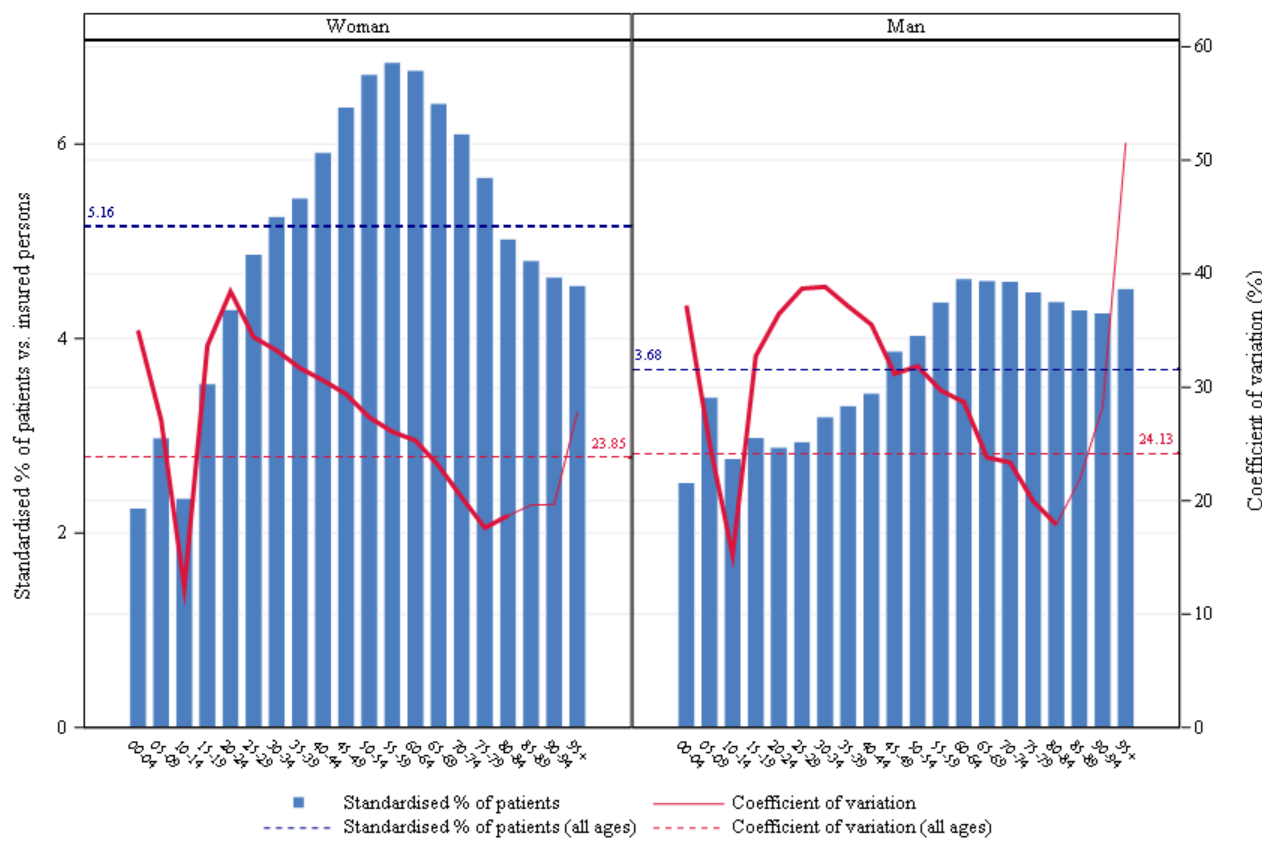
B. Insured consumers by sex and age group

	TOTAL
<i>Number of insured consumers</i>	510.305
Median age (years)	49
Mean age (years)	47,1
Max/Min Ratio of the median age (by district*)	1,06
Percentage of women	59,81%

Max/Min Ratio:

The max/min ratio measures the dispersion of values. It is calculated as the ratio of the maximum value found for the variable, in all districts*, to the minimum value, excluding outliers. If this minimum value is equal to zero, the max/min ratio cannot be calculated, and is reported as 'NA' ('not applicable').

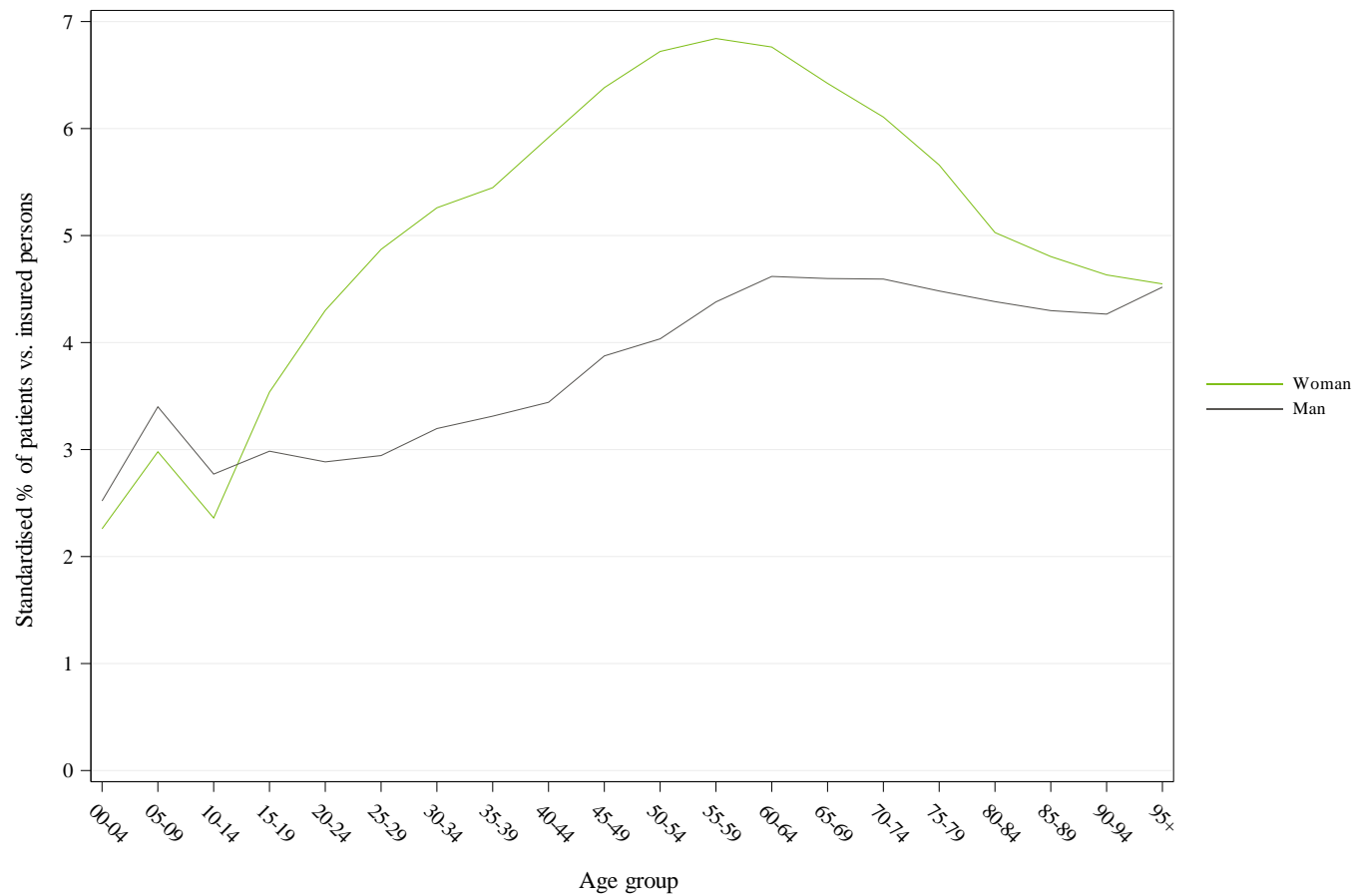
* Some districts are grouped together, see page 7, Standardisation.



This figure is made up of bar charts for each sex. The **coefficient of variation**, shown by the red line, measures the relative dispersion of the percentages of insured consumers observed for each district*, by age group and sex (standard deviation divided by the mean). This line is shown in bold for age groups where the coefficient of variation can be validly interpreted (i.e. for age groups in which there are sufficient insured persons per district* to allow for a proper comparison).

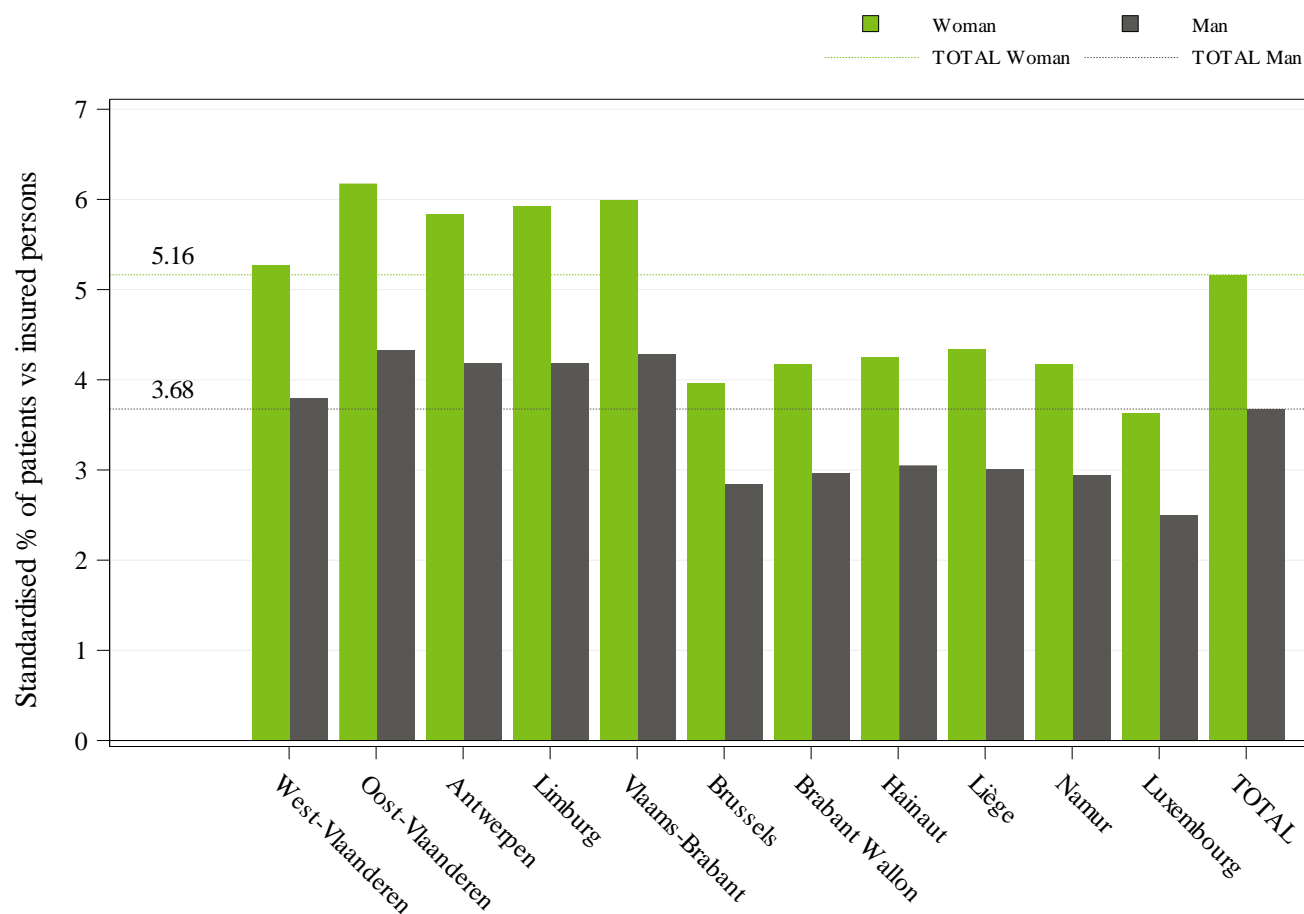
The left-hand vertical axis of the graph represents the percentage of insured consumers, and the right-hand axis the coefficient of variation. The horizontal axis shows the age groups. The horizontal dotted lines show the total values of the percentage of insured consumers (in blue) and of the coefficient of variation (in red).

Percentage of insured consumers and coefficient of variation by district*, by age group and sex



Comparison of the percentage of insured consumers by age group and sex

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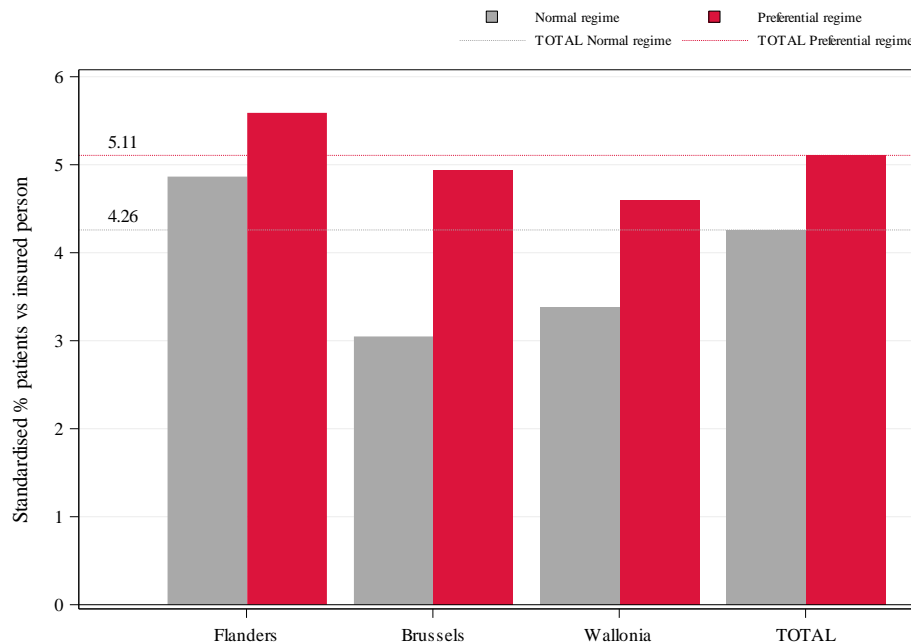


Percentage of insured consumers by province

This histogram shows the percentage of insured consumers by province and by sex. The grey bars show the rates for men, while the green bars show the rates for women, for each province. The grey and green broken lines show the percentage of insured consumers according to the same colour code.

C. Insured consumers by reimbursement scheme

	TOTAL
<i>Number of insured consumers</i>	510.305
% of insured consumers under the preferential scheme	5,11%
% of insured consumers under the general scheme	4,26%
Ratio Preferential scheme /General scheme	1,2



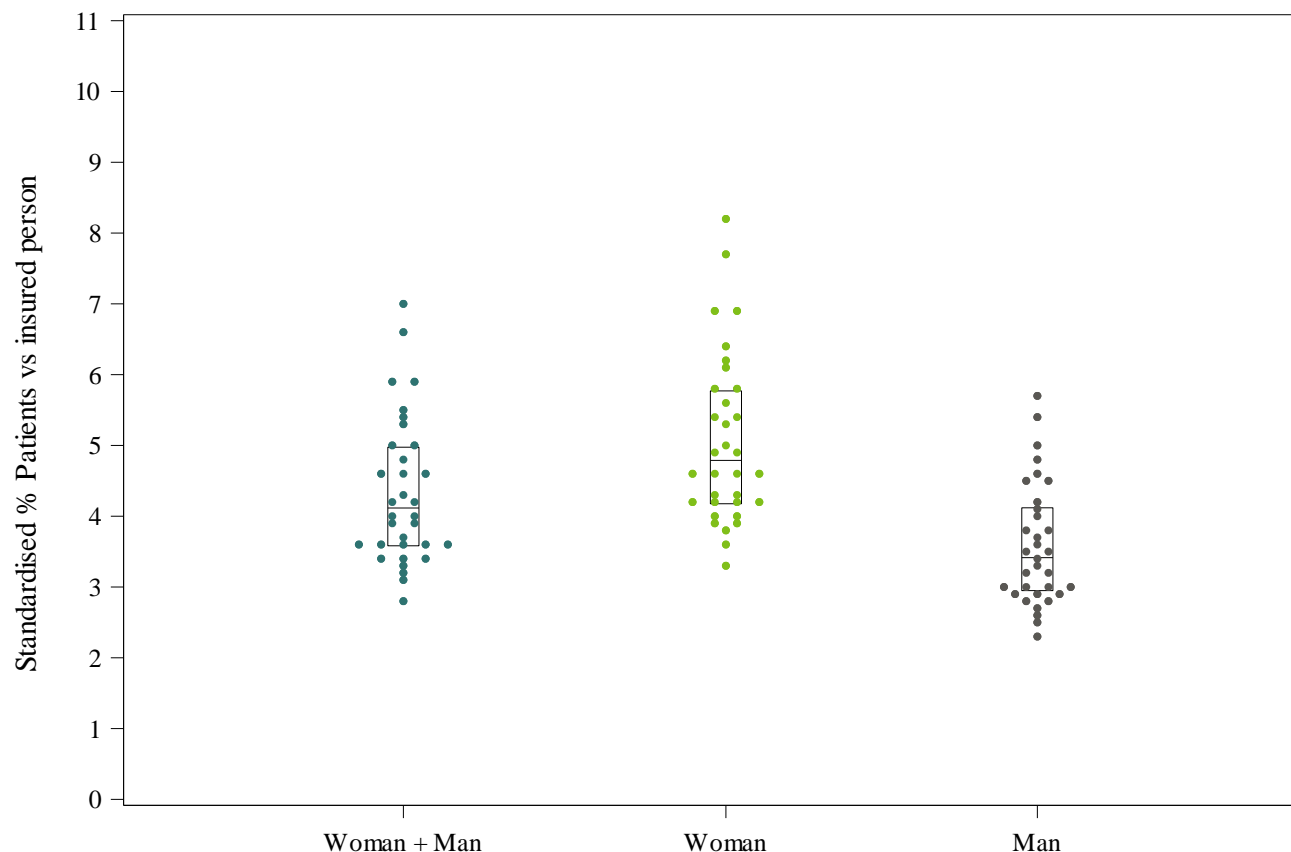
The graph shows the percentages of insured consumers with (in red) and without (in grey) the preferential reimbursement scheme, by region and in total. The red and grey dotted lines show the percentages of insured consumers, with and without the preferential reimbursement scheme, respectively.

Percentage of insured consumers by reimbursement scheme and by region

D. Geographical variations of insured consumers

	TOTAL
<i>Number of insured consumers</i>	510.305
Coefficient of Variation	23,84%
Max/Min Ratio of percentages insured consumers (by region)	1,47
Max/Min Ratio of percentages insured consumers (by district*)	2,49

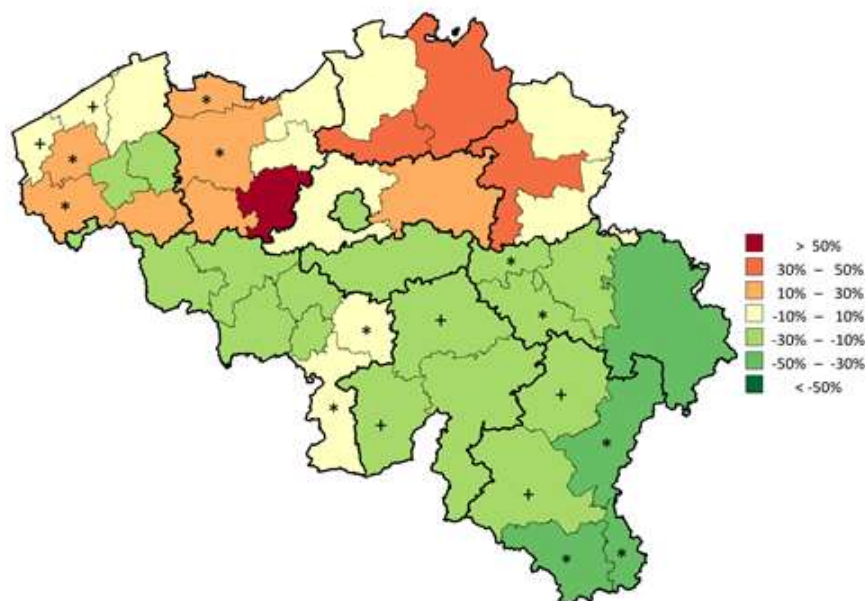
An 'NA' result indicates a ratio which cannot be calculated, i.e. the minimum value = zero.



A **dot plot** is a distribution chart, which is useful for highlighting groups in the data, gaps in the distribution and outliers. Here, each dot represents the percentage of insured consumers of a district*, for its entire population or broken down by sex.

The graph also shows a box with the 25th, 50th and 75th percentiles of the percentages of insured consumers for all districts*. The bottom line of the box represents the 25th percentile, while the upper line represents the 75th percentile. The line inside the box represents the 50th percentile.

'Dot plot' showing percentages of insured consumers by district*, by sex



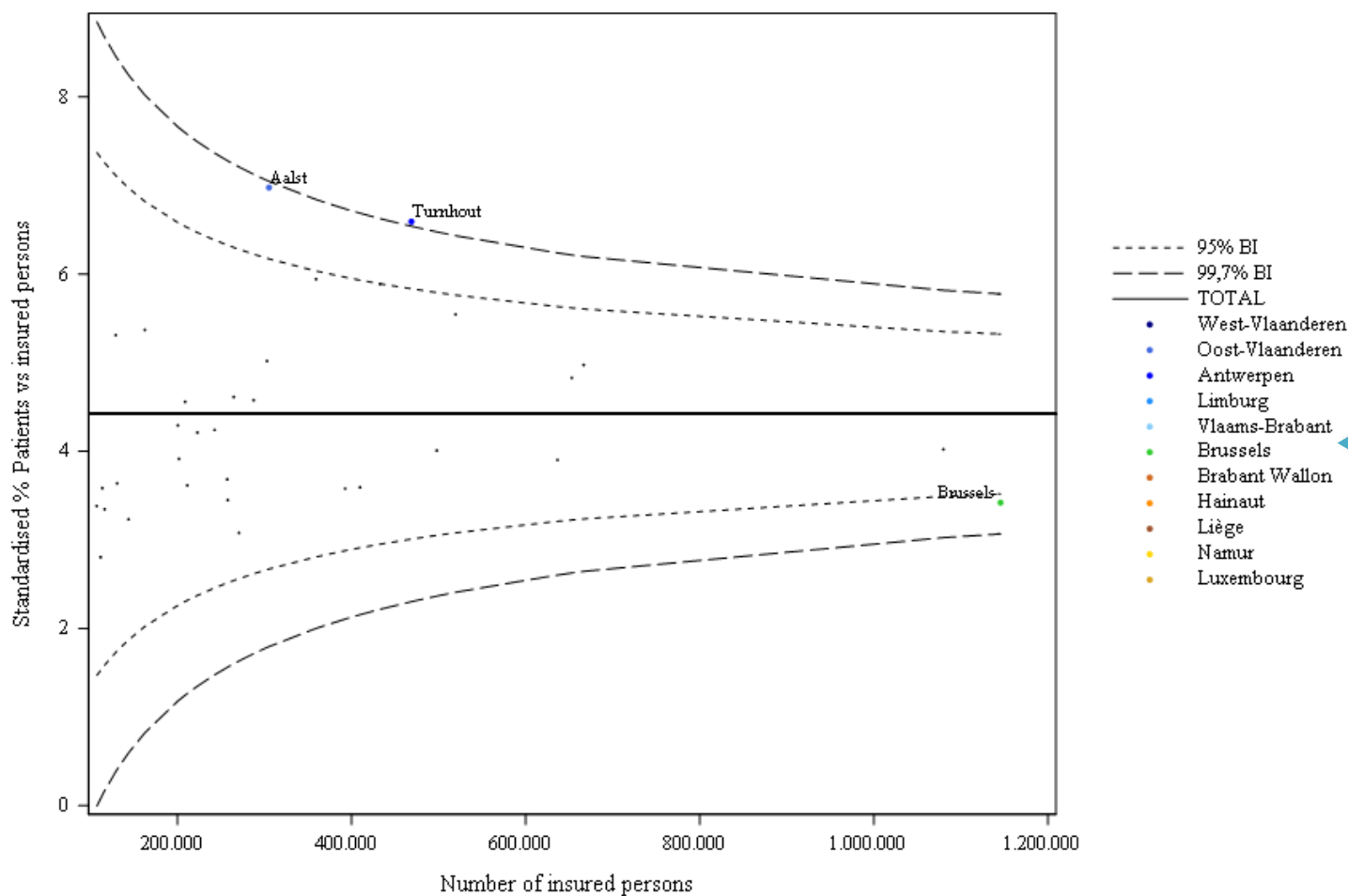
Map showing distribution of percentages of insured consumers, by district*

* Districts marked with * or + are grouped together within the same province.
see page 7, Standardisation

On this map of Belgium, thin lines show the boundaries of the districts*, while thick lines show the provincial borders. The districts* are coloured using a colour scale based on the level of rate of use in the district* compared to the Belgian national rate (overall rate). This ratio is expressed as a percentage: e.g. 0% if the district* rate is equal to the percentage of insured consumers in Belgium, 20% if the rate is 20% above the percentage of insured consumers, and -20% if the rate is 20% below the percentage of insured consumers. The differences are calculated using the last year analysed, and are displayed in bands of 20%. The following colour coding applies:

Colour	Category
Dark red	More than 50%
Red	Between 30% and 50%
Orange	Between 10% and 30%
Yellow	Between - 10% and 10%
Light green	Between -30% and -10%
Green	Between -50% and - 30%
Dark green	Less than -50%
White	Not used

N.B.: The interpretation of this map is to be done in parallel with the graph in funnel plot (next page)

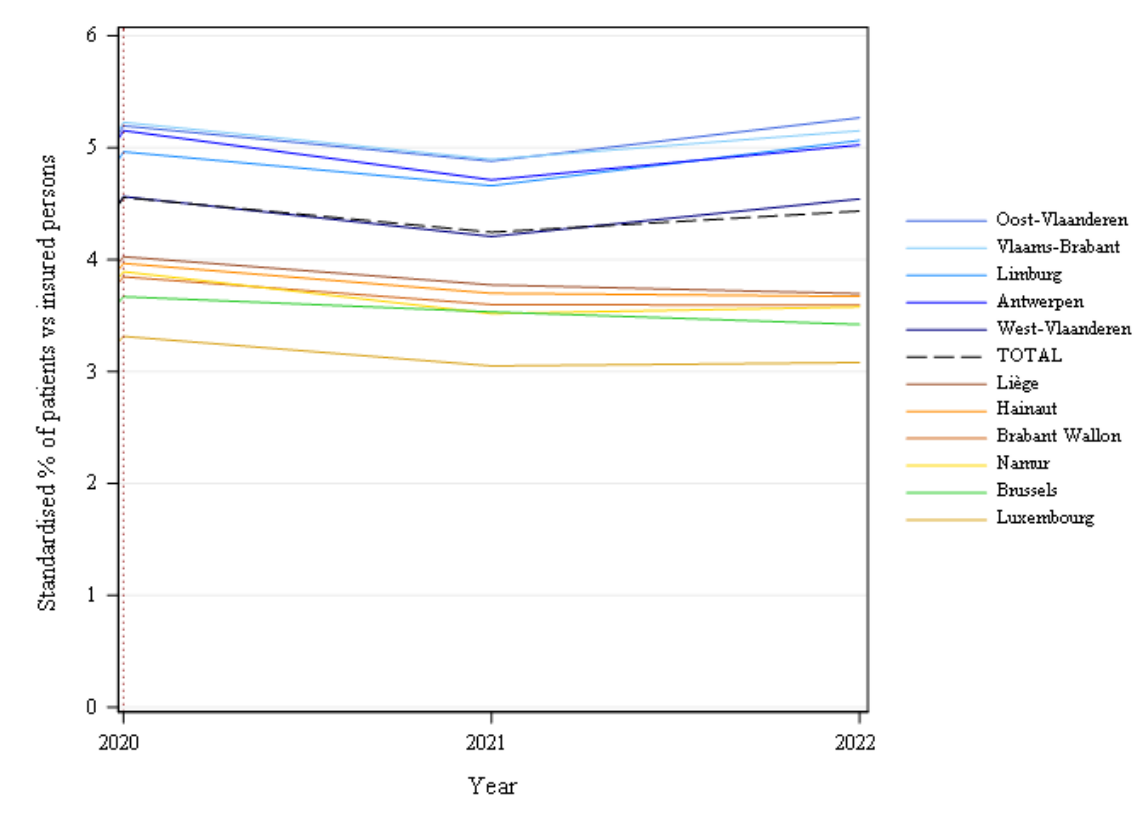


In this graph, the percentage of insured consumers in a district* is positioned versus the size of its population. Besides the dots representing the districts*, 95% and 99.7% **confidence intervals** are also shown on the graph. These are dependent of the size of the districts*. The thicker horizontal line shows the national percentage of insured consumers. The outlier districts* are identified as those districts* that fall outside the 99.7% confidence intervals, the zone between the 95% and 99.7% confidence intervals being considered as "warning zone".

N.B.: The interpretation of this graph is to be done in parallel with the map of the distribution of rates of use (previous page)

'Funnel plot' showing the percentages of insured consumers by district*

E. Evolution of insured consumers



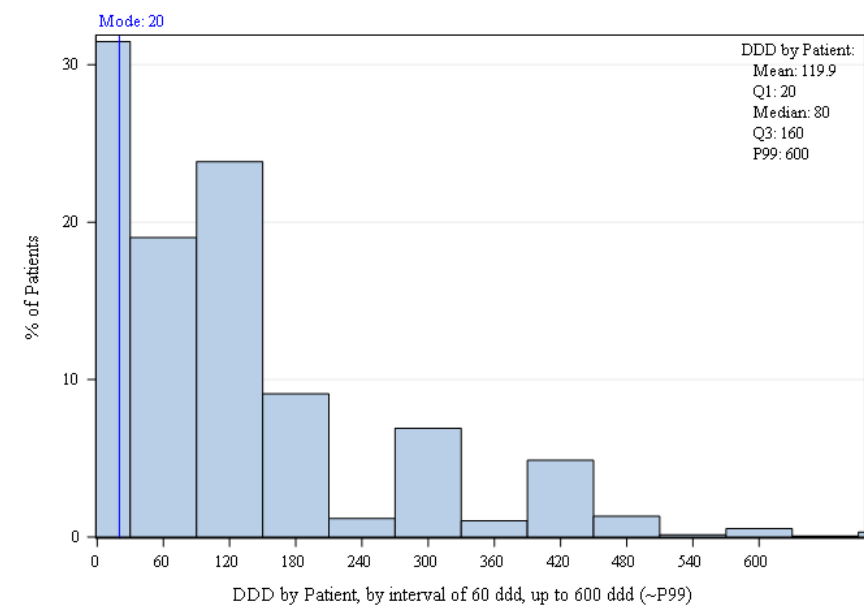
Evolution of percentage of insured consumers by province

3.2. Consumption per insured consumer

A. Quantity of medication consumed per insured consumer

	TOTAL
<i>Consumption of medication per year (DDD)</i>	61.183.521
<i>Number of consumers</i>	510.305
<i>Percentage of insured consumers</i>	4,43%
<i>Number of DDD per insured consumer</i>	120

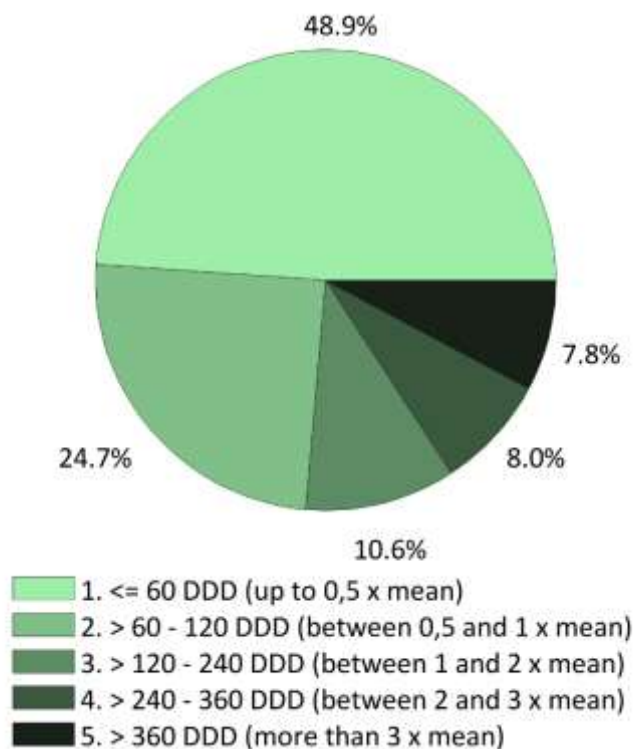
B. Distribution of insured consumers in consumption classes and by annual average



Distribution of insured consumers into consumption classes

The insured consumers are divided according to their annual consumption. High frequencies (peaks) in different classes may reflect differences in **treatment duration** or **dosage** (depending on the prescription, patient profile, pathology, compliance, etc.), but may also reflect other biases such as, among others, repetition of episodes over the year or the timing of initiation of chronic treatment.

Frequency	Per year
≤ 0,5 times the average annual consumption	48,89%
>0,5 and ≤1 times the average annual consumption	24,73%
>1 and ≤2 times the average consumption	10,57%
>2 and ≤ 3 times the average consumption	8,03%
>3 times the average annual consumption	7,79%

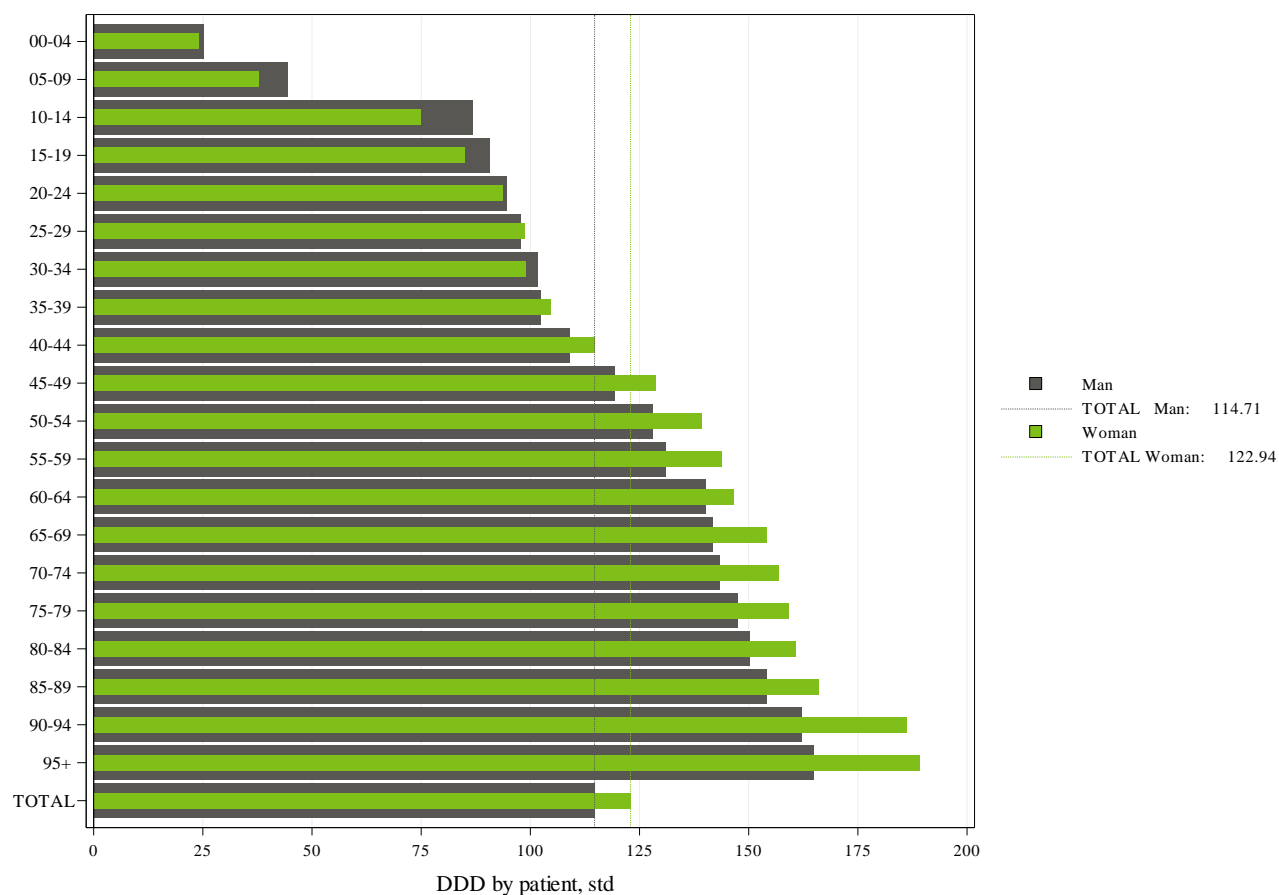


Distribution of insured consumers by average annual dose delivered

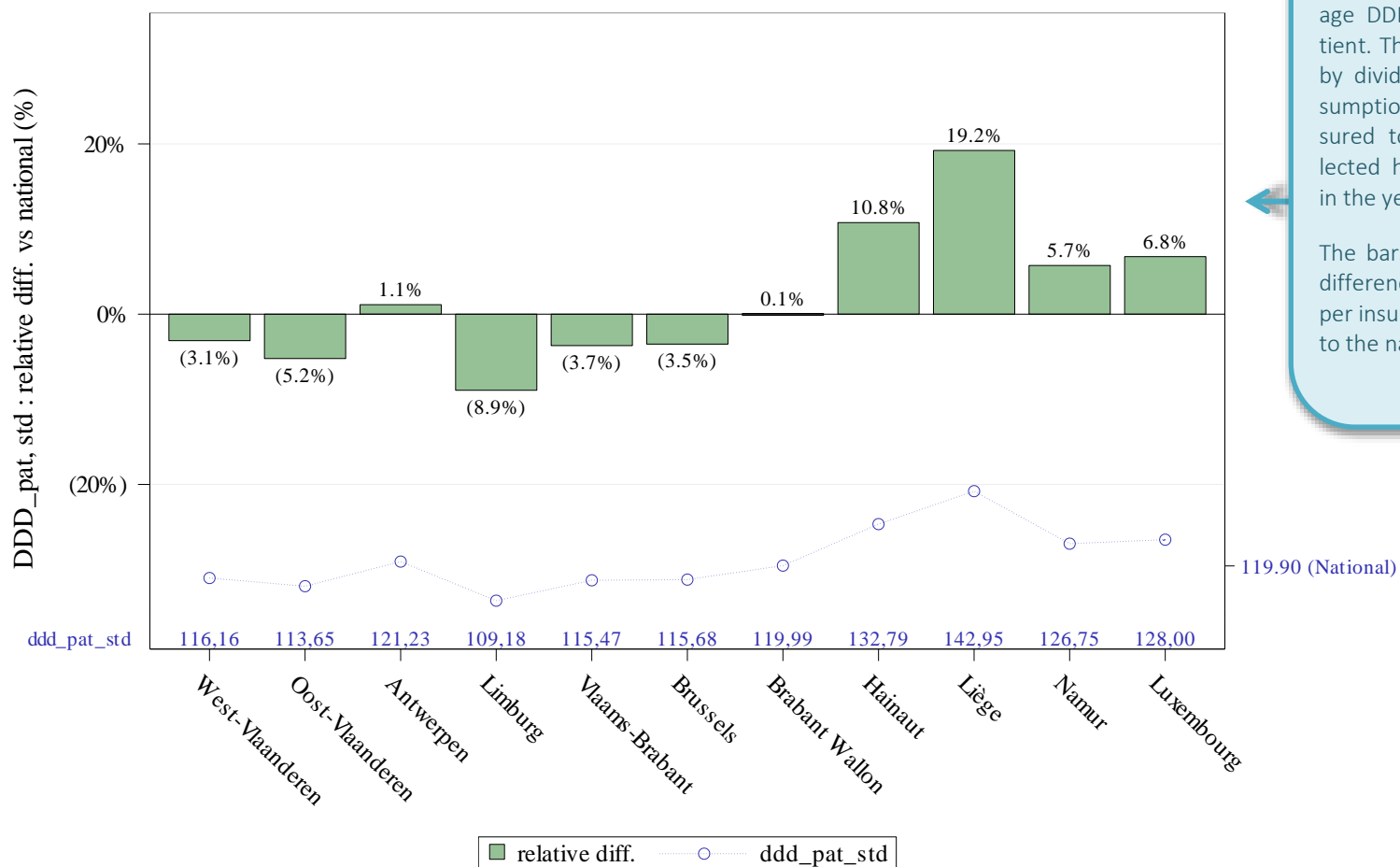
The insured consumers are divided according to their consumption in relation to the national average dose. Variations in doses may reflect differences in **treatment duration** or **dosage** (depending on the prescription, patient profile, pathology, compliance, etc.), but may also reflect other biases such as, among others, repetition of episodes over the year or the timing of initiation of chronic treatment.

C. Average quantity of medication consumed by sex and age per insured consumer

	Women	Men	Ratio W/M
Percentage of insured consumers	5,2%	3,7%	1,4
Number of DDD per insured consumer	122,9	114,7	1,07



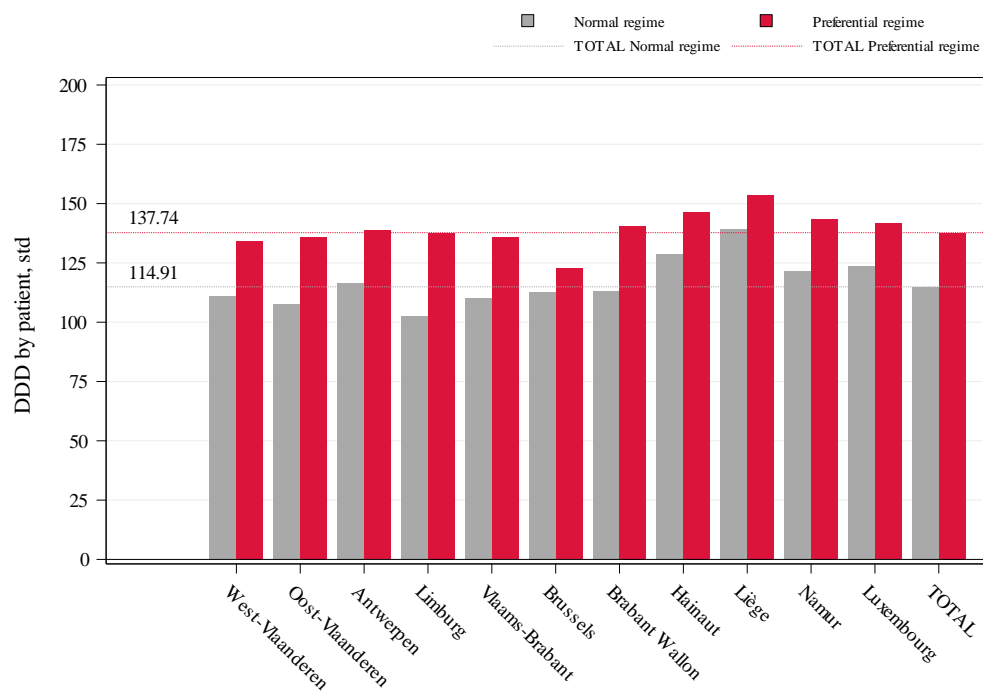
D. Average quantity of medication consumed per insured consumer by province



Consumption per insured consumer (DDD) by province and variation vs average national value

E. Average quantity of medication consumed per insured consumer by reimbursement scheme and by province

	Preferential scheme	General scheme	Ratio Preferential scheme /General scheme
Percentage of insured consumers	5,1%	4,3%	1,2
Number of DDD per insured consumer	137,7	114,9	1,2



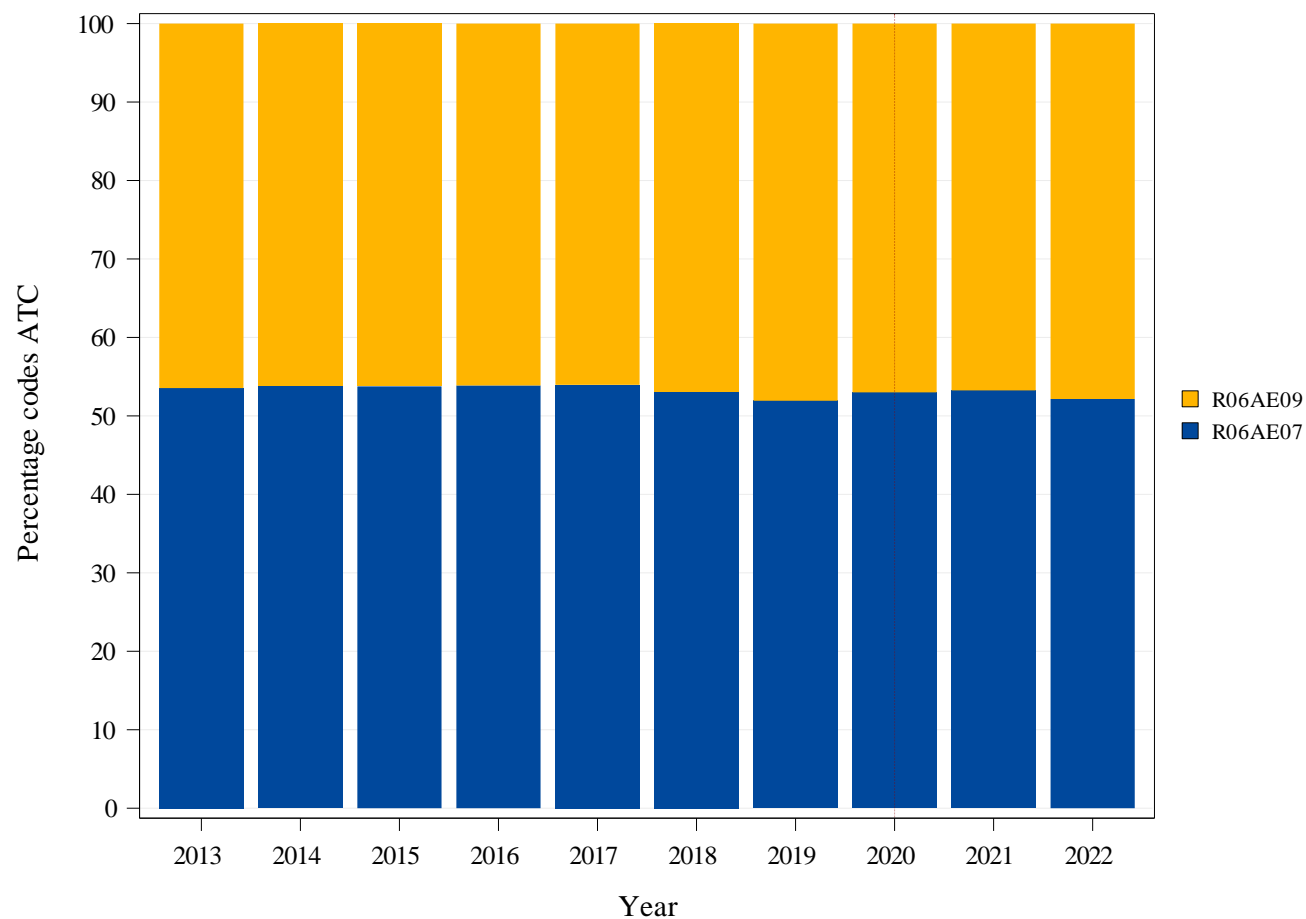
Consumption per insured consumer (DDD) by province and by reimbursement scheme

3.3. Volume of prescribed medication

A. Consumption of DDD per 100.000 insured

	TOTAL
<i>Consumption of medication per year (DDD)</i>	<i>61.183.521</i>
Consumption of DDD per 100.000 insured (delivered medication converted to DDD)	531.619

B. Volume distribution (DDD) of ATC codes delivered



See the ATC codes selected for the analysis on page 5 for further information on these codes (For ease of reading, the list is limited to the 23 most commonly issued ATC codes)

Note : The year 2020 was highlighted by a vertical line in order to draw the attention on the impact of the COVID-19

C. Specialisation of prescribers

Specialisation of the prescriber	Total prescribers	Concerned prescribers	% Prescribers	Median of prescribed DDD	Q3 of prescribed DDD	Volume of prescribed DDD	% DDD	% cheap DDD	Expenses	% Expenses
General practitioners	19.644	13.897	71%	2.674	4.982	49.359.843	81%	99%	4.246.759	79%
General practitioners in training	6.066	2.997	49%	980	1.820	3.750.614	6%	99%	350.303	7%
Dermatology-venereology	1.003	718	72%	640	1.510	989.376	2%	99%	85.556	2%
Specialists in training	10.070	4.092	41%	120	270	929.598	2%	98%	92.559	2%
Otorhinolaryngology	881	582	66%	480	1.260	775.086	1%	99%	75.069	1%
Pneumology	844	587	70%	640	1.440	770.714	1%	100%	59.535	1%
Paediatrics	2.177	1.232	57%	200	460	725.060	1%	92%	93.583	2%
Other specialities	45.584	13.192	29%	207	390	3.883.230	6%	100%	342.893	6%
Total	86.269	37.297	43%	400	2.045	61.183.521	100%	99%	5.346.257	100%



This table shows, in order, the following non-standardised data per specialities (figures for the year 2022):

- The number of prescribers who prescribed at least one medicine delivered;
- The number of prescribers who prescribe the ATC codes selected for this analysis;
- The percentage of prescribers prescribing these codes out of the number of providers who prescribed at least one medicine delivered;
- The median number and third quartile (= 75th percentile) of services per prescriber (prescribing codes);
- The volume of DDD prescribed, i.e. the volume of sales of medicines converted into DDD broken down by prescriber's specialty;
- The percentage of medicines prescribed, i.e. the ratio of the number of medicines dispensed by this speciality to the total number of medicines prescribed among the ATC codes selected;
- The percentage of low-cost drugs, i.e. the ratio of the number of medicines identified as "cheap" by national code number (CNK) to the total number of medicines dispensed among the selected ATC codes;
- Expenditure refers to the total costs borne by insurance (excluding patient share and non-insurance sales);
- The percentage of expenditure is the share of expenditure broken down by prescriber specialty in relation to total expenditure.

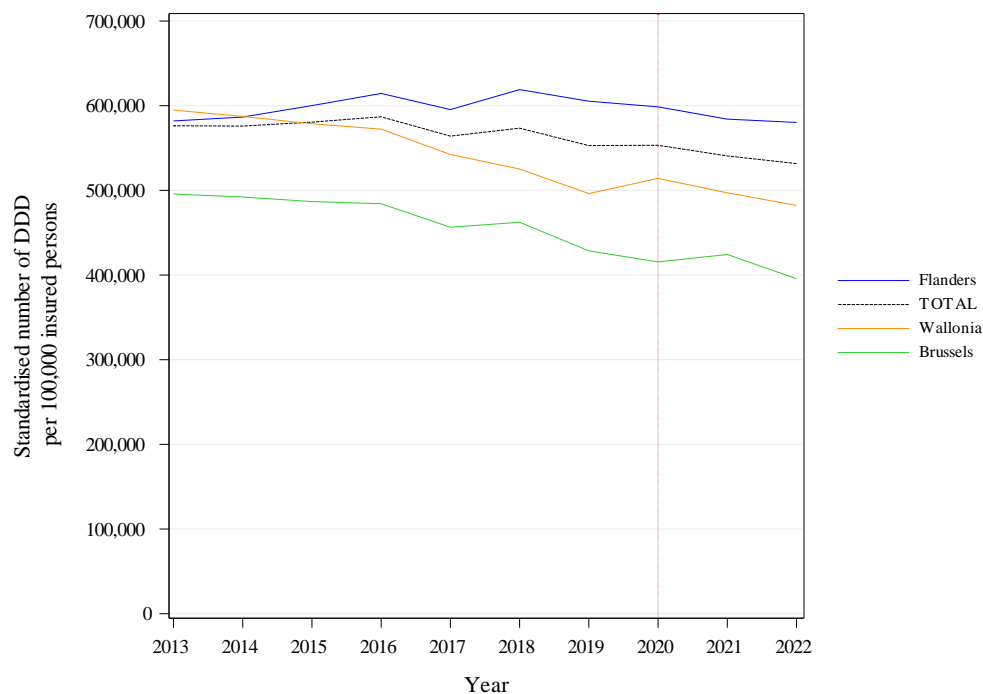
If applicable, specialties representing less than 1% of the total number of DDDs prescribed or with fewer than 5 prescribers are grouped together in the "Other specialties" category. For reasons of confidentiality, this "Other specialty" category will only be reported if there are at least 5 prescribers in total.

D. Evolution of DDD consumption per 100.000 insured persons

	TOTAL	
Annual consumption (DDD)	61.183.521	
Trend (2013-2022)	-0,89%	** (-1,46%)
Trend (2013-2019)	-0,69%	NS
Trend (2019-2022)	-1,30%	

These trends correspond to the average annual growth rate.

A non-significant statistical test indicates that the trend estimated by the model (in brackets) is stable, or that there is no break in the trend.



This graph shows a coloured curve for each region and a black curve for the entire Belgian population. The x-axis shows the years, and the y-axis shows the standardised consumption of DDD per 100.000 insured persons.

Note : The year 2020 was highlighted by a vertical line in order to draw the attention on the impact of the COVID-19 crisis.

Evolution of DDD consumption per 100.000 insured persons by region



This graph shows a colored line for each province and a black line for the entire Belgian population. The x-axis shows the years, and the y-axis shows the standardised consumption of DDD per 100.000 insured persons.

Note : The year 2020 was highlighted by a vertical line in order to draw the attention on the impact of the COVID-19 crisis.

Evolution of DDD consumption per 100.000 insured persons by province

		Consumption in DDD	Annual increase			Structural break
		2022 (per 10 ⁵ insured)	2013-2022	2013-2019	2019-2022	
Provinces	West Flanders	527.690	0,13%	0,21%	-0,02%	NA
	East Flanders	598.670	0,72%	1,39%	-0,60%	NA
	Antwerp	609.192	-0,20%	0,91%	-2,39%	NA
	Limburg	553.072	0,03%	0,87%	-1,63%	NA
	Flemish Brabant	594.873	-0,86%	-0,38%	-1,82%	NA
	Brussels	395.643	-2,47%	-2,39%	-2,63%	NA
	Walloon Brabant	430.950	-2,59%	-3,06%	-1,65%	NA
	Hainaut	487.555	-2,30%	-3,10%	-0,68%	NA
	Liège	528.423	-2,10%	-2,61%	-1,08%	NA
	Namur	453.468	-2,40%	-3,17%	-0,85%	NA
	Luxembourg	394.246	-2,70%	-3,60%	-0,87%	NA
Regions	Flanders	580.247	-0,03%	0,66%	-1,40%	NA
	Brussels	395.643	-2,47%	-2,39%	-2,63%	NA
	Wallonia	482.263	-2,30%	-2,98%	-0,94%	NA
TOTAL		531.619	-0,89%	-0,69%	-1,30%	NS

Evolution of DDD consumption by province and by region

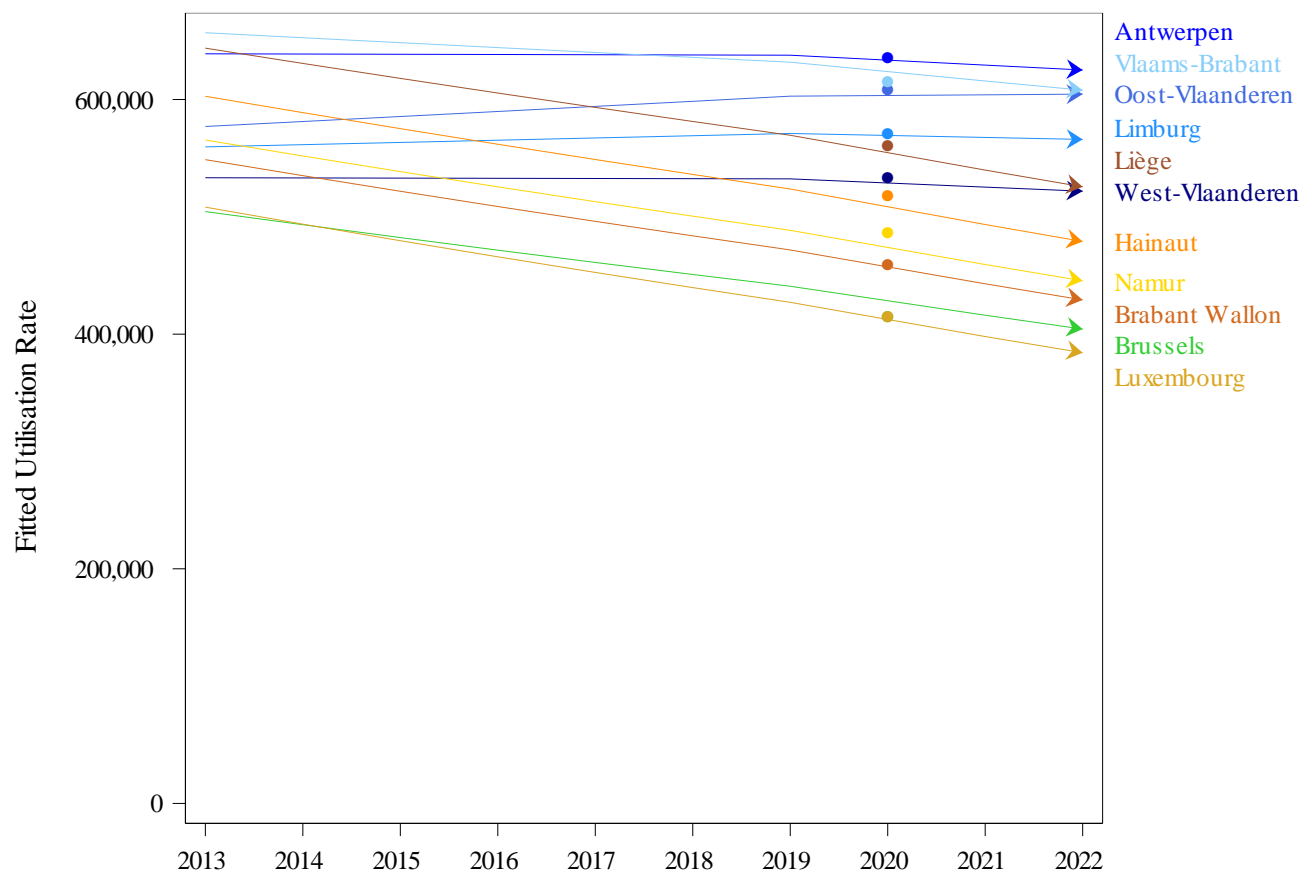
This table reports the standardised **consumption of DDD** for the last year analysed (2022), as well as the average **rates of increase**, by province, by region and in total, for the entire period ((2013-2022), for the last years (2019-2022) and for the period preceding these ((2013-2019).

To test whether the trend of the last years differs from the trend of the previous years, a two-stage linear mixed model was applied. The first step tests whether the trend of the last years is different from the previous period at the Belgian level. Then, if the test is significant, the second step tests whether the trend break differs from one region or province to another. Data for 2020 are excluded from the models.

The significance of the test for a change in trend is reported in the Structural break column : * P-value ≤ 0.05 / ** P-value ≤ 0.01 / *** P-value ≤ 0.001 and NS for a non-significant result.

NA' is shown where the ATC codes selected for the analysis have been used for the first time after the last three-year period considered or when the statistical tests cannot be carried out.

Medication - Antihistamines for systemic use



Regression lines per province showing a possibly different slope for the last years (2019-2022) compared to the years before (2013-2019).

Data of 2020 was excluded from this analysis, but is indicated on the graph for information.

Trend break assessment model by province – Regression lines

3.4. Expenditure borne by the health insurance and by the insured

A. Expenditure borne by the health insurance

	TOTAL
<i>Annual consumption (DDD)</i>	<i>61.183.521</i>
Annual expenditure	5.346.257€
Average cost per DDD	0,09€
Average annual expenditure per insured	0,46€
Max/Min Ratio of expenditure per insured (by region)	1,48
Max/Min Ratio of expenditure per insured (by district*)	2,24

An 'NA' result indicates a ratio which cannot be calculated, i.e. the minimum value = zero.

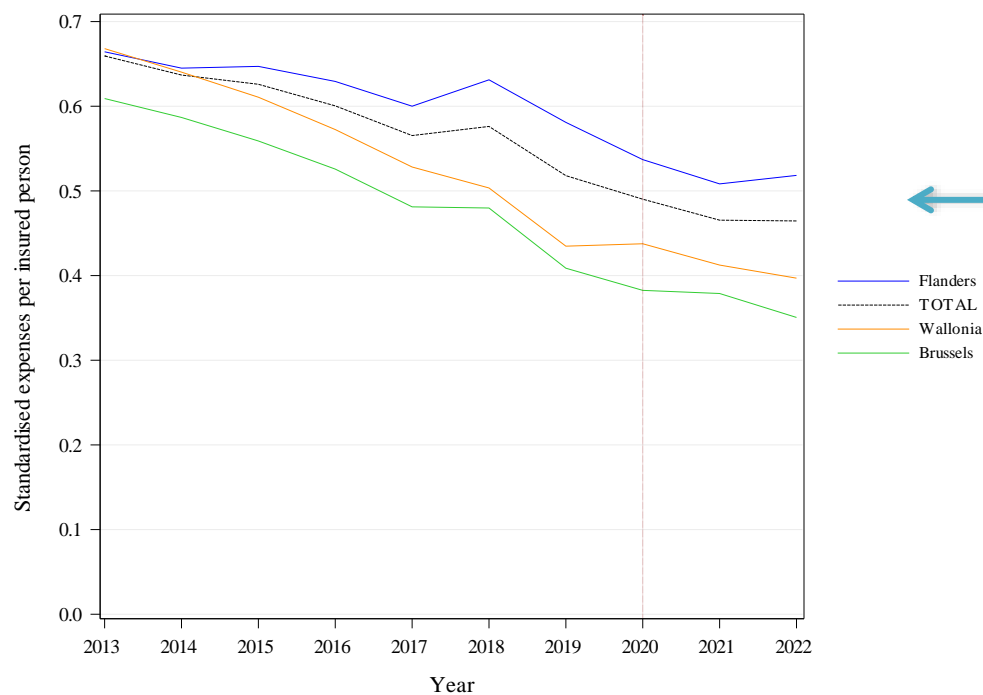
		Expenditure per insured
Provinces	West Flanders	0,5€
	East Flanders	0,5€
	Antwerp	0,5€
	Limburg	0,5€
	Flemish Brabant	0,5€
	Brussels	0,4€
	Walloon Brabant	0,4€
	Hainaut	0,4€
	Liège	0,4€
	Namur	0,4€
	Luxembourg	0,3€
Regions	Flanders	0,5€
	Brussels	0,4€
	Wallonia	0,4€
TOTAL		0,5€

Regional and provincial distribution of expenditure per insured

B. Evolution of expenditure per insured

	TOTAL
Annual expenditure	5.346.257€
Average annual expenditure per insured	0,46€
Trend (2013-2022)	-3,82%
Trend (2013-2019)	-3,94%
Trend (2019-2022)	-3,57%

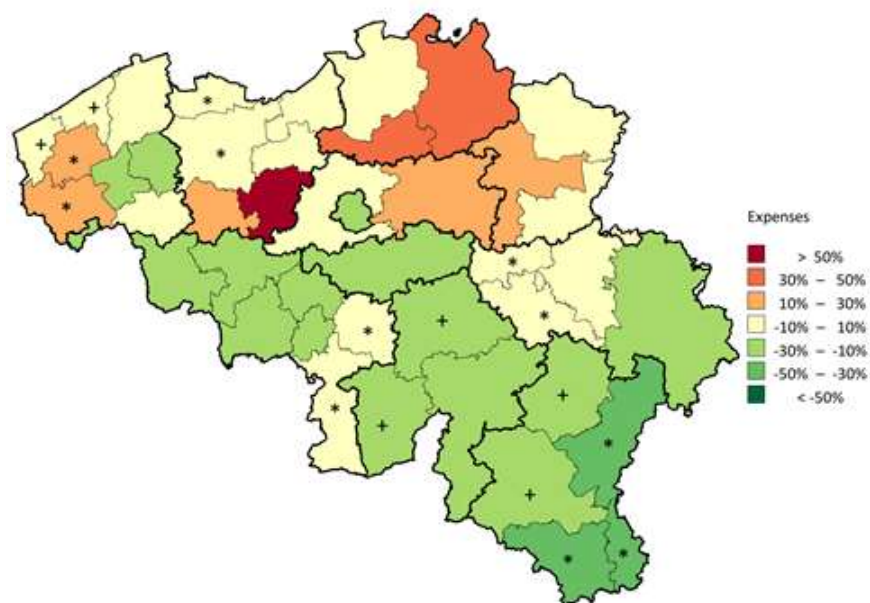
These trends correspond to the average annual growth rate.



This graph shows a coloured curve for each region and a black curve for the entire Belgian population. The x-axis shows the years, and the y-axis shows the standardised expenditure based on 2022 population data

Note : The year 2020 was highlighted by a vertical line in order to draw the attention on the impact of the COVID-19 crisis.

Evolution of expenditure per insured, by region



Map showing distribution of expenditure, by district*

On this map of Belgium, thin lines show the boundaries of the districts*, while thick lines show the provincial borders. The districts* are coloured using a colour scale based on the level of expenditure in the district* compared to Belgian national (overall) expenditure. This ratio is expressed as a percentage: e.g. 0% if expenditure in the district* is equal to the overall expenditure, 20% if it is 20% higher, and -20% if it is 20% lower. The percentages are calculated using the standardised expenditure of the last year analysed and are displayed in bands of 20%. The following colour coding applies:

Colour	Category
Dark red	More than 50%
Red	Between 30% and 50%
Orange	Between 10% and 30%
Yellow	Between - 10% and 10%
Light green	Between -30% and -10%
Green	Between -50% and - 30%
Dark green	Less than -50%
White	No expenditure

* Districts marked with * or + are grouped together within the same province.
see page 7, Standardisation

C. Evolution of expenditure per ATC code and per DDD

Code_atc	Description	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Average annual growth rate
R06AE07	CETIRIZINE	0,11	0,11	0,11	0,10	0,10	0,10	0,09	0,08	0,08	0,08	-3,74%
R06AE09	LEVOCETIRIZINE	0,12	0,11	0,11	0,11	0,10	0,11	0,10	0,09	0,09	0,10	-2,24%

Evolution of expenditure per ATC code and per DDD in Euros

(For readability, this list is limited to the 23 most commonly issued ATC codes in 2022)

D. Expenditure borne by the insured consumer (patient share)

	TOTAL
<i>Annual consumption (DDD)</i>	61.183.521
Annual expenditure	5.346.257€
Total share of patients	5.123.473€
Average annual patient share per insured consumer¹	10,04€
% borne by the insured consumer²	48,94%

¹ The average financial contribution paid per year per insured consumer of the medicine is calculated by dividing the total share of patients by the number of insured consumers.

² This is the share of the insured consumer (patient share) in relation to the total cost of the medicine supplied under the insurance scheme (i.e. excluding sales outside health insurance).

4. KEY DATA SUMMARY

Main prescribers:		General practitioners	81%
CONTEXT			
Percentage of sales not covered by the health insurance (NIHDI) ¹			28,2%
PROFILE OF INSURED CONSUMERS			
Percentage of insured consumers			4,43%
Median age			49 y.
Max/min ratio ² of the median age (by district*)			1,06
Percentage of women			59,8%
Ratio Preferential rate/General rate			1,2
Coefficient of variation (2022)			23,8%
Max/min ratio ² of percentage of insured consumers (by district*)			2,49
CONSUMPTION			
Annual consumption (DDD)			61.183.521
Consumption of DDD (per 100.000 insured persons)			531.619
Average annual consumption per insured consumer (in DDD)			120
Percentage insured consumers with more than 3 times the average consumption			7,79%
Coefficient of variation ³ (2013-2015)			13,12%
Coefficient of variation ³ (2020-2022)			16,92%
Trend ⁴ (2013-2022)			-0,89%
Trend ⁵ (2013-2019)			-0,69%
Trend ⁵ (2019-2022)			-1,30%
DIRECT EXPENDITURE (based on DDD)			
Annual expenditure borne by the insurance			5.346.257€
Average annual expenditure per insured			0,46€
Average patient share per insured consumer			48,9%
Max/Min Ratio ² of expenditure per insured (by district*)			2,24
Percentage low-cost medication			99,3%
Trend (2013-2022)			-3,82%
Trend (2019-2022)			-3,57%

¹ Approximate value estimated from the discrepancy between the sales declarations of wholesalers to pharmacies converted into DDD and what is paid by the health insurance and the patients' share (see Annex D). This is a contextual indicator.

² An 'NA' result indicates a ratio, which cannot be calculated, i.e. the minimum value equals zero.

³ The test compares the coefficients of variation for the two periods and indicates whether the difference is statistically significant.

⁴ The test indicates whether the observed slope is statistically significantly different from 0%.

⁵ The test indicates whether the break in trend between the two periods is statistically significant.

5. APPENDICES

A. Analysis of variance (ANOVA), except Brussels (based on insured-consumers)

Statistical significance of the differences observed in 2022	
<i>By region?</i>	***
<i>By sex?</i>	***
<i>By reimbursement scheme?</i>	***
<i>By sex and per region?</i>	NS
<i>By reimbursement scheme and per region?</i>	NS
<i>By sex and per reimbursement scheme?</i>	***
<i>By sex and reimbursement scheme and per region?</i>	NS

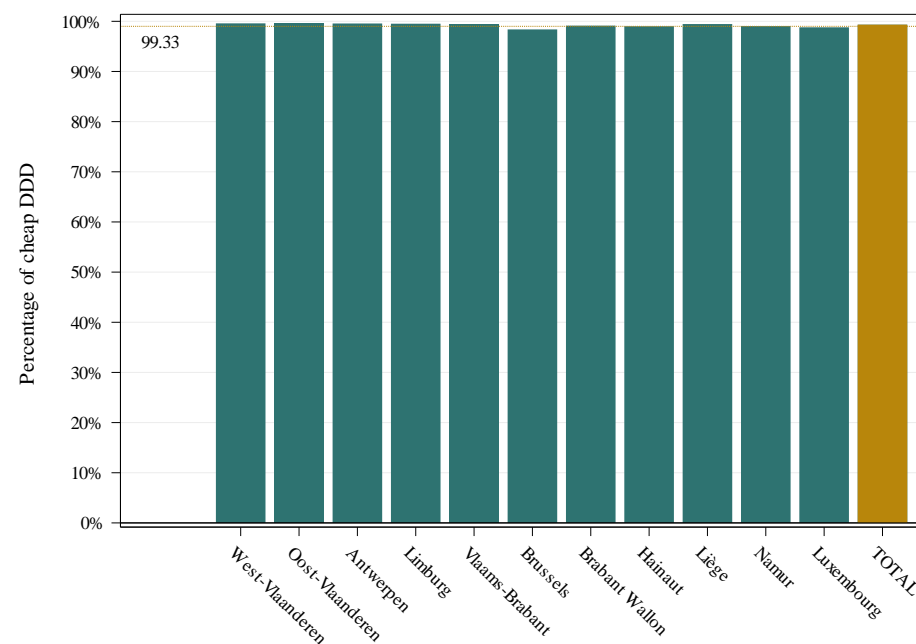
In order to be able to assess the significance of the observed differences, a linear mixed **ANOVA** model was fitted to the data of all districts* of the Walloon and Flemish regions, after standardising for age. The model has region, sex and reimbursement scheme as fixed effects (main effects) and also contains all two-way and three-way interactions between these effects.

In order to interpret the analysis correctly, first the three-way interaction (last row of the table) should be evaluated, followed by the two-way interactions and finally by the main effects. If the three-way interaction is significant, the interpretation of the model should be done at this level only and the two-way interactions and main effects should not be interpreted. If the three-way interaction is not significant, the two-way interactions are evaluated. Every effect that appears in a significant interaction should be interpreted at the interaction level and not at the main effect level. Only if a main effect is not part of a significant interaction should the interpretation be made directly at the main effect level.

The **asterisks** represent the level of statistical significance of the tests: * P-value $\leq 0,05$ / ** P-value $\leq 0,01$ / *** P-value $\leq 0,001$ or NS for a non-significant result.

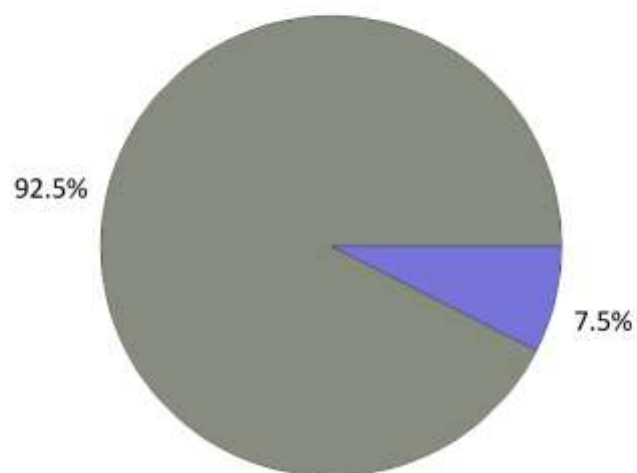
B. Percentage of low-cost medication

	TOTAL
<i>Annual consumption (DDD)</i>	61.183.521
Percentage of low-cost medication	99,3%
Max/min ratio of % low-cost (by district*)	1,01



Percentage of 'low-cost' medication delivered nationally and provincially

This graph shows the percentage of low-cost DDD vs the total number of DDD delivered. Besides one bar per region, an additional bar is displayed for the Belgian population. The dotted line also depicts this total ratio.



■ G ■ R

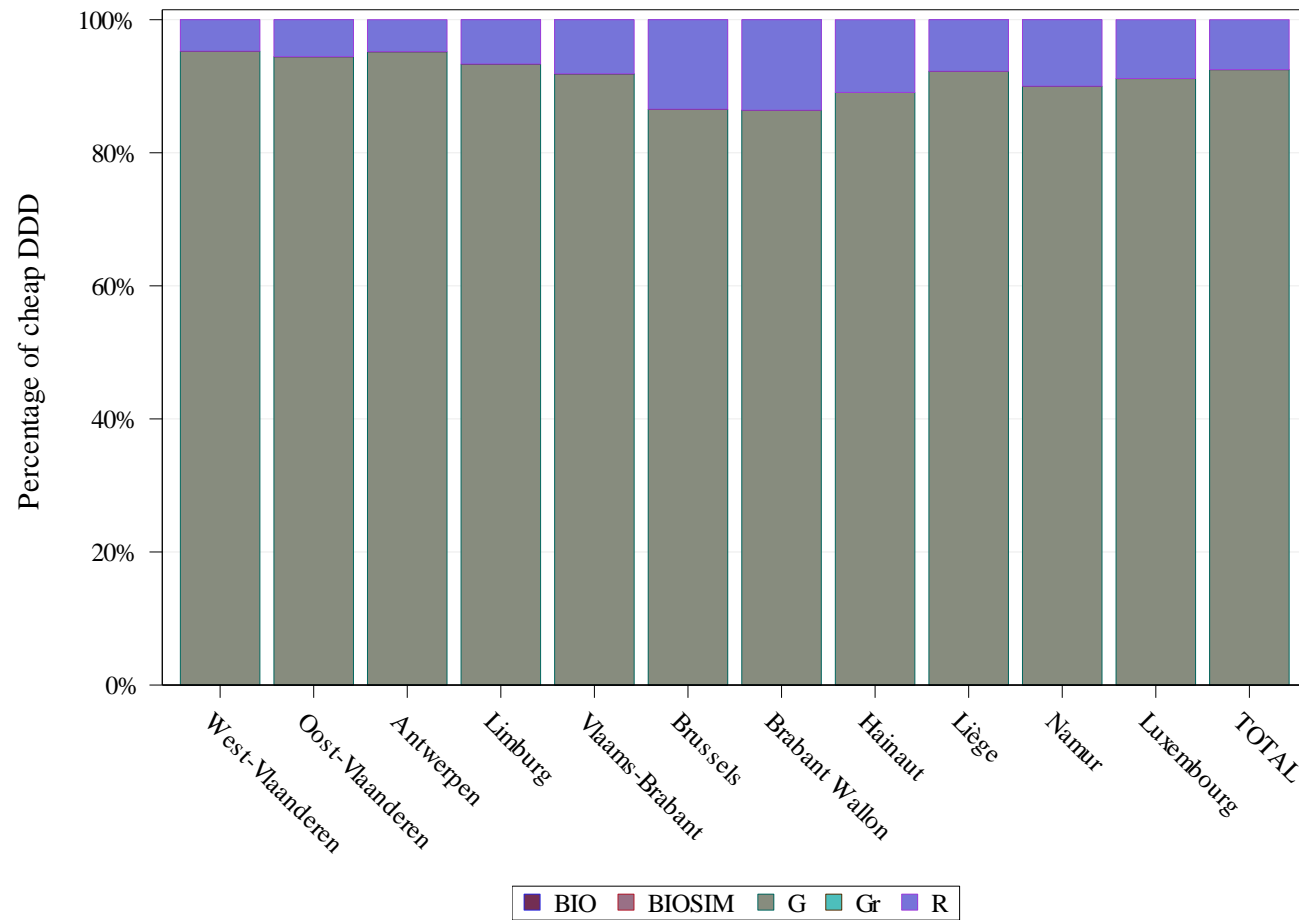
Distribution of DDD by "low-cost" drug class

% low-cost medication	
G	92,50%
R	7,50%
Gr	0,00%
BIOSIM	0,00%
BIO	0,00%

The percentage of low-cost medication is calculated per CNK code (The CNK code is a unique identification number per package, assigned to all drugs and parapharmaceuticals (medical devices, food supplements, cosmetics ...) delivered in pharmacies).

The "low-cost" status is given based on the situation in August of the year of this report.

The letter G refers to generic medicines, while Gr stands for reference generic medicines, R = branded reference drugs, BIOSIM stands for biosimilar medicines and BIO for biological medicines.

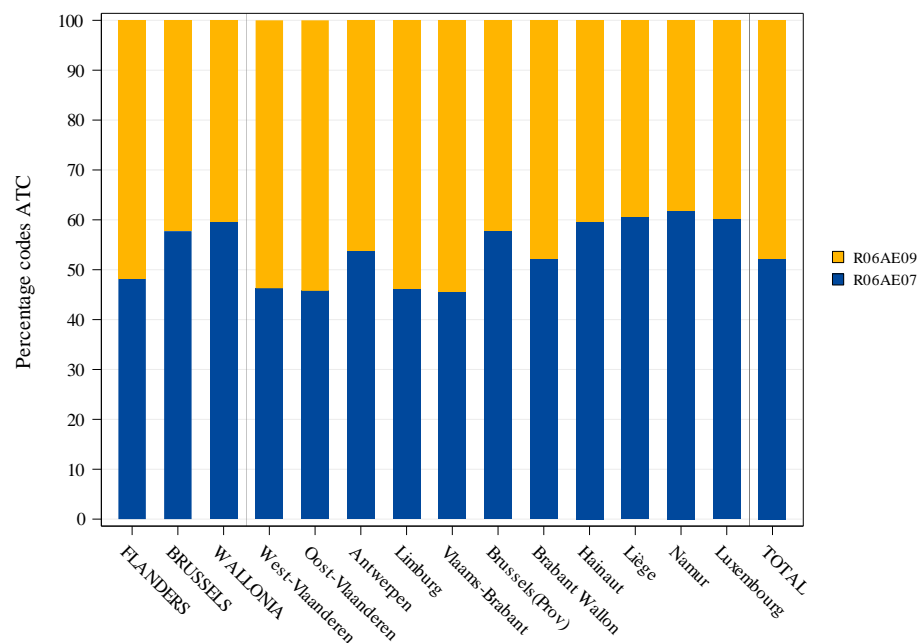


Type of low-cost drug (DDD) by province

G and Gr: low-cost generic (r= reference),
R: branded medicine,
BIO(SIM) stands for biological and biosimilar drugs.

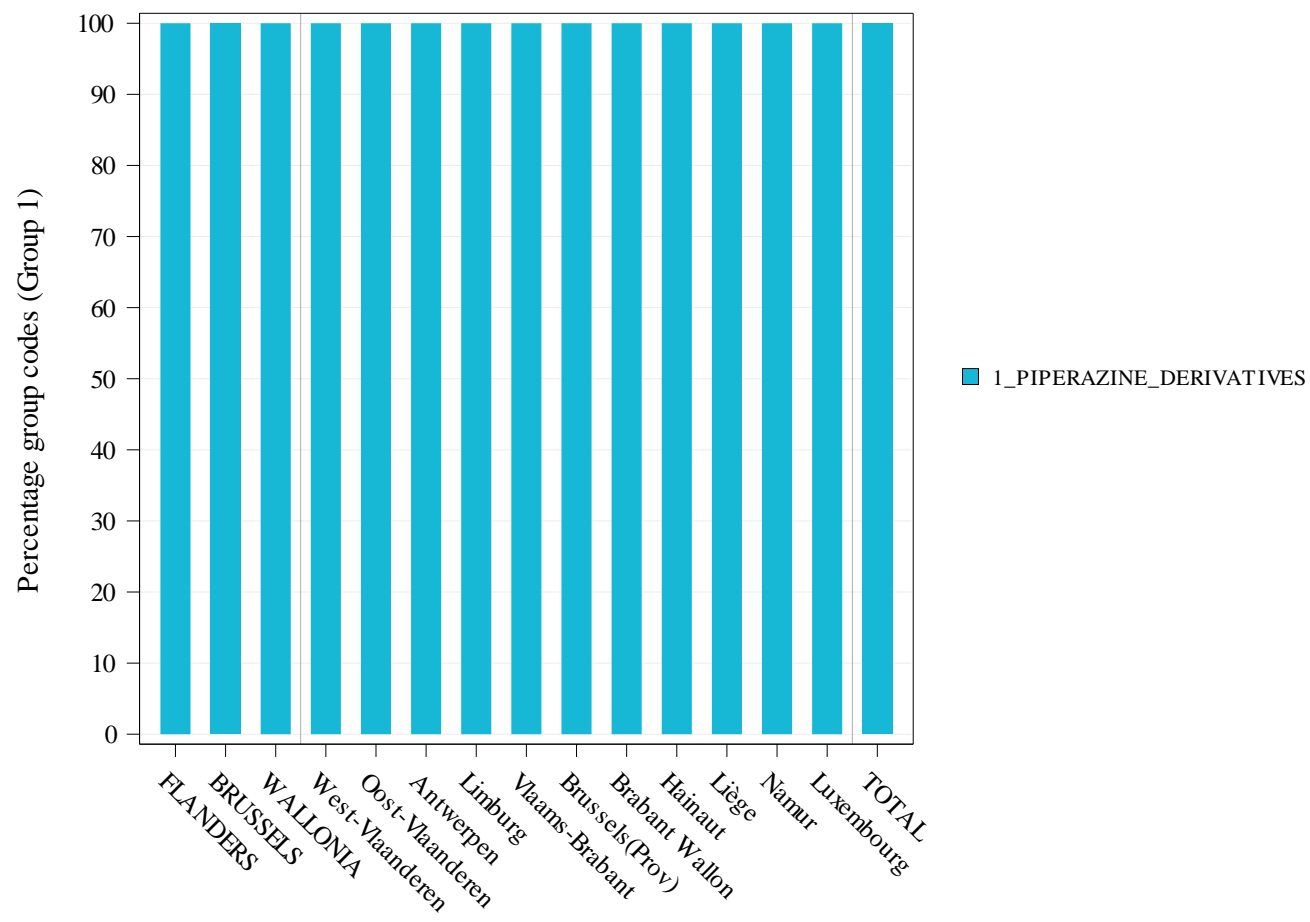
C. Variations in the type of medication delivered (based on DDD)

➔ Variations in prescription based on ATC codes:



ATC-Code	Description
R06AE09	LEVOCETIRIZINE
R06AE07	CETIRIZINE

➔ Variations in prescription by group of medication:



D. Sales volumes outside the health insurance

	2022
<i>Total sales volume (in DDD)¹</i>	85.821.638
<i>Sales volume in health insurance (in DDD)</i>	61.639.956
% of sales volume outside health insurance	28,2%

¹ The total sales volume converted into DDD is based on the database "LMPB" provided by IQVIA and is converted into DDD according to the WHO references. Volumes are summarised at ATC 5 level and do not take into account potential selection criteria (age, gender or other) applicable to the analysis

Medication - Antihistamines for systemic use

ATC5-Code	Description	Total volume	Volume reimbursed	% not reimbursed*
R06AE	PIPERAZINE DERIVATIVES	85.821.638,00	61.639.956,00	28,18%
TOTAL		85.821.638,00	61.639.956,00	28,18%

Share sold outside health insurance per ATC group (2022)

**% not reimbursed: estimate of the percentage of sales not covered by the health insurance (NIHDI)*

Volumes are summarised at ATC 5 level and do not take into account potential selection criteria (age, gender or other) applicable to the analysis