# **Medical practice variations**

# **Blepharochalasis (Adjusted)**

Analysis of the distribution and evolution of medical practice 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

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### **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 2016-2018<sup>1</sup>. 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 2016<sup>2</sup>. 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.

'Variations in medical practice' 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 analyses<sup>3</sup> of practice in the area of Blepharochalasis (Adjusted), 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.

<sup>&</sup>lt;sup>1</sup> (Institut national d'assurance maladie-invalidité, 2016)

<sup>&</sup>lt;sup>2</sup> (Institut national d'assurance maladie-invalidité, 2016)

<sup>&</sup>lt;sup>3</sup> Readers interested in the methodology used in these quantitative analyses should consult the document entitled 'Variations in practice – Methodology'.

### **2.** Specific method of analysis

#### A. NIHDI nomenclature codes selected for analysis

The NIHDI nomenclature codes selected for the analysis are listed below:

Outpatient	Inpatient	Rates	Expenses	Label	Creation	Deletion	Group N	Value
245733	245744	ye s	yes	Plastie pour dermatochalasis de la paupière supérieure, par paupière	01-04-1985		N18	N200
245755	245766	ye s	yes	Intervention chirurgicale pour blépharochalasis	01-04-1985	30-06-2016	N18	

This table shows the NIHDI nomenclature codes selected for this analysis, stating whether or not they were included in the analyses of services and expenditure, and giving, for each one, a description, dates of creation and deletion, where appropriate, their N group (in the NIHDI nomenclature) and their value.

#### **B.** Past history of nomenclature codes

Outpatient	Inpatient	Date	Label
245733	245744	01-04-1985	Plastique cutanée de la paupière
245733	245744	01-07-2016	Plastie pour dermatochalasis de la paupière supérieure, par paupière

This table displays the historic evolution of the definitions of the NIHDI-nomenclature codes taken into account for this analysis, if modifications were implemented during the period 2012-2022.

#### C. Source of data and analysis period

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

Document N	for the utilisation rate and amount of expenses of insured persons (who meet the selection criteria) whose age, sex, preferential regime and residence are known 2012-2022
Document P	for the utilisation rate and amount of expenses of insured persons (who meet the selection criteria) by type of medical specialities in 2022
Document P, SHA, ADH	for the practice occurrences and analysis of patient care settings in 2021
-	-

Analysis period

2012-2022

'N Documents' are monthly data sent by the sickness funds to NIHDI, within three months. These data show the number of services provided, dates and the fees involved. Every six months, these data are compiled by the insurers, which also add data on patients: age, gender, social category and district of residence. N Documents, however, cannot be used to analyse the combinations of services received by individual patients.

'P Documents' are six-monthly data sent by the sickness funds to NIHDI, within four months. These data show the services provided, the serviceprovider, the prescriber, the place of provision of service, and the hospital where patients were treated. P Documents can be used to monitor medical consumption and pricing, but not (yet) to analyse services per patient.

'Documents SHA, ADH' are sent annually and within six months by the insurer-organisations to the NIHDI. They include all the services provided respectively in day admission and standard hospitalisation, in general hospitals per hospital stay.

#### D. Specific selection criteria

Several filters may have been applied to the data, so that only one section of the population 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				
-	-				

#### E. Standardisation

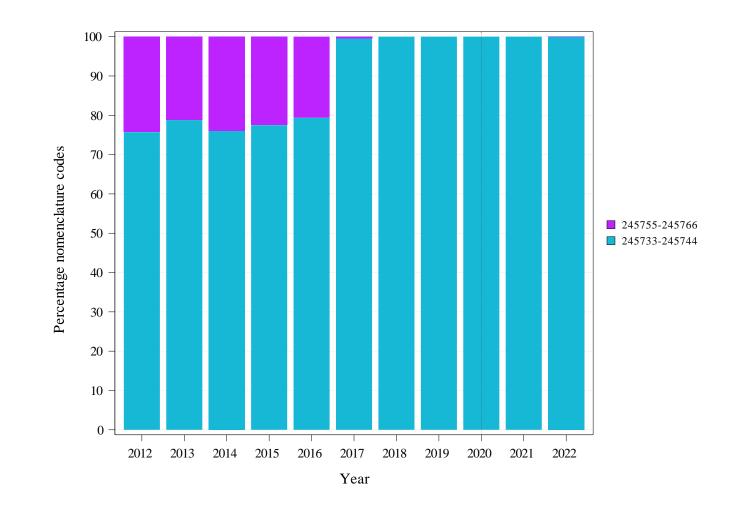
The data are standardised before analysis per year, based on age, sex and preferential regime per arrondissement, province and region (standardization based on population in 2022).

**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. R**ESULTS

#### A. National standardised rate of use

	TOTAL
Average number of interventions per year	4.534
Standardised rate of use	39
per 100 000 insured persons	39



#### B. Breakdown of nomenclature codes provided, by volume

See page 4 for details about the NIHDI nomenclature codes selected for analysis. Note : The year 2020 was highlighted by a vertical dashed line, in order to draw the attention on the impact of the COVID-19 crisis.

#### C. Specialisation of healthcare providers

Specialisation of the provider	<b>Total providers</b>	<b>Concerned providers</b>	% Providers	Median of H.C. services	Q3 of H.C. services	% Total H.C. services
Ophthalmological surgery	1152	199	17%	11	25	89,94%
Plastical surgery	269	98	36%	2	3	7,10%
Otorhinolaryngology	693	2	0%	56	107	2,49%
Other specialities	2373	13	1%	1	2	0,48%
Total	4487	312	7%	5	15	100,00%

•

This table shows the following non-standardised data, by medical specialities (figures for the year 2022):

- The number of service-providers per specialisation who have recorded at least one service (the figures are exceptionally extrapolated from a single semester if an \* is indicated in the header, otherwise the full year is taken into account);
- The number of service-providers recording services under the nomenclature codes selected for this analysis;
- The service-providers for these codes as a percentage of the total number of service-providers recording provision of at least one service;
- The median number and third quartile of services per service-provider (recording provision under these codes);
- The service percentage, i.e. the number of services recorded for this specialisation as a percentage of total services provided.

#### **D.** Specialisation of prescribers

Specialisation of the prescriber	<b>Total prescribers</b>	<b>Concerned prescribers</b>	% Prescribers	Median of prescriptions	Q3 of prescriptions	% Prescriptions
Not applicable	0	0	0%	0	0	100,00%

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

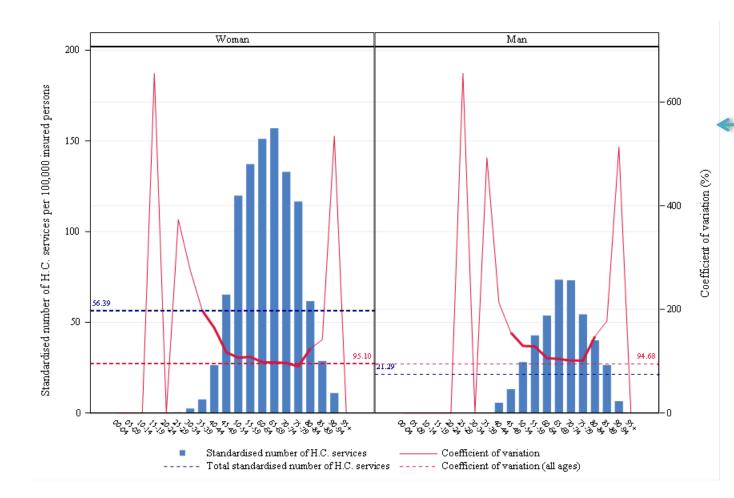
- The number of prescribers who have prescribed at least one service (the figures are exceptionally extrapolated from a single semester if an \* is indicated in the header, otherwise the full year is taken into account);
- The number of prescribers prescribing the nomenclature codes selected for this analysis;
- The prescribers prescribing these codes as a percentage of the number of prescribers prescribing at least one service;
- The median number and third quartile of services per prescriber (prescribing these codes);
- The percentage of services prescribed, i.e. the number of prescriptions issued for this specialisation as a percentage of total services prescribed.

#### E. Standardised rate of use by sex and age group

	TOTAL
Average number of interventions per year	4.534
Median age (years)	63
Mean age (years)	62,75
Max/Min Ratio of the median age (by district)	1,19
Percentage of women	73,52%

Max/Min Ratio:

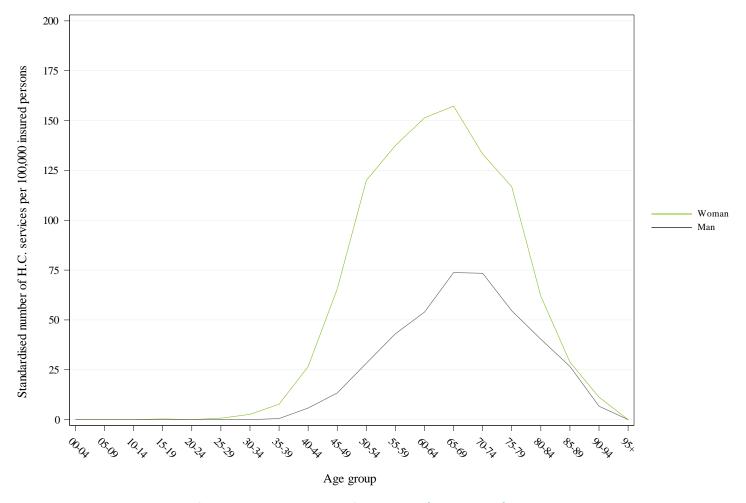
The max/min ratio measures the dispersion of values. It is calculated as the ratio of the maximum value found for the variable, in all districts, to the minimum value. If this minimum value is equal to zero, the max/min ratio cannot be calculated, and is reported as 'NA' ('not applicable').



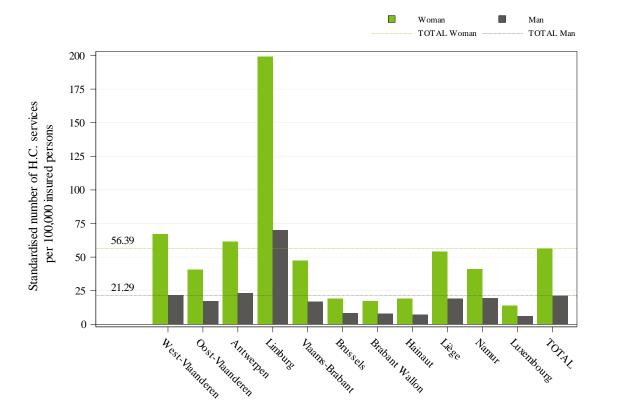
# Standardised rate of use per 100 000 insured persons, and coefficient of variation for the districts, by age group and sex, for the year 2022

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 standardised rates of use 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 standardised rate of use, and the righthand axis the coefficient of variation. The horizontal axis shows the age groups. The horizontal dotted lines show the total values of the standardised rates of use (in blue) and of the coefficient of variation (in red).



Comparison of the standardised rates of use by sex (per 100 000) in 2022

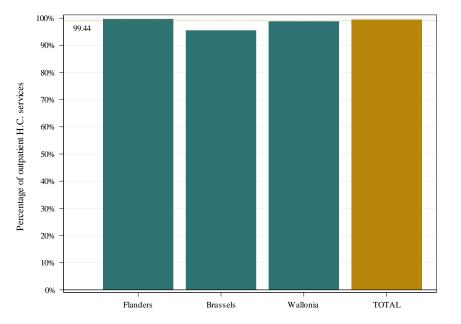


This histogram shows standardised rates of use by province and by sex. The grey bars show the rates for men, while the green bars show the rates for women, for each province. The grey and green broken lines show the total standardised rates of use, again grey for men, green for women.

Standardised rate of use per 100 000 insured persons, by sex and by province for the year 2022

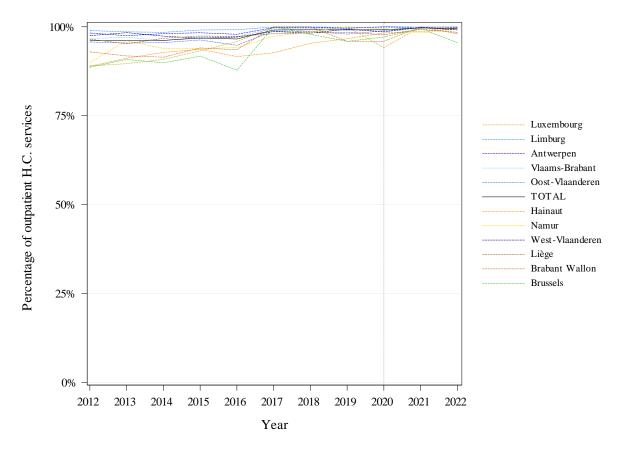
F. Standardised rate of use: hospital and outpatient care

	TOTAL
Average number of interventions per year	4.534
Percentage of out-patient care	99,44%
Max/min ratio of out-patient care percentage (by district)	1.05



This graph shows the percentage of outpatient services (including hospital day admissions), i.e. the number of outpatient services provided as a percentage of total services (outpatient and hospital stays). Besides the bar per region, there is a bar for the entire Belgian population. A dotted line also shows this overall ratio.

Percentage of outpatient care, total and by region



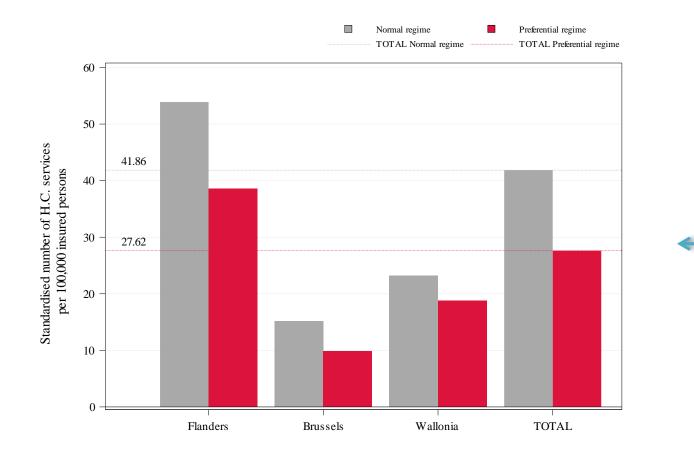
Change over time in the percentage of outpatient care, by province

#### N.B.:

- The year 2020 was highlighted by a vertical dashed line, in order to draw the attention on the impact of the COVID-19 crisis
- A complementary document to this chapter, about the handling of patients per health care sector, is enclosed in this report (cf. p.36)

### G. Standardised rate of use by reimbursement scheme

	TOTAL
Average number of interventions per year	4.534
Percentage provided under the preferential reimbursement scheme	14,89%
Standardised rate of use with preferential reimbursement scheme	28
(per 100 000)	20
Standardised rate of use without preferential reimbursement scheme	42
(per 100 000)	76
Ratio Preferential scheme /General scheme	0,66



This graph shows the standardised rates of use with (in red) and without (in grey) the preferential reimbursement scheme, by region and in total. The red and grey dotted lines show the overall standardised rates of use, with and without the preferential reimbursement scheme, respectively.

Standardised rate of use by reimbursement scheme and by region

#### H. Trends in standardised rates of use

Average number of interventions per year	TOTAL 4.534	Statistical significance
Trend (2012-2022)	-4,09%	*** (-8,73%)
Trend (2012-2019)	-8,54%	***
Trend (2019-2022)	7,17%	ጥ ጥ ጥ

70 60 Standardised number of H.C. services per 100,000 insured persons 50 40 Flanders TOTAL Wallonia Brussels 30 20 10 0 . 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 Year

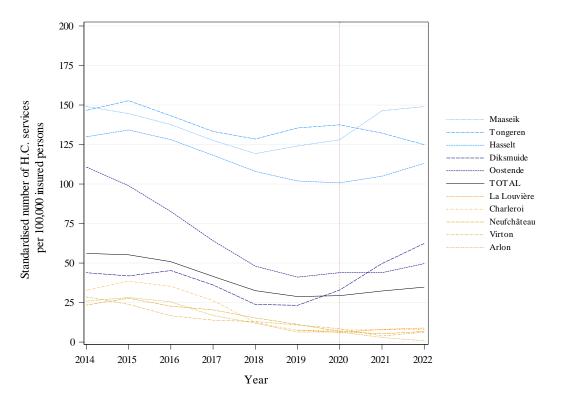
These trends correspond to the average annual growth rate.

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 rate of use per 100 000 insured persons.

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

Trends in the standardised rate of use per 100 000 insured persons, by region



Trends in the standardised rate of use per 100 000 insured persons, by district

This graph shows a colored line for each district and a black line for the entire Belgian population. The x-axis shows the years, and the y-axis shows the standardised rate of use per 100 000 insured persons.

To better highlight changes over time, the rates shown are **rolling averages** of the rates for the three years preceding the year in question (including the year itself).

The graph only shows the five districts with the highest average rates and the five districts with the lowest average rates over the last 3 years studied.

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

		Rate of use		Annual increase		
		<b>2022</b> (per 10 <sup>5</sup> insured)	2012- 2022	2012- 2019	2019- 2022	Structural break
	West Flanders	45,16	-2,99%	-9,39%	13,74%	NA
	East Flanders	<i>29,33</i>	-4,64%	-12,45%	16,40%	NA
	Antwerp	42,79	-4,07%	-9,01%	8,53%	NA
	Limburg	135,38	-0,52%	-1,73%	2,35%	NA
ces	Flemish Brabant	32,72	-1,01%	-5,22%	9,58%	NA
Provinces	Brussels	14,07	-7,58%	-11,59%	2,53%	NA
Pro	Walloon Brabant	13	-12,70%	-20,85%	9,75%	NA
	Hainaut	13,17	-8,80%	-15,92%	10,26%	NA
	Liège	36,78	-8,71%	-12,91%	1,89%	NA
	Namur	30,57	-5,30%	-11,42%	10,68%	NA
	Luxembourg	9,72	-9,35%	-9,50%	-9,00%	NA
ns	Flanders	51	-2,53%	-6,67%	7,88%	NA
Regions	Brussels	14,07	-7,58%	-11,59%	2,53%	NA
Re	Wallonia	22,44	-8,59%	-13,90%	5,10%	NA
	TOTAL	39,15	-4,09%	-8,54%	7,17%	***

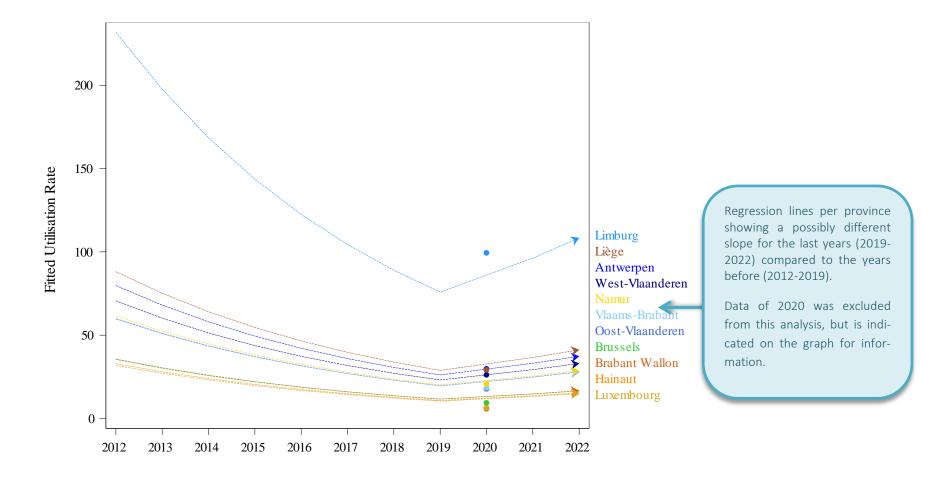
Trends in the rates of use, by province and region

This table reports the standardised **rates of use** 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 (2012-2022), for the last years (2019-2022) and for the period preceding the last years (2012-2019)

In order to find out whether the trend in the last years differs from that in the years before, a linear mixed model was fitted in two steps. In the first step a change in trend on the national level is tested. If this test is significant, in a second step, the model tests whether the difference in trend is significant for each province, region and at the national level. The data of 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  $\leq 0.05 / **$  P-value  $\leq 0.01 / ***$  P-value  $\leq 0.001$  and NS for a non-significant result.

'NA' is shown where the nomenclature codes selected for the analysis have not been used for the entire last period or when the statistical tests cannot be evaluated.



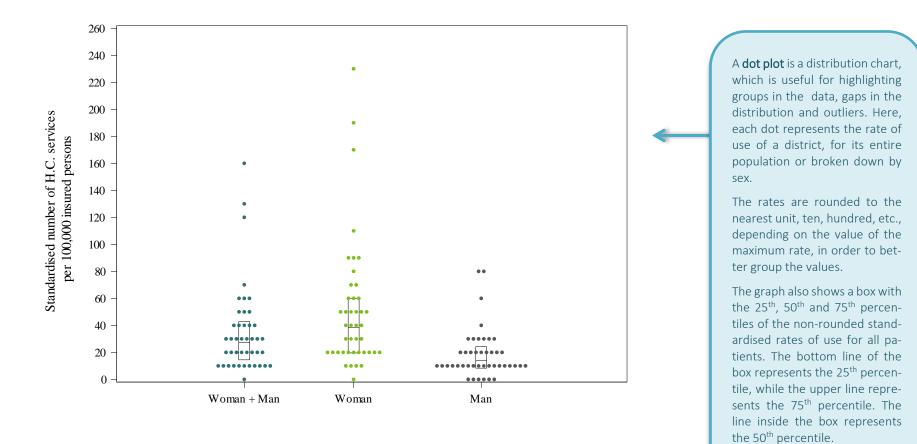
Trend break assessment model by province – Regression lines

I. Geographical variations in standardised rates of use

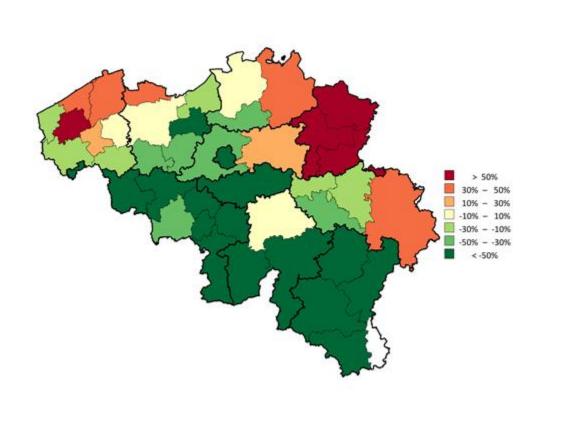
	TOTAL
Average number of interventions per year	4.534
Coefficient of Variation (2022)	93,84
Max/Min Ratio* of the standardised rates of use (by region)	3,62
Max/Min Ratio* of the standardised rates of use (by district)	NA

Coefficient of Variation (2020-2022)	99,84
Coefficient of Variation (2012-2014)	60,57
Statistically significant difference? ( $p \le 0.05$ )	No

\* An 'NA' result indicates a ratio which cannot be calculated, i.e. the minimum value = zero (cf. E. Standardised rate of use by sex and age group)



'Dot plot' showing standardised rates of use by district, by sex

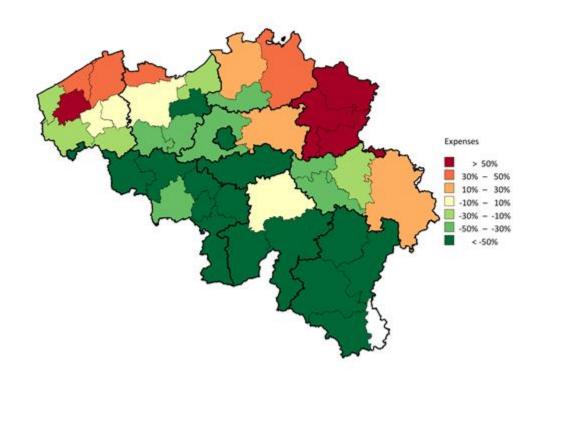


#### Map showing distribution of standardised rates of use, by district

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 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 overall rate, 20% if the rate is 20% above the overall rate, and -20% if the rate is 20% below the overall rate. The percentages are calculated using the standardised rates of the last year analysed, and are displayed in bands of 20%. The following colour coding applies:

Colour	Category		
	More than 50%		
	Between 30% and 50%		
	Between 10% and 30%		
	Between - 10% and 10%		
	Between -30% and -10%		
	Between -50% and - 30%		
	Less than -50%		
	Not used		

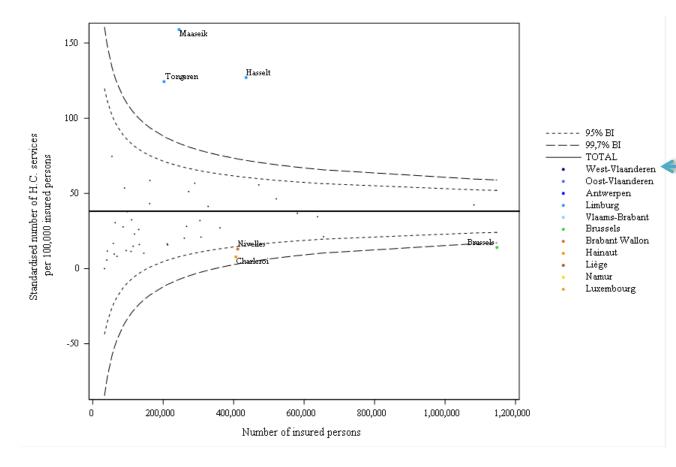
N.B.: The interpretation of this map is to be done in parallel with the graph in funnel plot (p.28)



#### Map showing distribution of standardised 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	
	More than 50%	
	Between 30% and 50%	
	Between 10% and 30%	
	Between - 10% and 10%	
	Between -30% and -10%	
	Between -50% and - 30%	
	Less than -50%	
	No expenditure	



In this graph, the standardised rate of use 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 standardised rate of use. 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, 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 <u>map of</u> <u>the distribution of rates of use</u> (p.26)

'Funnel plot' showing the standardised rates of use by district, by the number of insured persons

J. Standardised healthcare expenditure borne by the insurance

	TOTAL
Average number of interventions per year	4.534
Average annual expenditure (€)	1.381.342
Average cost per intervention (€)	304,66
Average annual expenditure per insured (€)	0,12
Max/Min Ratio* of expenditure per insured	4,06
(by region)	,
Max/Min Ratio* of expenditure per insured	NA
(by district)	

\* An 'NA' result indicates a ratio which cannot be calculated, i.e. the minimum value = zero (cf. E. Standardised rate of use by sex and age group)

_		Standardised expenditure (per insured)
	West Flanders	0,13€
	East Flanders	0,09€
	Antwerp	0,13€
10	Limburg	0,43 €
Provinces	Flemish Brabant	0,1€
vin	Brussels	0,04 €
Pro	Walloon Brabant	0,04 €
	Hainaut	0,04 €
	Liège	0,11€
	Namur	0,09€
	Luxembourg	0,03 €
ns	Flanders	0,16€
Regions	Brussels	0,04 €
8	Wallonia	0,07€
	TOTAL	***€

Regional and provincial distribution of standardised expenditure (2022)

Nomenclature	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Average annual growth rate
245733-245744	285,75	292,22	293,15	286,15	291,37	269,91	292,29	294,56	297,73	300,79	304,66	0,64%
245755-245766	114,53	115,96	117,80	117,86	118,35	112,92	0,00	0,00	0,00	0,00	0,00	NA

Change over time in expenditure, by service and by nomenclature code

## 4. Key Data Summary

	ΤΟΤΑ	L
PROVIDERS & PRESCRIBERS		
Main healthcare providers:Ophthalmological surgery	89,94%	
Main prescribers: Not applicable	-	
RATE OF USE	-	-
Number of interventions (per year)	4.534	-
Standardised rate of use (per 100 000 insured persons)	39,15	
≥ 2 occurrences per patient (2021) <sup>4</sup>	89,2%	
Percentage of outpatient care	99,44%	-
POPULATION	-	
Median age	63 years	-
Max/min ratio <sup>5</sup> of the median age (by district)	1,19	
Percentage of women	73,52%	
Ratio Preferential rate/General rate	0,66	
TRENDS	-	-
<b>Trend</b> <sup>6</sup> (2012-2022)	-4,09%	***
<b>Trend</b> <sup>6</sup> (2012-2019)	-8,54%	***
<b>Trend</b> <sup>6</sup> (2019-2022)	7,17%	***
GEOGRAPHICAL VARIATIONS		-
<b>Coefficient of variation</b> <sup>6</sup> (2012-2014)	60,57	
<b>Coefficient of variation</b> <sup>6</sup> (2020-2022)	99,84	NS
Max/min <sup>5</sup> Ratio of number of interventions <sup>6</sup> (per 100 000 insured persons, by region)	3,62	
Max/min Ratio <sup>5</sup> of number of interventions (per 100 000 insured persons, by district)	NA	
DIRECT EXPENDITURE	-	-
Average annual expenditure	1.381.342 €	
Average annual expenditure per insured	<b>0,12</b> €	
Max/Min Ratio <sup>5</sup> of expenditure per insured (by region)	4,06	
Max/Min Ratio <sup>5</sup> of expenditure per insured (by district)	NA	
Average cost of interventions	304,66 €	
CODING VARIATIONS & PRACTICE ALTERNATIVES <sup>4</sup>	1	
Variations in practice coding <sup>6</sup> (by province)	NA	NA
Variations in the choice of practice alternatives <sup>6</sup> (by province)	NA	NA

<sup>&</sup>lt;sup>4</sup> More detailed results are shown in a document enclosed to this report.

<sup>&</sup>lt;sup>5</sup> An 'NA' result indicates a ratio, which cannot be calculated, i.e. the minimum value equals zero.

<sup>&</sup>lt;sup>6</sup> If the result(s) show(s) a significant difference, the level of statistical significance is symbolized by one to three asterisks (increasingly significant). Otherwise, NS is displayed (not significant). 'NA' indicates the test is not applicable.

### **5.** APPENDICES

#### A. Analysis of variance (ANOVA), except Brussels

Statistical significance of the differences observed in 2022		
By region?	Yes	***
By sex?	Yes	***
By reimbursement scheme?	Yes	**
By sex and per region?	Yes	***
By reimbursement scheme and per region?	Yes	*
By sex and per reimbursement scheme?	No	NS
By sex and reimbursement scheme and per region?	No	NS

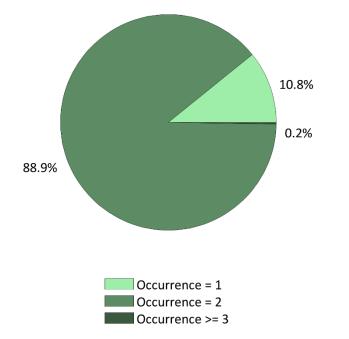
In order to be able to assess the significance of the observed differences, a linear mixed **ANOVA** model was fitted to the data of all districts of the Walloon and Flemish regions, after standardising for age. The model has region, sex and reimbursement scheme as fixed effects and also contains all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

In order to interpret the model correctly, first the three-way interaction 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 main effects that appears in a significant interaction should be interpreted at the level of the interaction and not at the level of that main effect. Main effects can only be interpreted directly if they don't appear in a significant interaction.

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.** Frequency of practice occurrences

Frequency	Per year	Per day
2 occurrences	88,9%	88,6%
≥ 3 occurrences	0,2%	0,2%
≥ 2 occurrences	89,2%	88,8%



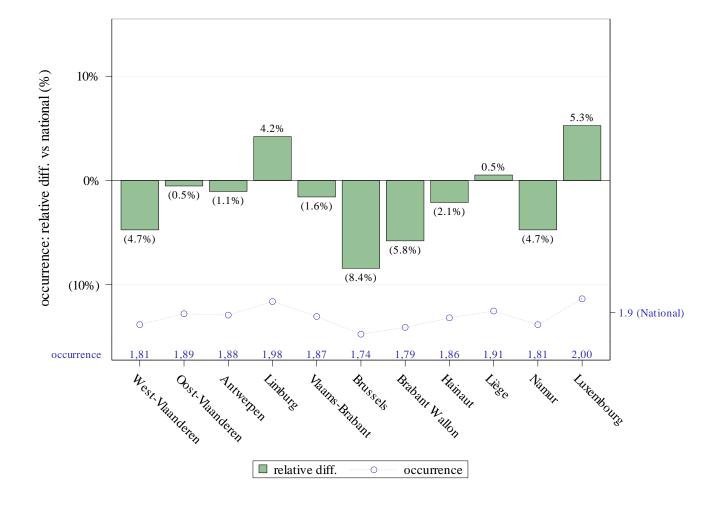
Distribution of practice recurrences per year (2021)

Some practices may be billed several times for the same patient in the same year or even on the same day. This may be due to a **repetition of the practice**, but also to an anatomical effect, which may lead, depending on the organ concerned, to performing the same practice **bilaterally**, which may therefore cause a double occurrence on the same day.

In order to interpret the results per day validly, it is useful to note that the same patient may be counted several times if, for example, he or she has received two identical services simultaneously, twice a year.

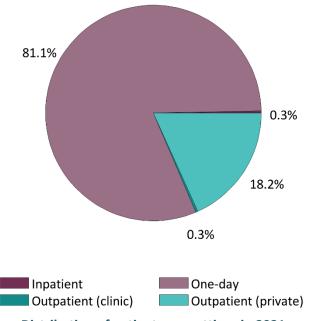
These frequency analyses of occurrences are carried out over the year **2021** using the following databases: Documents P, ADH and SHA.

Values « **n.a.** » are indicated if the data were not available at the time of this report.



Frequency of practice occurrences by province and variation vs national value (2021)

#### C. Patient care settings



Distribution of patient care settings in 2021

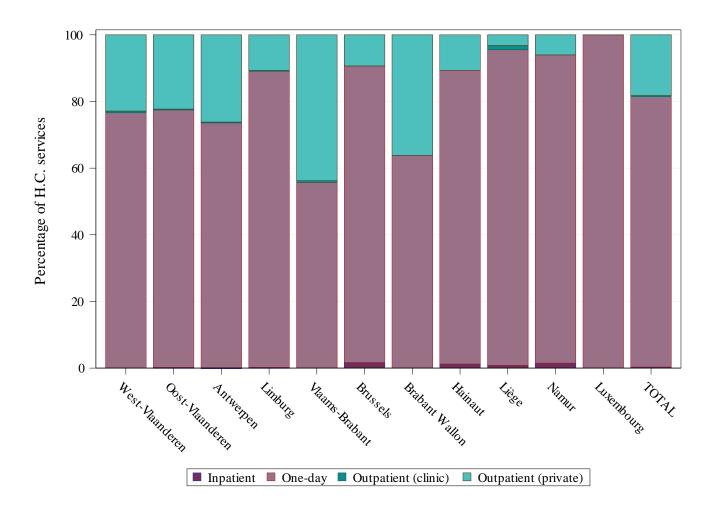
Outpatient (private)	18,2%
Outpatient (polyclinic)	0,3%
(Day) Hospital	81,1%
Hospital (stay)	0,3%

**Care Settings** 

In addition to the chapter on <u>standardised inpatient and outpatient use rates</u> (see p.16), the analysis of patient care settings can be refined by identifying the outpatient (private and polyclinic) and inpatient (day or standard hospitalisation) sub-sectors.

These analyses are carried out over the year **2021** using the following databases: Documents P, ADH and SHA.

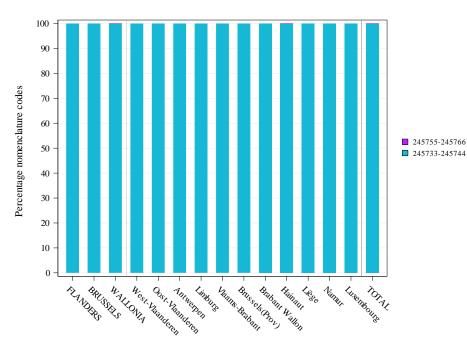
Values « n.a. » are indicated if the data were not available at the time of this report.



Distribution of patient care settings by province (2021)

#### D. Coding variations and practice alternatives

#### → Variations in coding:



Volume b	reakdown	of	nomenclature	codes

Significance	By region	By province
Use of Nomenclature codes <sup>7</sup>	NA	NA

Outpatient	Inpatient	Label
245733	245744	Plastie pour dermatochalasis de la paupière supérieure, par paupière
245755	245766	Intervention chirurgicale pour blépharochalasis

<sup>7</sup>The calculation of significance is carried out here by comparing the geographical differences in the use of the different nomenclature codes to code the practice.

The **asterisks** represent the level of statistical significance of Chi-square test: \* P-value  $\leq 0,05 / **$  P-value  $\leq 0,01 / ***$  P-value  $\leq 0,001$ . **NS** and **NA** respectively indicate that the variations are not significant or not applicable.