2020

ECFS Patient Registry

Annual Data Report

European Cystic Fibrosis Society
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Annual Data Report

2020 data

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Preface

After two years of unforeseen challenges and uncertainties due to the outbreak of the SARS-CoV-2 pandemic in early spring 2020 we are pleased to share with you the 2020 Annual Report from the European Cystic Fibrosis Society Patient Registry (ECFSPR). The ECFSPR is still growing in coverage around Europe, and this 16th report now contains demographic and clinical data of 52,246 consenting CF patients from 39 countries. The epidemiological data is provided by national cystic fibrosis (CF) registries and individual CF centres throughout Europe and neighbouring countries.

As a result of the pandemic, many CF centres all around Europe have been struggling with enormous clinical workload in 2020, with often limited resources to continue with the regular registry activities. In several regions, on-site patient care had to be reduced to the required minimum, to shield patients and hospital staff. Still, we are proud and thankful to our contributors that the ECFSPR has been able to continue collecting, analysing and publishing data during these difficult times. This achievement has been made possible only due to huge efforts of the contributing CF centres and national CF registries and we would like to thank all our stakeholders for their extraordinary engagement. This engagement enables the ECFSPR to fulfil its mission to continue to provide a reliable and comprehensive picture of clinical outcomes in CF across Europe.

Following a data quality project that started in 2018, with a temporary interruption during the pandemic, and included on-site visits in selected CF centres and at national CF registries, we are now presenting results of data quality in the ECFSPR for the first time in the current report. High data quality and completeness are mandatory to ensure robust and reliable data especially in the frame of the ongoing pharmacovigilance studies that are conducted in the ECFSPR since 2020. As a result of these studies, the ECFSPR is able to reimburse the efforts in time and human resources of its contributors for 2020 and the following years, ensuring sustainability of the data collection Europe-wide.

In this report, we introduce some changes in the content. The former chapter on complications and therapy has been broken down into two separate chapters. Furthermore, a separate chapter is now dedicated on CFTR modulator therapy. Over the next few years, we aim to further improve the content and the design of the report.

For more than 10 years the ECFSPR collaborates closely with CF centres and national CF registries to ensure that their data is as complete and high quality as possible. Our continuous collaboration with CF Europe and the national patient organisations guarantees that the registry data is used to benefit the community and we are grateful to all people with CF, and their families, throughout Europe, for their willingness to participate in the European CF Patient Registry.

Finally, I would like to thank the ECFSPR staff, the Executive and Scientific Committees, and all people who voluntarily contribute to our working groups and the numerous projects undertaken by the Registry, as well as our sponsors and supporters who provide the financial background to make the ECFSPR possible and sustainable.

Sincerely,

Andreas Jung, ECFSPR Director

To the people with cystic fibrosis

This report is about you and how cystic fibrosis (CF) affects you and other people all over Europe. The report is based on information collected by individual CF centres and the national CF registries that participate in the European Cystic Fibrosis Society Patient Registry (ECFSPR). We have tried to make the presentation of this data as clear as possible and hope that you will find the report interesting and easy to understand.

With each ECFSPR Annual Report we publish a separate At-a-Glance report containing key information from the report, specifically for the people with CF and their families, and anyone wishing to know a little more about the disease: www.ecfs.eu/projects/ecfs-patient-registry/annual-reports. Interactive maps with country-specific information are available on the homepage of our website: www.ecfs.eu/ecfspr.

We continue to develop country posters with information and basic statistics from the Registry for display in CF centres. The posters are published online at www.ecfs.eu/ecfspr/posters. The data in the posters will be regularly updated.

News, updates and other interesting information are regularly posted on social media. Find us on Facebook www.facebook.com/EuropeanCysticFibrosisPatientRegistry/, Twitter @ECFSRegistry, and now also on Instagram www.instagram.com/ecfspr/ and LinkedIn www.linkedin.com/company/84849296/admin/.

We will continue to work with patient organisations on increasing awareness of the Registry among people with CF and their families. If you have suggestions on how we can improve or if anything is unclear, you are welcome to contact us by email at ecfs-pr@uzleuven.be.

To discuss the results from your country presented in this report we encourage you to contact your CF centre.

For more detailed information about the Registry please visit the patient-dedicated page on our website www.ecfs.eu/projects/ecfs-patient-registry/information-about-ecfspr-cf-patients.

More information on how we handle your data and how you can exercise your rights is available in the Privacy Notice www.ecfs.eu/sites/default/files/general-content-files/working-groups/ecfs-patient-registry/Privacy%20notice_Update_ECFSPR_vs%205_0.pdf.

Introduction

The European Cystic Fibrosis Society Patient Registry (ECFSPR)

The ECFSPR collects demographic and clinical data of consenting people with cystic fibrosis from Europe and neighbouring countries. Data is collected using a common set of variables and definitions, and is sent to the ECFSPR in one of the following ways:

- National CF registries (or individual centres with local databases) extract data from their own database and import the data into the ECFSPR software;
- Individual centres enter data directly into the ECFSPR software.

Collection of data at a local level must be approved by local data protection authorities in accordance with European data protection legislation. Data stored in the central database is pseudonymised, and only year/ month of birth and randomised centre and patient codes are used as identifiers.

Data is available for scientific purposes on application. All requests are reviewed by the ECFSPR Scientific Committee, and, based on their recommendation, the country coordinators in the Steering Group (composed of national representatives of the countries that contribute data to the ECFSPR) decide if the data from their country can be used for a request; this decision is final. Requests originating from Industry are also reviewed by the ECFS Clinical Trials Network. All applications must meet the European and individual country data protection legislation regarding patient anonymity.

For more information, please visit our website www.ecfs.eu/ecfspr.

General Considerations

It is possible that some national registries use data definitions and parameters that do not fully correspond to those employed by the ECFSPR, either because some types of information are not collected, or they are collected by the national registry using a different method. When the national registries upload their data they are asked to state whether their variable definitions meet those of the ECFSPR or not. Where major discrepancies between the definitions occur, those variables have been omitted from the annual report for that country; in the case of minor discrepancies an explanatory footnote has been added to the graphs and tables. For example, the ECFSPR collects information on the presence of chronic *Pseudomonas aeruginosa* infection according to the modified Leeds criteria, and/or the presence of elevated *Pseudomonas* antibodies (see Appendix 3, page 152). If a national registry collects such information as “at least one positive *Pseudomonas aeruginosa* culture this year”, this information would be too different from the ECFSPR definition of chronic *Pseudomonas aeruginosa*, and we would set this variable to “missing” for that particular country. If, instead, a country defines chronic *Pseudomonas aeruginosa* as “the presence of more than four positive cultures in 6 months”, the data of this variable would be included in the annual report since the definition is much closer to the ECFSPR definition and a footnote would be added to the relevant tables and graphs.

If a country does not collect a certain variable, we have omitted that country from the relevant graphs in the report; all of the data, however, is presented in the tables. The same applies for countries where the information for a variable is missing for more than 10% of the patients. The countries with less than 5 patients in an age group (e.g. less than 5 adults) are excluded from both the graphs and the tables. The number of missing values is important when interpreting the results, since it is impossible to know if a

person with CF with a missing value for a given complication has this complication or not, meaning given frequencies are less accurate. For example, in a country where 7% of the people with CF have liver disease but 20% have unknown/missing information on liver disease, the true frequency of liver disease will be anything between 7 and 27%.

You will find some differences between the findings of the national registries' own reports and the ECFSPR report. This is because some variable values are recoded or computed in different ways. For example, some national registries compute the age of the patient at the date of the annual visit and consider 16 years as the cut-off for adult age. The ECFSPR computes the age at FEV1/height/weight measurement and the age at follow-up (the end of the year) and considers 18 years as the cut-off for adult age. Since clinical outcomes do not change very much over a 12-month period, we do not consider this to be a serious obstacle to interpretation. Another example: for lung function values such as FEV1 the raw data values, reported in litres, are not informative unless they are expressed in relation to the age, sex and height of the patient. We therefore needed to transform the raw values into new variables in order to compare lung function between people with CF and countries. We used common reference populations for all data when calculating the values as a percentage of predicted from the raw data. Slightly different values can be obtained when using another reference population on the same raw data. It is important to use a common method of calculation when comparing different countries, just as the national registries choose a common method of calculation when they compare the individual centres in that country.

The estimated coverage, i.e. the percentage of people with CF included in the national registry or national data presented by the country, varies; see table 1.1, page 9. These differences can influence how the data is interpreted, and we therefore advise comparisons to be made only between countries with similar coverage.

Date of the database that is used to create the tables and graphs in this report is 19 January 2022.

Glossary and Abbreviations[1]

AL:	Albania
AM:	Armenia
AT:	Austria
BE:	Belgium
BG:	Bulgaria
BY:	Belarus
CH:	Switzerland
CY:	Cyprus
CZ:	Czech Republic
DE:	Germany
DK:	Denmark
ES:	Spain
FR:	France
GB:	United Kingdom of Great Britain and Northern Ireland
GE:	Georgia
GR:	Greece
HR:	Croatia
HU:	Hungary
IE:	Ireland
IL:	Israel
IS:	Iceland
IT:	Italy
LT:	Lithuania
LU:	Luxembourg
LV:	Latvia
MD:	Republic of Moldova
MK:	North Macedonia
NL:	The Netherlands
NO:	Norway
PL:	Poland
PT:	Portugal
RO:	Romania
RS:	Serbia
RU:	Russian Federation
SE:	Sweden
SI:	Slovenia
SK:	Slovak Republic
TR:	Turkey
UA:	Ukraine

[1] Reference: www.iban.com/country-codes

Summary of data report

Outcome		Females	Males	Total
Patients registered in the ECFSPR	n	24799	27447	52246
	(%)	(47.5%)	(52.5%)	
Age at follow-up (in years; patients alive on 31/12/2020)	mean	21.5	22.1	21.8
	median	18.8	19.8	19.4
Patients ≥ 18 years (patients alive on 31/12/2020)	n	12788	14780	27568
	(%)	(51.9%)	(54.2%)	(53.1%)
Age at diagnosis*	mean (years)	4.2	4.0	4.1
	median (months)	3.6	3.6	3.6
Patients with at least one F508del allele recorded*	n	18776	20629	39405
	(%)	(80.7%)	(80.7%)	(80.7%)
Patients living with lung transplant**	n	1426	1373	2799
	(%)	(6.1%)	(5.4%)	(5.7%)
Patients living with liver transplant**	n	102	209	311
	(%)	(0.4%)	(0.8%)	(0.6%)
Patients deceased in 2020***	n	165	194	359
	(%)	(0.7%)	(0.7%)	(0.7%)
Age at death (years)***	mean	32.4	34.9	33.7
	median	30.0	32.5	32.0

* Only patients seen during the year are presented. The total number of patients presented is 49,111.

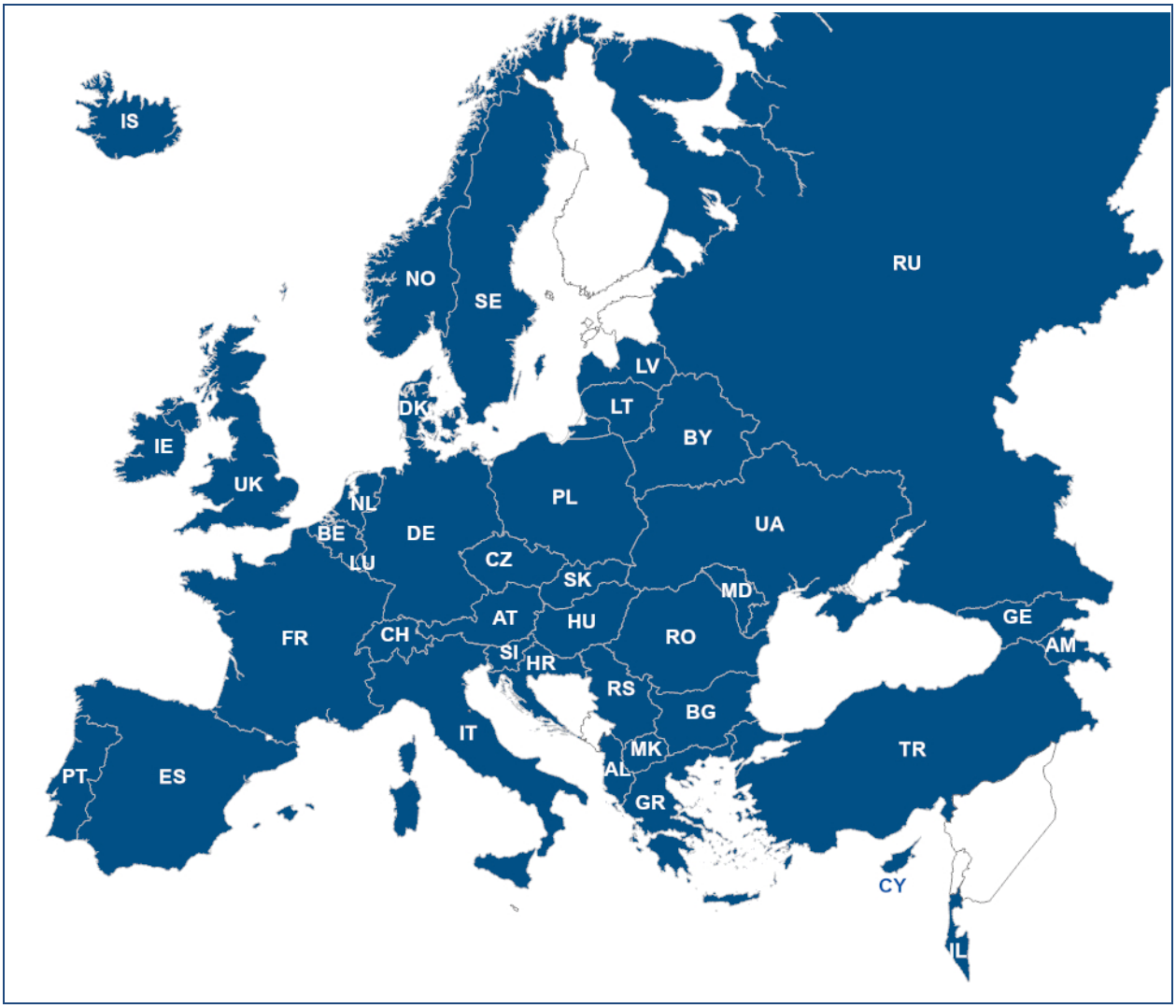
** Only patients alive at 31/12/2020 are presented. The total number of patients presented is 48,795.

*** Only patients seen during the year are presented. For the United Kingdom, all patients with a confirmed diagnosis of CF were included (N=10,837). The total number of patients presented is 50,026.

Data report

1. Demographics

Figure 1.1 Map of countries that contributed to the ECFSPR in year 2020.



Marked in blue are the countries that contributed 2020 data.

Table 1.1 Number of patients in year 2020, by country.

Country	Patients registered, not lost to follow-up	Patients seen	Estimated coverage
Albania	135	81	80%
Armenia	30	25	>70%
Austria	853	833	>90%
Belarus[1]*	151	151	90%
Belgium*	1352	1334	>90%
Bulgaria	202	194	>70%
Croatia**	147	132	>95%
Cyprus	30	23	>80%
Czech Republic*	666	631	99%
Denmark*	541	497	99%
France*	6954	6954	>90%
Georgia[1]	84	73	>80%
Germany*	6669	6667	80%
Greece[2]*	431	387	60%
Hungary*	499	496	98%
Iceland	14	14	
Ireland*	1289	1234	89%
Israel**	585	518	>95%
Italy*	5841	5801	98%
Latvia	48	46	>90%
Lithuania	37	34	52%
Luxembourg[3]	27	23	>60%
Rep of Moldova	55	49	>90%
The Netherlands*	1560	1545	95%
North Macedonia	144	122	>90%
Norway*	330	325	85%
Poland	1341	1180	>60%
Portugal**	367	357	>95%
Romania	254	228	50%
Russian Federation*	3611	2393	88%
Serbia	210	158	>90%
Slovak Republic**	299	269	>90%
Slovenia	114	111	>95%
Spain	2505	2351	85%
Sweden*	702	702	>95%
Switzerland**	1013	1000	>99%
Turkey	2101	2082	>60%
Ukraine	218	169	24%
United Kingdom[4]*	10837	9922	99%
Total	52246	49111	

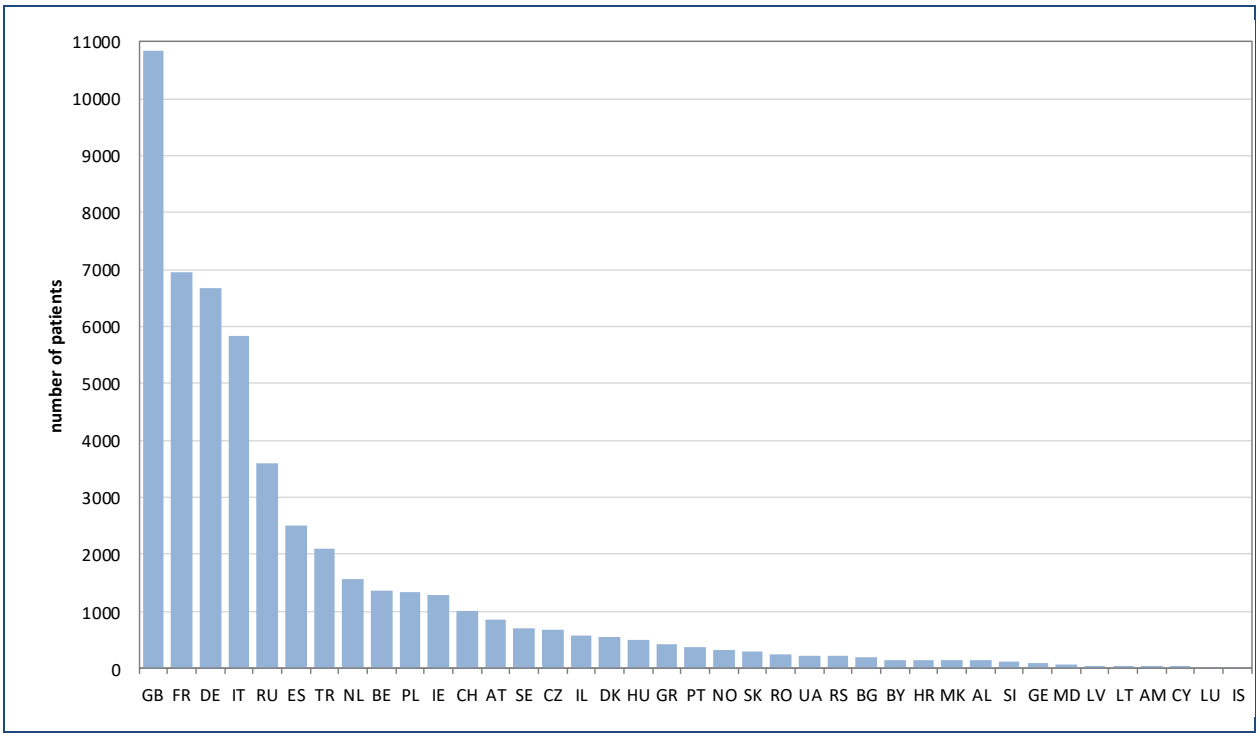
* Countries with an established national CF registry.
** These countries are defined as a national registry, since all centres in the country participate in the ECFSPR.

1 Belarus and Georgia have 0% coverage for adults.
2 Greece: A paediatric centre didn't provide data for follow-up year 2020.
3 Luxembourg: An adult centre didn't provide data for follow-up year 2020.
4 United Kingdom: In the graphs of this report we use GB as abbreviation for United Kingdom of Great Britain and Northern Ireland.

The column “Patients registered, not lost to follow-up” shows the patients that attend centres and includes patients that were not seen by clinical staff during the year but are known to be alive that year. NB: The ECFSPR recommends marking a patient as “lost to follow-up” if a patient has not been seen for the third consecutive year and nothing is known about his/her condition.

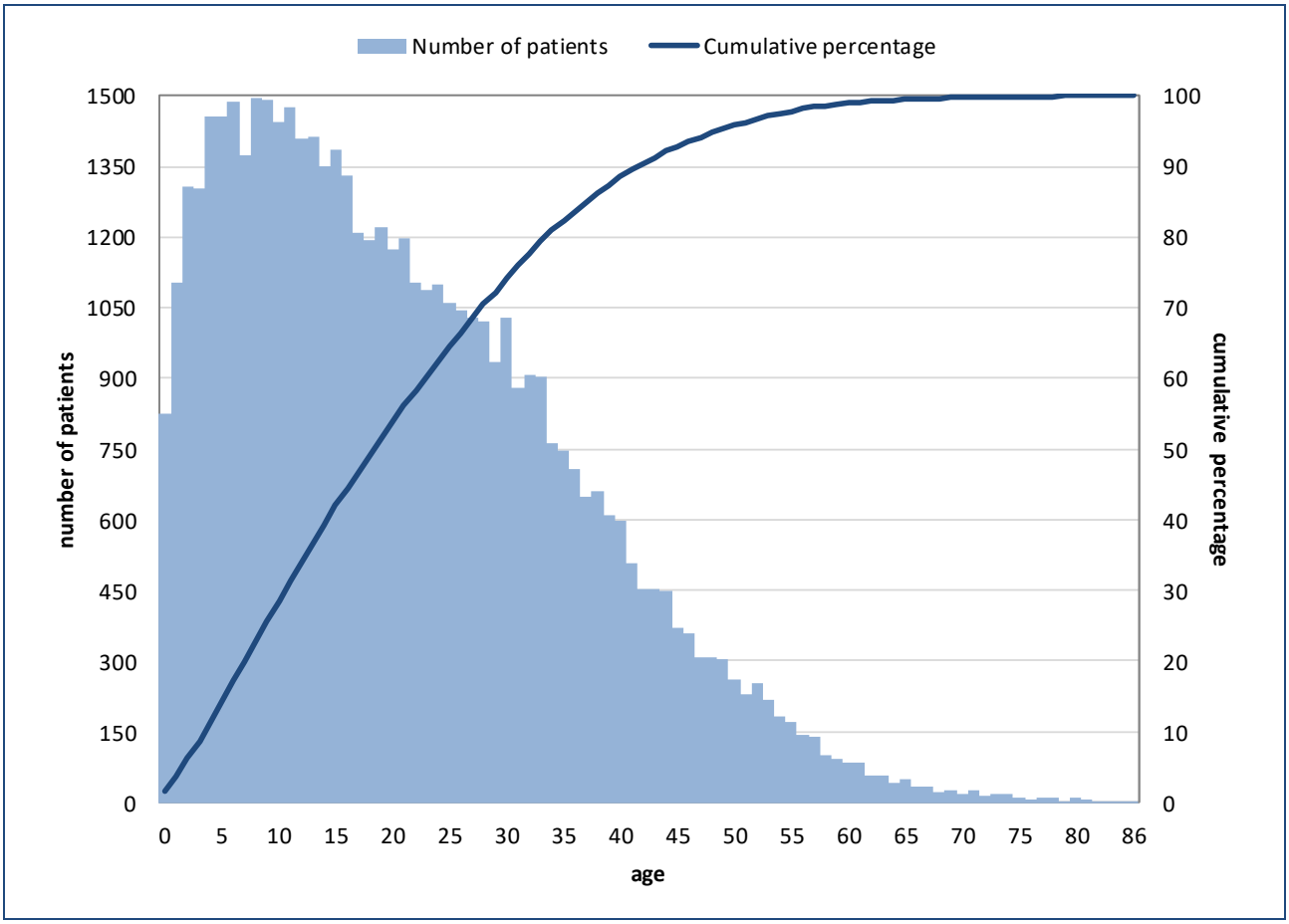
The column “patients seen” presents only the patients who have attended the clinic during the year. The column “Estimated coverage 2020” shows the estimated percentage of people with CF living in that country who are included in the national registry / national data collection as reported by the country. For some countries, one individual centre may include almost all patients, e.g. Latvia and Serbia.

Figure 1.2 Number of patients registered in the ECFSPR in year 2020, by country.



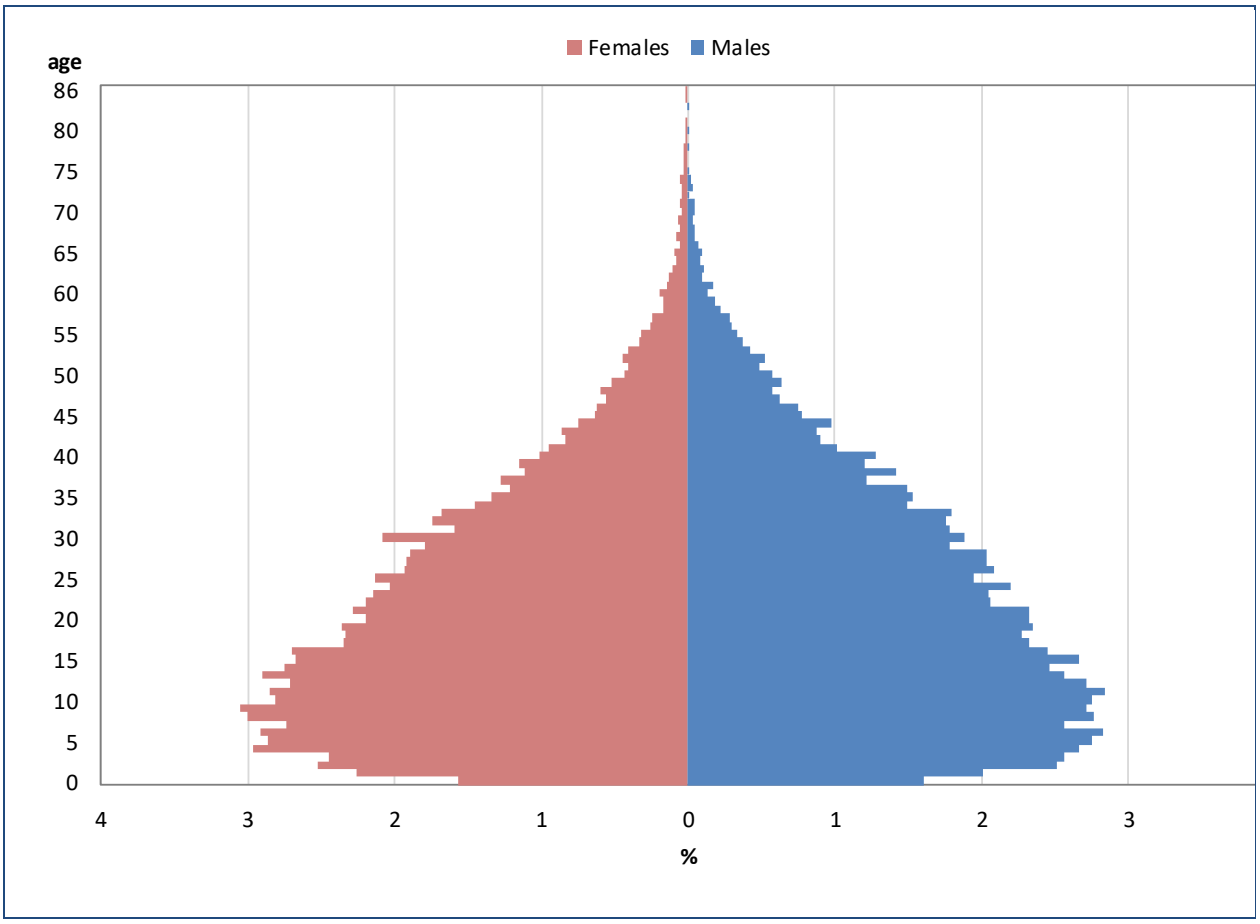
Each vertical bar shows the number of registered patients (excluding lost to follow-up) living in that country in 2020. Please refer to table 1.1 for the coverage in each country.

Figure 1.3 Age at follow-up distribution. Patients alive on 31/12/2020.



Each blue vertical bar represents the number of patients of that age alive in 2020. The cumulative percentage (the dark blue line) describes how many patients (as a percentage) are below a certain age (e.g. 50% of the patients are younger than 19 years of age).

Figure 1.4 Age at follow-up distribution by sex. Patients alive on 31/12/2020.



The pyramid shows the percentage of patients of different ages as horizontal bars. The right side of the pyramid (blue) shows, for males, how many patients (as a percentage) are a certain age, the left side (red) shows the same for females. The lower percentage of patients at the bottom of the pyramid is a result of the fact that some patients have not yet been diagnosed (mean age at diagnosis is 4.1 years, see table 2.1).

Table 1.2 Proportion of children (<18 years) and adults (≥18 years), by country. Patients alive on 31/12/2020.

Country	Children (<18 years) number (%)	Adults (≥18 years) number (%)
Albania	111 (82.22)	24 (17.78)
Armenia	25 (83.33)	5 (16.67)
Austria	384 (45.34)	463 (54.66)
Belarus	151 (100)	0 (0)
Belgium	471 (35.07)	872 (64.93)
Bulgaria	116 (57.71)	85 (42.29)
Croatia	90 (61.64)	56 (38.36)
Cyprus	11 (36.67)	19 (63.33)
Czech Republic	334 (50.61)	326 (49.39)
Denmark	207 (38.40)	332 (61.60)
France	2737 (39.60)	4174 (60.40)
Georgia	82 (98.80)	1 (1.20)
Germany	2745 (41.52)	3867 (58.48)
Greece	95 (22.04)	336 (77.96)
Hungary	255 (51.31)	242 (48.69)
Iceland	8 (57.14)	6 (42.86)
Ireland	503 (39.27)	778 (60.73)
Israel	181 (31.15)	400 (68.85)
Italy	2300 (39.48)	3525 (60.52)
Latvia	34 (70.83)	14 (29.17)
Lithuania	15 (40.54)	22 (59.46)
Luxembourg	25 (92.59)	2 (7.41)

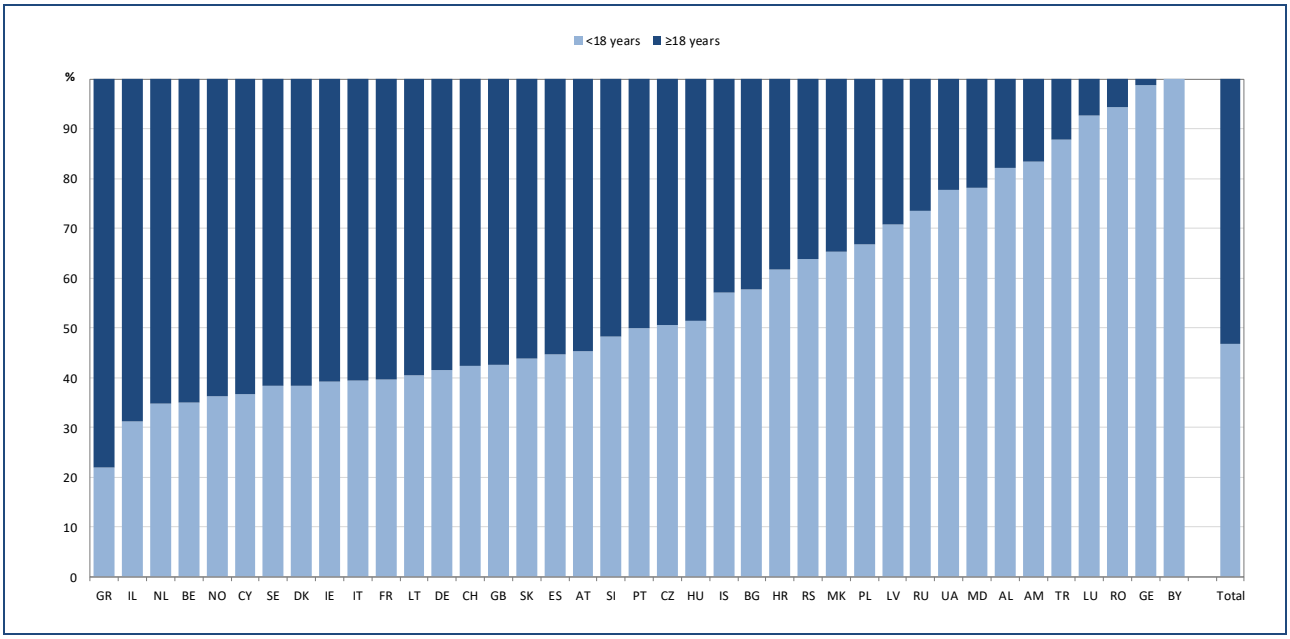
Note: Belarus and Georgia have 0% coverage for adults.

Note: Greece: A paediatric centre didn't provide data for follow-up year 2020, which accounts for the high percentage of adult patients.
Luxembourg: An adult centre didn't provide data for follow-up year 2020, which accounts for the low percentage of adult patients.

[table 1.2 continued]

Country	Children (<18 years) number (%)	Adults (≥18 years) number (%)
Rep of Moldova	43 (78.18)	12 (21.82)
The Netherlands	539 (34.80)	1010 (65.20)
North Macedonia	94 (65.28)	50 (34.72)
Norway	120 (36.36)	210 (63.64)
Poland	889 (66.74)	443 (33.26)
Portugal	179 (50.00)	179 (50.00)
Romania	237 (94.42)	14 (5.58)
Russian Federation	2641 (73.59)	948 (26.41)
Serbia	134 (63.81)	76 (36.19)
Slovak Republic	127 (43.79)	163 (56.21)
Slovenia	55 (48.25)	59 (51.75)
Spain	1115 (44.73)	1378 (55.27)
Sweden	267 (38.36)	429 (61.64)
Switzerland	428 (42.42)	581 (57.58)
Turkey	1829 (87.85)	253 (12.15)
Ukraine	168 (77.78)	48 (22.22)
United Kingdom	4574 (42.59)	6166 (57.41)
Total	24319 (46.87)	27568 (53.13)

Figure 1.5 Proportion of children (<18 years) and adults (≥18 years), by country and overall. Patients alive on 31/12/2020.



Note: Belarus and Georgia have 0% coverage for adults.

Note: Greece: A paediatric centre didn't provide data for follow-up year 2020, which accounts for the high percentage of adult patients.
Luxembourg: An adult centre didn't provide data for follow-up year 2020, which accounts for the low percentage of adult patients.

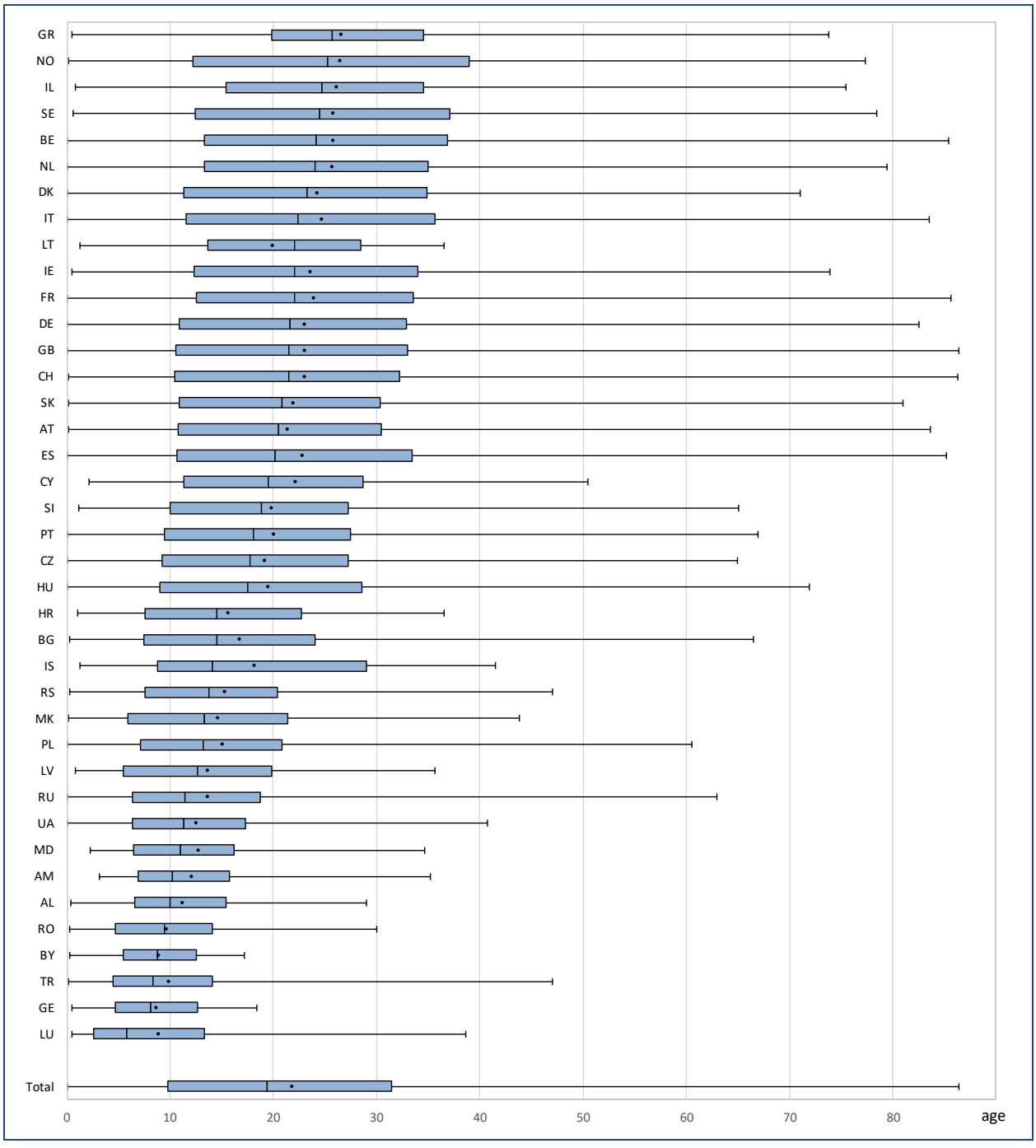
This graph shows the percentage of patients in each country who are adults (dark blue) or children (light blue). The percentage of adults varies considerably between the different countries, but this is partly an effect of the way the patients are included. For example, for some countries only a few individual centres send data to the ECFSPR, or the proportion of children and adults may reflect only the proportion of paediatric and adult centres in that country who participate in the ECFSPR and not the real proportion in the country. Please refer to table 1.1, page 9, for national coverage.

Table 1.3 Age at follow-up: descriptive statistics, by country and overall. Patients alive on 31/12/2020.

Country	N	Mean (average age)	Min (age of the youngest patient)	25th pctl (25% of the patients are younger than this age)	Median (half the patients are younger than this age)	75th pctl (75% of the patients are younger than this age)	Max (age of the oldest patient)
Albania	135	11.2	0.4	6.6	10.0	15.4	29.0
Armenia	30	12.1	3.2	6.9	10.2	15.8	35.2
Austria	847	21.4	0.2	10.8	20.5	30.5	83.7
Belarus	151	8.9	0.3	5.5	8.8	12.5	17.2
Belgium	1343	25.8	0.1	13.3	24.2	36.9	85.4
Bulgaria	201	16.7	0.3	7.5	14.5	24.0	66.5
Croatia	146	15.6	1.0	7.6	14.5	22.7	36.5
Cyprus	30	22.2	2.2	11.3	19.5	28.7	50.5
Czech Republic	660	19.2	0.1	9.2	17.7	27.3	65.0
Denmark	539	24.3	0.0	11.3	23.3	34.9	71.0
France	6911	23.9	0.0	12.5	22.1	33.6	85.6
Georgia	83	8.7	0.5	4.7	8.1	12.7	18.4
Germany	6612	23.0	0.0	10.9	21.6	32.9	82.5
Greece	431	26.6	0.5	19.9	25.7	34.6	73.8
Hungary	497	19.5	0.0	9.0	17.5	28.6	71.9
Iceland	14	18.2	1.3	8.8	14.1	29.0	41.5
Ireland	1281	23.6	0.5	12.3	22.1	34.0	73.9
Israel	581	26.1	0.8	15.4	24.7	34.5	75.5
Italy	5825	24.7	0.0	11.6	22.4	35.7	83.5
Latvia	48	13.6	0.8	5.5	12.7	19.8	35.7
Lithuania	37	20.0	1.3	13.7	22.1	28.5	36.5
Luxembourg	27	8.9	0.5	2.6	5.8	13.3	38.6
Rep of Moldova	55	12.8	2.3	6.5	11.0	16.2	34.7
The Netherlands	1549	25.7	0.1	13.3	24.1	35.0	79.5
North Macedonia	144	14.6	0.2	5.9	13.3	21.4	43.8
Norway	330	26.5	0.2	12.2	25.3	39.0	77.3
Poland	1332	15.1	0.1	7.1	13.2	20.8	60.5
Portugal	358	20.1	0.1	9.5	18.1	27.5	67.0
Romania	251	9.7	0.3	4.7	9.4	14.1	30.0
Russian Federation	3589	13.7	0.1	6.3	11.4	18.7	63.0
Serbia	210	15.3	0.3	7.6	13.8	20.4	47.1
Slovak Republic	290	21.9	0.2	10.9	20.8	30.4	81.0
Slovenia	114	19.9	1.2	10.0	18.9	27.3	65.1
Spain	2493	22.8	0.1	10.7	20.2	33.4	85.2
Sweden	696	25.8	0.6	12.4	24.5	37.1	78.5
Switzerland	1009	23.1	0.2	10.5	21.5	32.2	86.3
Turkey	2082	9.9	0.2	4.5	8.3	14.1	47.0
Ukraine	216	12.5	0.0	6.4	11.3	17.3	40.7
United Kingdom	10740	23.1	0.0	10.6	21.5	33.0	86.4
Total	51887	21.8	0.0	9.8	19.4	31.5	86.4

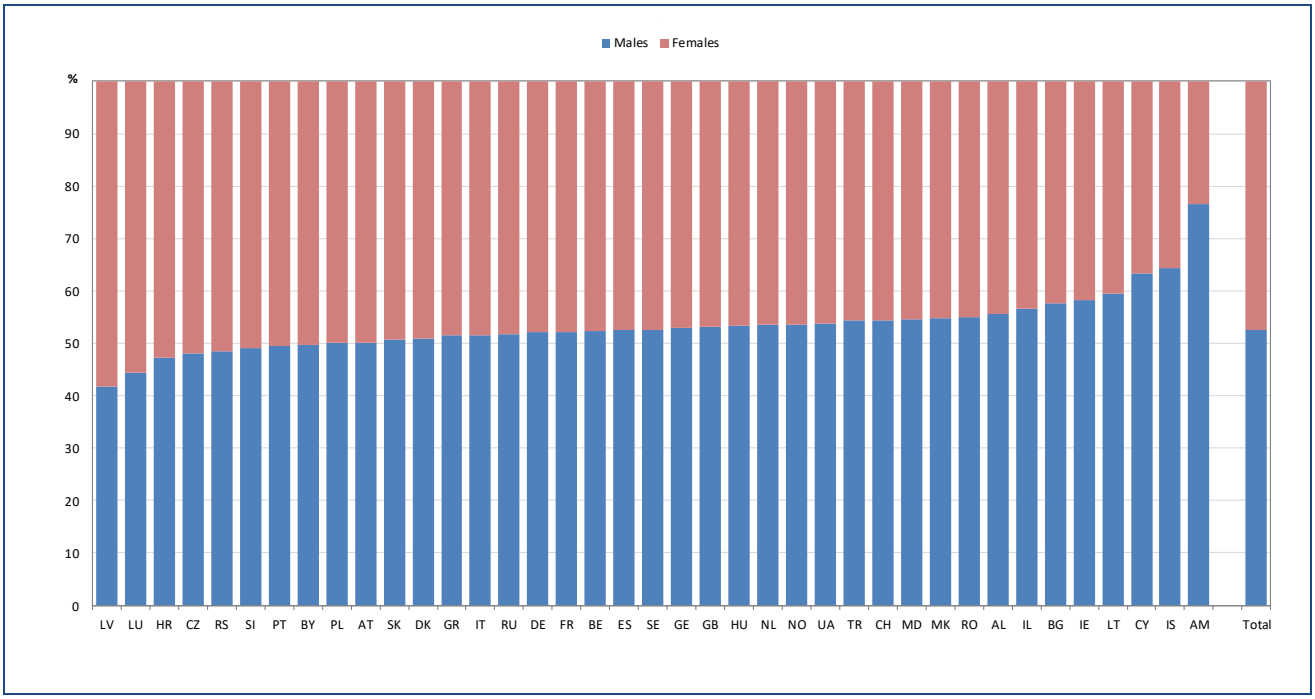
This table shows the descriptive statistics for age at follow-up of the patients by country and overall. Only patients who were alive on 31/12/2020 are included.

Figure 1.6 Age at follow-up: boxplot, by country and overall. Patients alive on 31/12/2020.



This boxplot is a graphic representation of the age detailed in table 1.3. For each country the borders of the box are first and third quartile, the dash (black line crossing the blue box) is the median, the black dot is the mean and the whiskers (lines with a T-shaped end) are the minimum and the maximum.

Figure 1.7 Sex distribution, by country and overall. Patients alive on 31/12/2020.



Sex distribution of all patients. Overall (see "Total") in the ECFSPR there are slightly more male than female patients.

2. Diagnosis

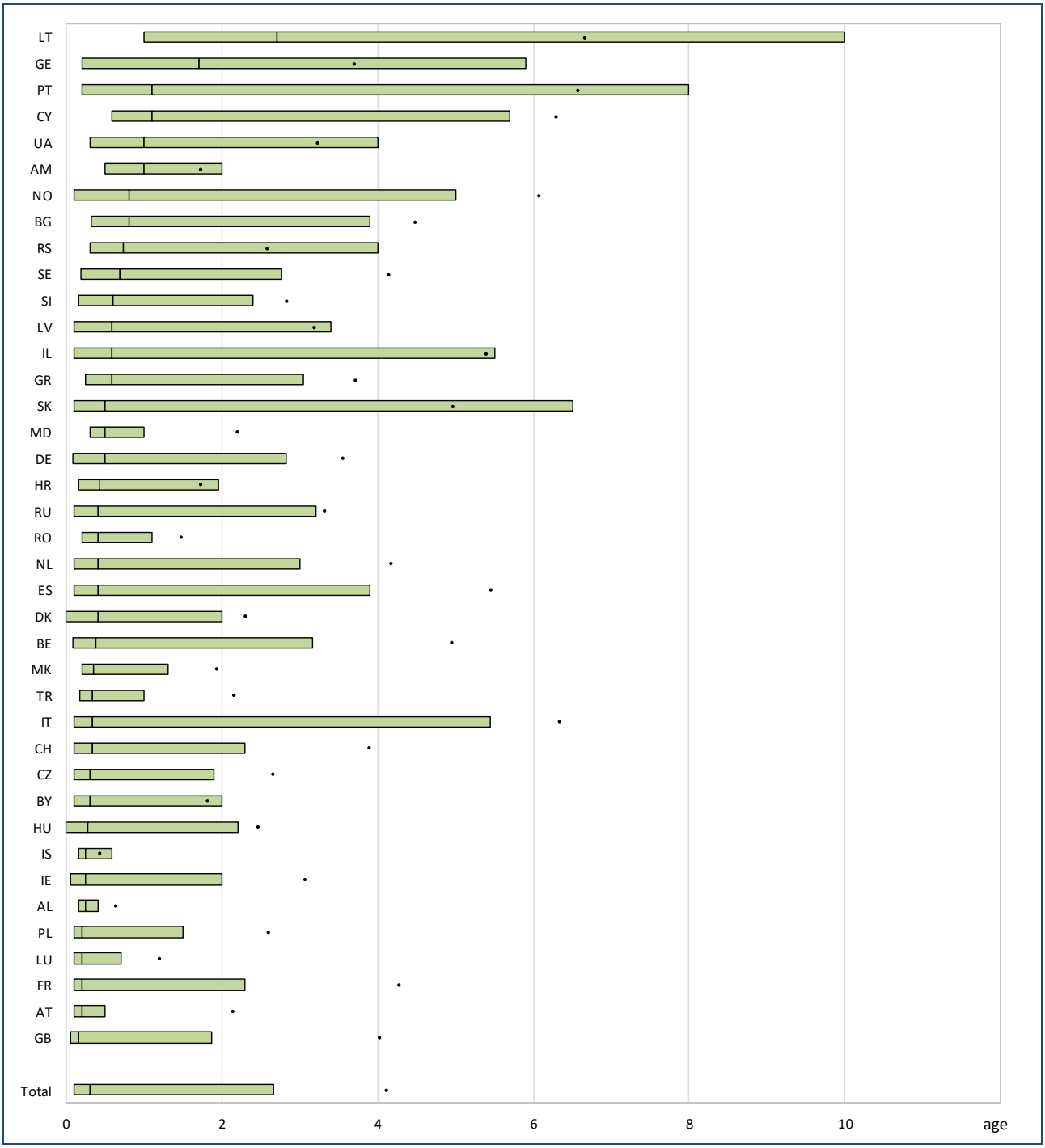
Hereafter, only patients seen during the year are presented.

Table 2.1 Age at diagnosis (in years): descriptive statistics, by country and overall. All patients seen in 2020.

Country	N	N miss	Mean (average age at diagnosis)	Min (lowest age at diagnosis)	25th pctl (25 % of the patients were diagnosed before this age)	Median (half the patients were diagnosed before this age)	75th pctl (75% of the patients were diagnosed before this age)	Max (highest age at diagnosis)
Albania	81	0	0.63	0.00	0.16	0.25	0.40	14.00
Armenia	25	0	1.72	0.10	0.50	1.00	2.00	6.17
Austria	769	64	2.13	0.00	0.10	0.20	0.50	61.00
Belarus	151	0	1.80	0.01	0.10	0.30	2.00	15.00
Belgium	1331	3	4.94	0.00	0.08	0.38	3.16	82.57
Bulgaria	190	4	4.48	0.00	0.32	0.80	3.90	64.30
Croatia	124	8	1.72	0.00	0.16	0.42	1.95	22.00
Cyprus	21	2	6.28	0.01	0.59	1.10	5.69	48.09
Czech Republic	625	6	2.64	0.00	0.10	0.30	1.90	47.00
Denmark	497	0	2.30	0.00	0.00	0.40	2.00	42.67
France	6892	62	4.27	0.00	0.10	0.20	2.30	81.20
Georgia	71	2	3.69	0.00	0.20	1.70	5.90	16.30
Germany	6428	239	3.55	0.00	0.08	0.50	2.83	69.41
Greece	375	12	3.70	0.00	0.25	0.58	3.04	55.68
Hungary	448	48	2.46	0.00	0.00	0.28	2.20	39.00
Iceland	14	0	0.42	0.00	0.15	0.25	0.58	1.20
Ireland	1227	7	3.06	0.00	0.05	0.25	2.00	75.83
Israel	514	4	5.38	0.00	0.10	0.58	5.50	56.00
Italy	5695	106	6.33	0.00	0.10	0.33	5.45	77.62
Latvia	46	0	3.17	0.00	0.10	0.59	3.40	25.60
Lithuania	33	1	6.65	0.40	1.00	2.70	10.00	24.00
Luxembourg	23	0	1.19	0.00	0.10	0.20	0.70	17.00
Rep of Moldova	49	0	2.19	0.10	0.30	0.50	1.00	19.00
The Netherlands	1460	85	4.17	0.00	0.10	0.40	3.00	66.00
North Macedonia	122	0	1.92	0.00	0.20	0.35	1.30	29.20
Norway	315	10	6.06	0.00	0.10	0.80	5.00	69.00
Poland	1165	15	2.59	0.00	0.10	0.20	1.50	46.70
Portugal	346	11	6.57	0.00	0.20	1.10	8.00	58.00
Romania	222	6	1.47	0.00	0.20	0.40	1.10	14.60
Russian Federation	2385	8	3.31	0.00	0.10	0.40	3.20	59.50
Serbia	156	2	2.57	0.10	0.30	0.73	4.00	18.60
Slovak Republic	242	27	4.96	0.00	0.10	0.50	6.50	59.00
Slovenia	110	1	2.83	0.00	0.15	0.60	2.40	37.50
Spain	2317	34	5.45	0.00	0.10	0.40	3.90	75.00
Sweden	692	10	4.13	0.00	0.18	0.69	2.77	68.68
Switzerland	889	111	3.89	0.00	0.10	0.33	2.30	81.90
Turkey	2059	23	2.15	0.00	0.17	0.33	1.00	43.60
Ukraine	168	1	3.22	0.00	0.30	1.00	4.00	38.50
United Kingdom	9881	41	4.02	0.00	0.05	0.15	1.86	81.35
Total	48158	953	4.11	0.00	0.10	0.30	2.66	82.57

Note: For Hungary, Slovak Republic and Switzerland the information on age at diagnosis is missing for more than 10% of the patients.

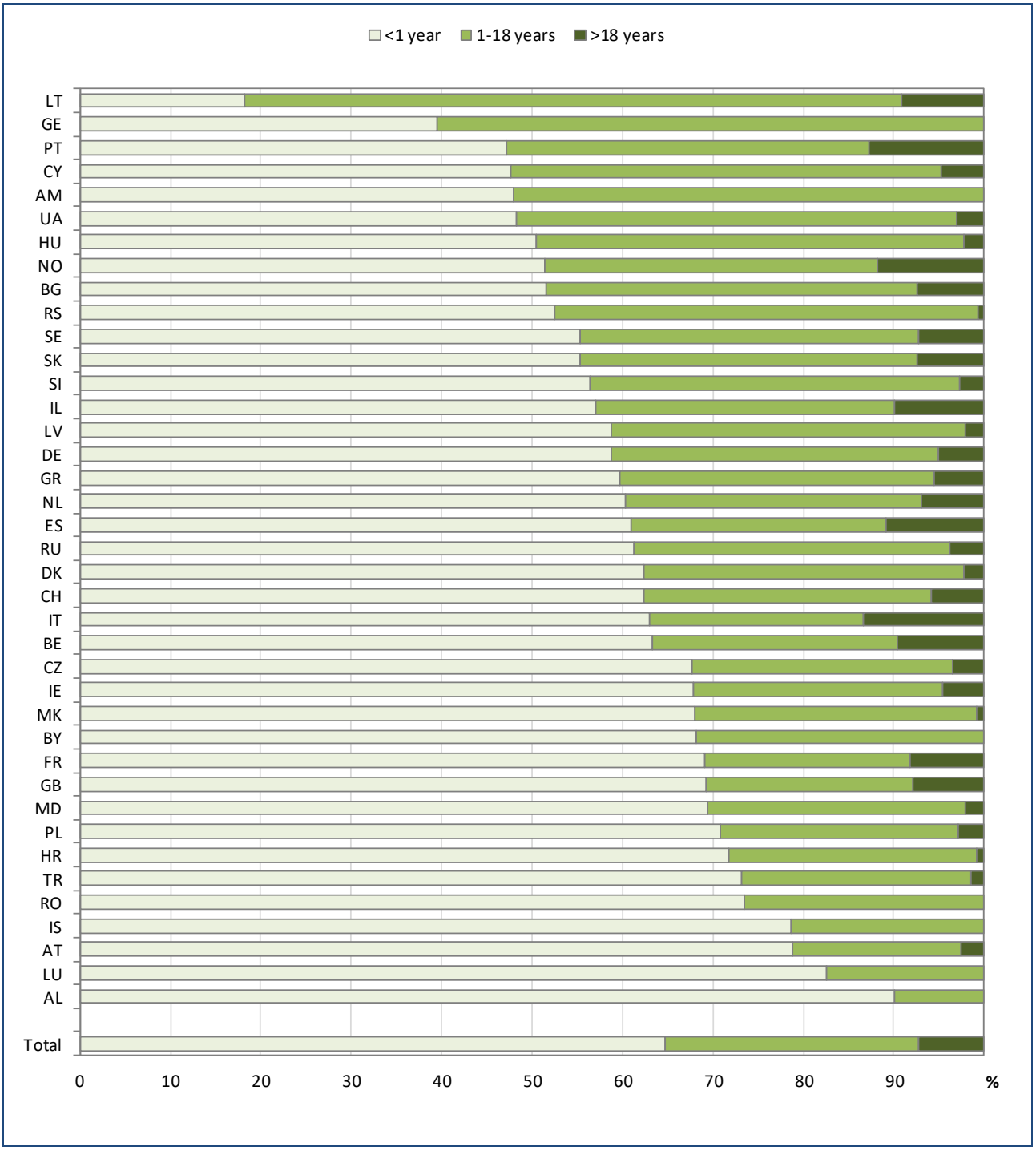
Figure 2.1 Age at diagnosis (in years): boxplot, by country and overall. All patients seen in 2020.



Note: For Hungary, Slovak Republic and Switzerland the information on age at diagnosis is missing for more than 10% of the patients.

This boxplot is a graphic representation of age at diagnosis as detailed in table 2.1. For each country the borders of the box are the first and third quartiles, the dash (black line crossing the green box) is the median, the black dot is the mean. The whiskers that are the minimum and the maximum values are not shown because the maximum values are really high for some countries and this would have shrunk the boxes at the left side of the graph.

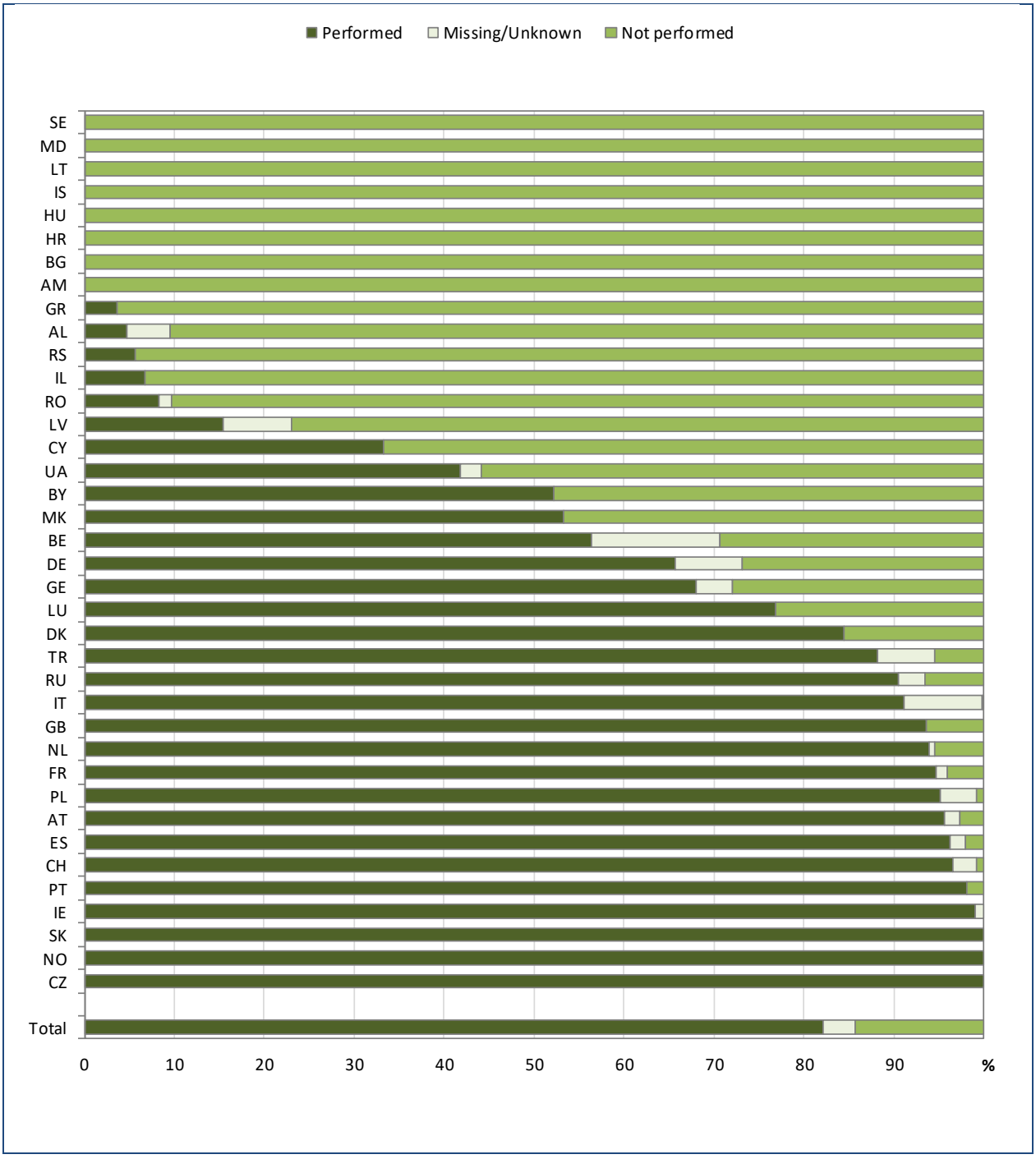
Figure 2.2 Proportion of patients diagnosed younger than 1 year, between 1 and 18 years, and older than 18 years, by country and overall. All patients seen in 2020.



Note: For Hungary, Slovak Republic and Switzerland the information on age at diagnosis is missing for more than 10% of the patients.

This graph shows the percentage of patients according to the age of diagnosis. Light green horizontal bars represent patients diagnosed younger than 1-year, green bars the patients diagnosed between 1 and 18 years, and the dark green bars represent patients diagnosed older than 18 years. The bars sum to 100%.

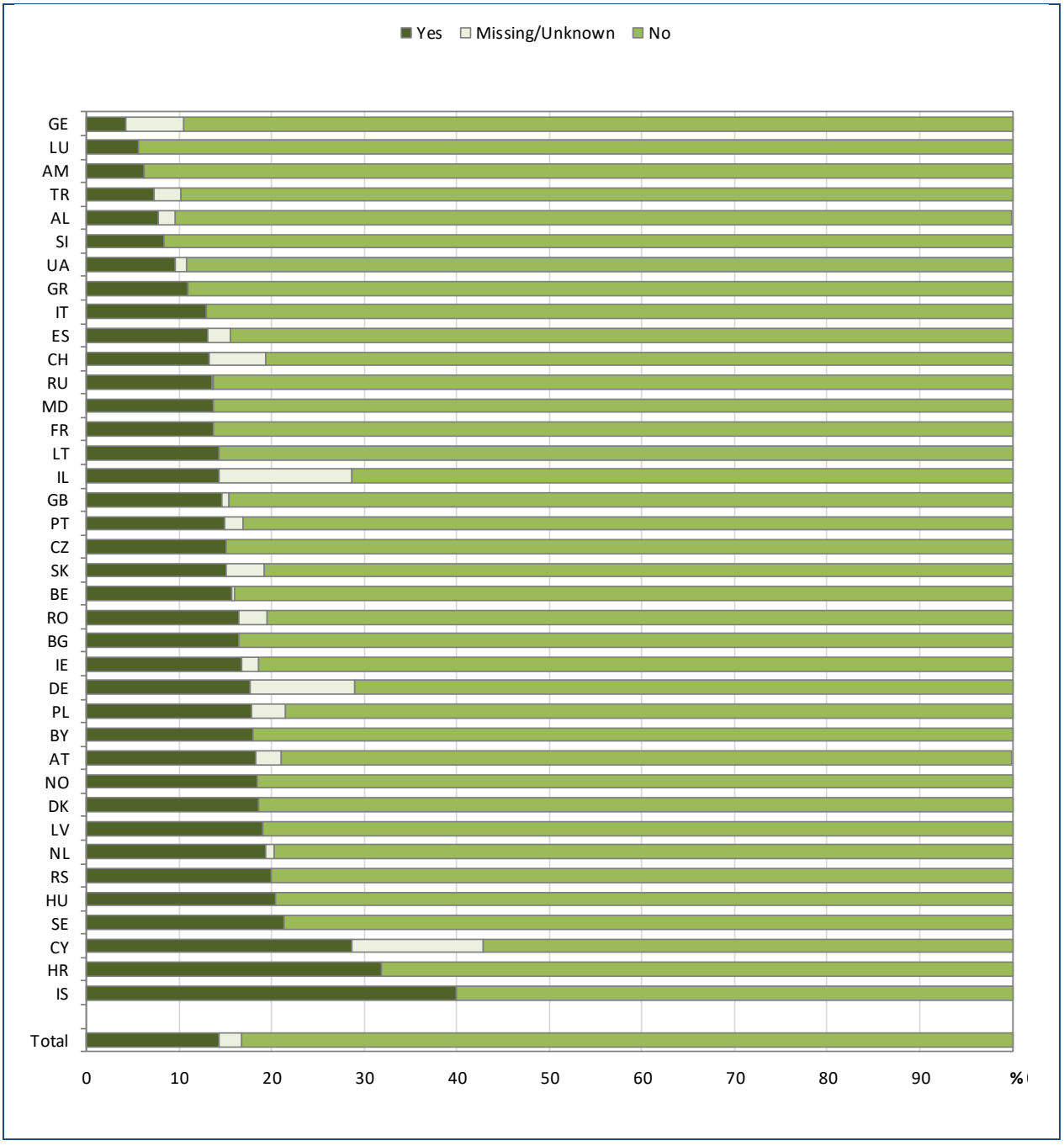
Figure 2.3 Proportion of patients who underwent neonatal screening, by country and overall. Patients 5 years old or younger seen in 2020.



Note: For Belgium, France and United Kingdom positive answers ("neonatal screening performed") are reported only when neonatal screening is one of the factors that led to CF diagnosis.

This graph shows the percentage of patients at the age of 5 years or younger in 2020 who were screened at birth. Dark green horizontal bars represent neonatal screening "performed", light green ones "not performed". This graph shows that, in the five years previous to 2020, in many countries the CF patients underwent neonatal, i.e. newborn screening, and that in some countries there is no neonatal screening programme. In total, 79% of all children of 5 years old or younger registered in the ECFSPR in 2020 were screened at birth. This estimate also reflects the fact that not all the countries carry out newborn screening.

Figure 2.4 Patients with meconium ileus, by country and overall. Patients aged 10 years or younger.



Note: For Cyprus, Germany and Israel the information on meconium ileus is missing for more than 10% of the patients ≤10 years.

3. Genetics

Cystic fibrosis is caused by mutations of the 'CFTR' gene; one on each allele. One mutation is inherited from the mother and one from the father. If both mutations are the same, the person is homozygous for this mutation. If these are two different mutations, the person is considered to be heterozygous.

We supplied the countries with a list of the 1600 most common mutations based on the Cystic Fibrosis Mutation database (CFTR1). If the patient had a mutation that was not present in the database, the country had the possibility to enter the name of the mutation as free text. During the data cleaning process, the genotypes not on our list were checked for obvious misspellings or alternative names and, if identified as a known mutation, renamed. Although there are different naming conventions for mutations, we use the original mutation name (legacy name) in this report, since more than 90% of the mutations in the database use this nomenclature.

Please note that, although not presented in the report, information on complex alleles is captured and available.

If DNA analysis to look for CFTR mutations was never carried out, we asked the countries to report "Not done" in the genotype field. If DNA analysis was done, but only one or no mutations were found, we asked the countries to write "Unknown" for the unidentified mutations. Please bear in mind that there are differences from country to country in how DNA testing is carried out: some countries use standard kits that test only a limited number of common mutations (e.g. 28), and other countries perform DNA-analyses of the whole gene until the mutation is identified.

Table 3.1 Proportion of patients with DNA analysis and the result of this, by country and overall. All patients seen in 2020.

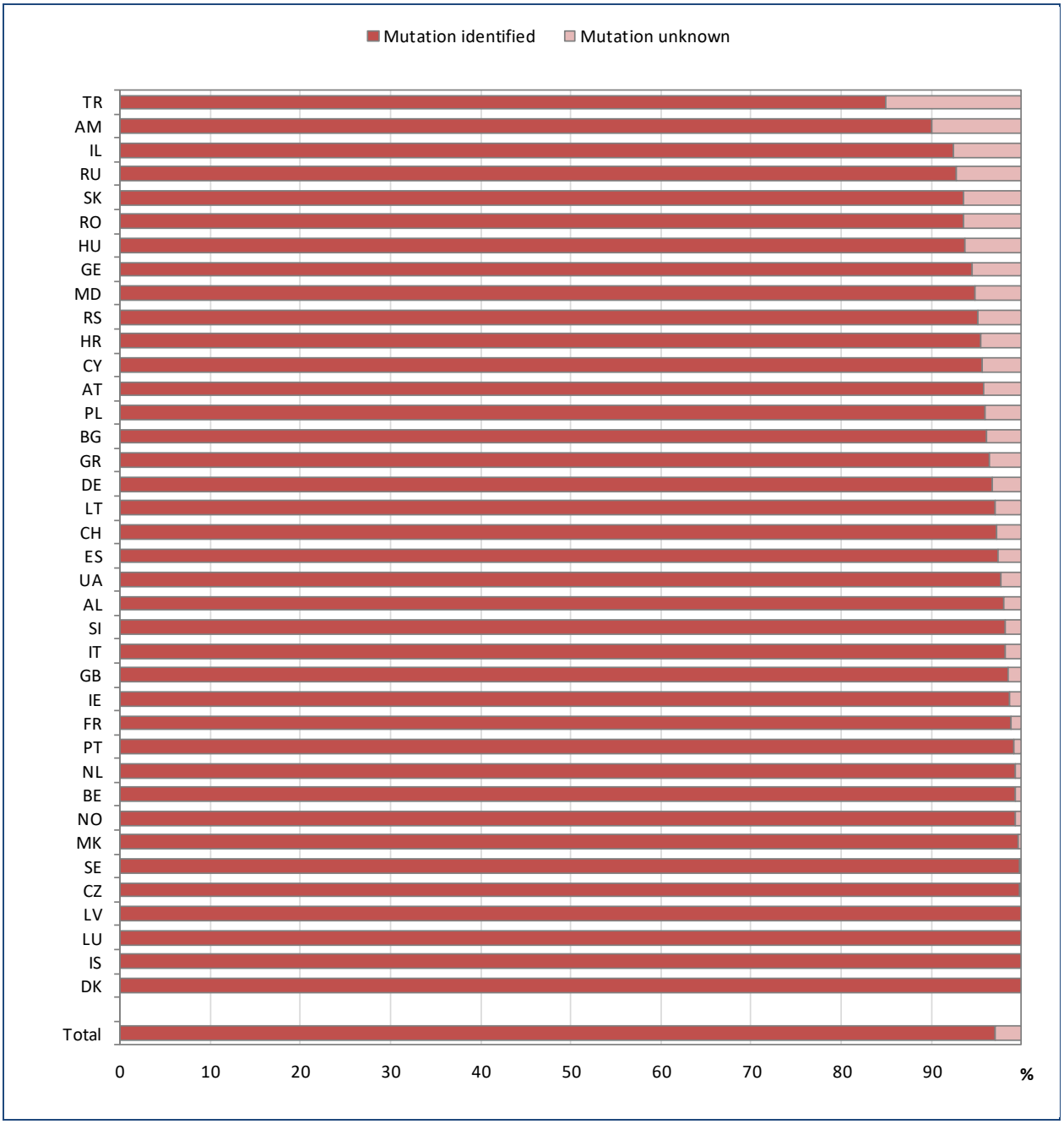
Country	Genotyping		Among genotyping done	
	not done	done	at least one mutation unknown	two mutations identified
	number (%)	number (%)	number (%)	number (%)
Albania	5 (6.17)	76 (93.83)	3 (3.95)	73 (96.05)
Armenia	0 (0)	25 (100)	5 (20.00)	20 (80.00)
Austria	0 (0)	833 (100)	51 (6.12)	782 (93.88)
Belarus	0 (0)	151 (100)	44 (29.14)	107 (70.86)
Belgium	0 (0)	1334 (100)	17 (1.27)	1317 (98.73)
Bulgaria	0 (0)	194 (100)	12 (6.19)	182 (93.81)
Croatia	0 (0)	132 (100)	10 (7.58)	122 (92.42)
Cyprus	0 (0)	23 (100)	2 (8.70)	21 (91.30)
Czech Republic	0 (0)	631 (100)	3 (0.48)	628 (99.52)
Denmark	0 (0)	497 (100)	0 (0)	497 (100)
France	0 (0)	6954 (100)	126 (1.81)	6828 (98.19)
Georgia	9 (12.33)	64 (87.67)	6 (9.38)	58 (90.63)
Germany	17 (0.25)	6650 (99.75)	342 (5.14)	6308 (94.86)
Greece	0 (0)	387 (100)	24 (6.20)	363 (93.80)
Hungary	3 (0.60)	493 (99.40)	52 (10.55)	441 (89.45)
Iceland	0 (0)	14 (100)	0 (0)	14 (100)
Ireland	0 (0)	1234 (100)	28 (2.27)	1206 (97.73)
Israel	2 (0.39)	516 (99.61)	52 (10.08)	464 (89.92)
Italy	2 (0.03)	5799 (99.97)	172 (2.97)	5627 (97.03)
Latvia	0 (0)	46 (100)	0 (0)	46 (100)
Lithuania	0 (0)	34 (100)	2 (5.88)	32 (94.12)
Luxembourg	0 (0)	23 (100)	0 (0)	23 (100)

[table 3.1 continued]

Country	Genotyping		Among genotyping done	
	not done	done	at least one mutation unknown	two mutations identified
	number (%)	number (%)	number (%)	number (%)
Rep of Moldova	0 (0)	49 (100)	4 (8.16)	45 (91.84)
The Netherlands	5 (0.32)	1540 (99.68)	20 (1.30)	1520 (98.70)
North Macedonia	1 (0.82)	121 (99.18)	1 (0.83)	120 (99.17)
Norway	0 (0)	325 (100)	3 (0.92)	322 (99.08)
Poland	2 (0.17)	1178 (99.83)	71 (6.03)	1107 (93.97)
Portugal	0 (0)	357 (100)	5 (1.40)	352 (98.60)
Romania	2 (0.88)	226 (99.12)	25 (11.06)	201 (88.94)
Russian Federation	96 (4.01)	2297 (95.99)	287 (12.49)	2010 (87.51)
Serbia	2 (1.27)	156 (98.73)	13 (8.33)	143 (91.67)
Slovak Republic	0 (0)	269 (100)	29 (10.78)	240 (89.22)
Slovenia	1 (0.90)	110 (99.10)	4 (3.64)	106 (96.36)
Spain	1 (0.04)	2350 (99.96)	116 (4.94)	2234 (95.06)
Sweden	0 (0)	702 (100)	3 (0.43)	699 (99.57)
Switzerland	4 (0.40)	996 (99.60)	39 (3.92)	957 (96.08)
Turkey	101 (4.85)	1981 (95.15)	398 (20.09)	1583 (79.91)
Ukraine	0 (0)	169 (100)	7 (4.14)	162 (95.86)
United Kingdom	44 (0.44)	9878 (99.56)	279 (2.82)	9599 (97.18)
Total	297 (0.60)	48814 (99.40)	2255 (4.62)	46559 (95.38)

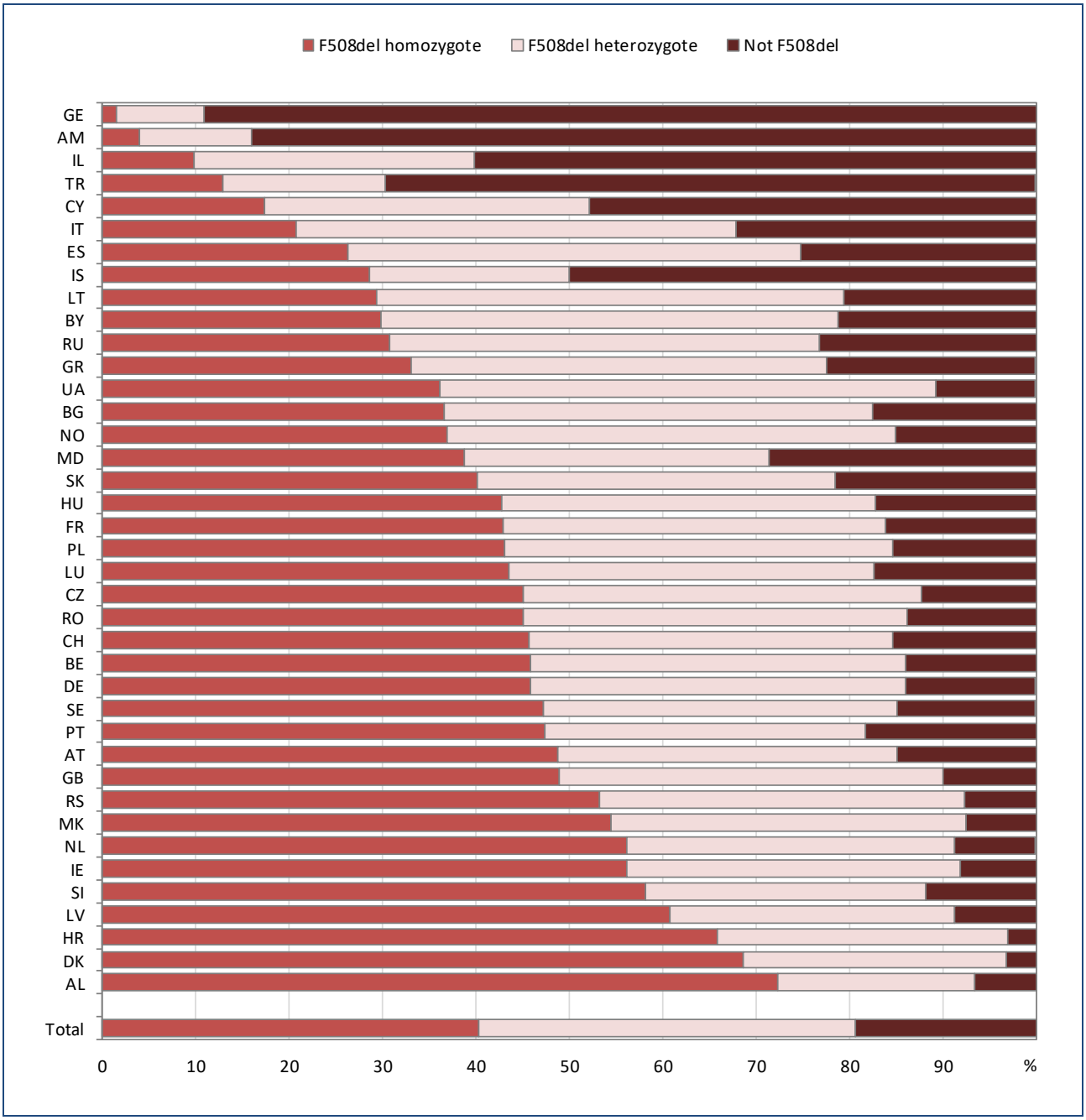
The table shows how many patients underwent DNA analysis to identify the CFTR mutations (column “genotyping done”) and, for those patients, how many patients had both mutations identified (column “two mutations identified”) and for how many one or both mutations remained unidentified (column “at least one mutation unknown”).

Figure 3.1 Proportion of identified mutations, by country and overall. Only patients with DNA analysis.



This graph shows the percentage of mutations that are not identified (in light pink) after DNA analysis, by country and overall. One “allele” means one of the two CFTR genes. The number of non-identified alleles varies greatly from country to country; this is partly due to the different approaches to DNA testing. Overall, more than 3% of mutations remain unidentified after DNA analysis, leaving 5.48% of the patients with at least one mutation unidentified.

Figure 3.2 Prevalence of F508del homozygous and heterozygous patients, by country and overall. All patients seen in 2020.



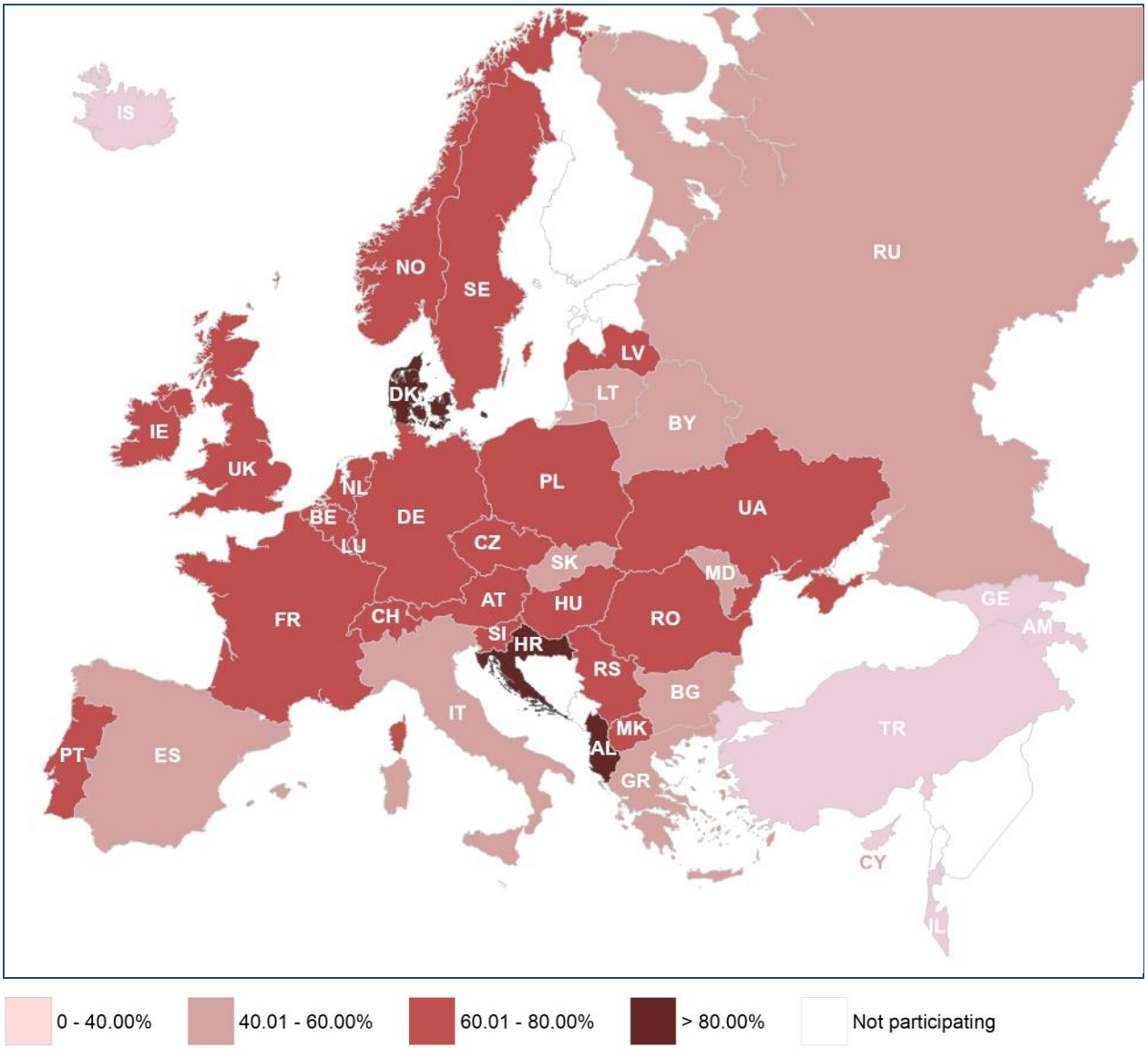
F508del is the name of the most commonly occurring CFTR mutation in the world. Patients who carry two F508del mutations are often described as having "classic CF", but other combinations of mutations may cause the same degree of disease. We have grouped the patients in F508del homozygous (patients who have two F508del mutations), F508del heterozygous (patients who have one F508del mutation and another known mutation, different from F508del), and patients without F508del mutations. Only patients for whom the genotype is known have been included in this graph. "Unknown" mutations have been classified as "other", since F508del is included in all genotyping kits and would have been identified. Please note that the genotype grouping in this graph does not reflect the severity of the disease in the countries.

Table 3.2 Allelic frequencies of the 18 most common mutations in the ECFSPR database.

Mutation name	Number of alleles	Percentage among tested	Country with highest allele frequency
F508del	58974	60.41	Albania (82.9%)
G542X	2683	2.75	Armenia (8.0%)
N1303K	2133	2.18	Iceland (46.4%)
G551D	1230	1.26	Ireland (8.3%)
W1282X	1049	1.07	Israel (22.6%)
2789+5G->A	1045	1.07	Greece (3.2%)
3849+10kbC->T	976	1.00	Lithuania (10.3%)
CFTRdele2,3	934	0.96	Belarus (10.9%)
R117H	928	0.95	Ireland (3.0%)
1717-1G->A	862	0.88	Switzerland (2.9%)
R553X	826	0.85	Lithuania (5.9%)
2183AA->G	695	0.71	Armenia (10.0%)
D1152H	612	0.63	Israel (5.0%)
621+1G->T	606	0.62	Greece (6.5%)
R347P	581	0.60	Luxembourg (4.4%)
G85E	516	0.53	Israel (2.6%)
3272-26A->G	506	0.52	Belgium (2.1%)
R1162X	500	0.51	Slovenia (5.0%)

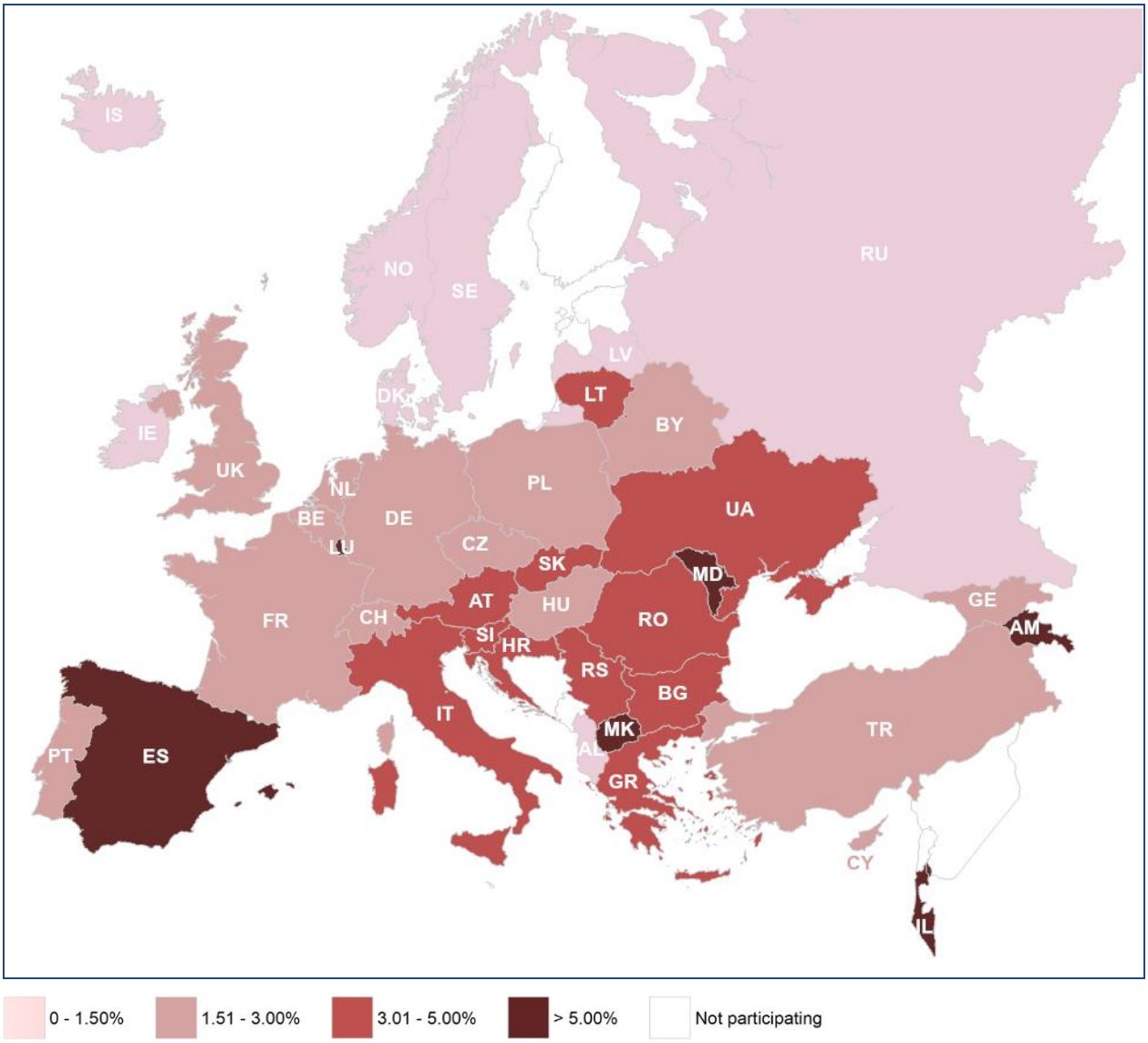
This table presents the allele frequency of the 18 most commonly occurring mutations found in the ECFSPR database. The last column reports in which country this particular mutation is most frequent. F508del is, by far, the most frequent mutation.

Figure 3.3 Geographical distribution of mutation F508del.



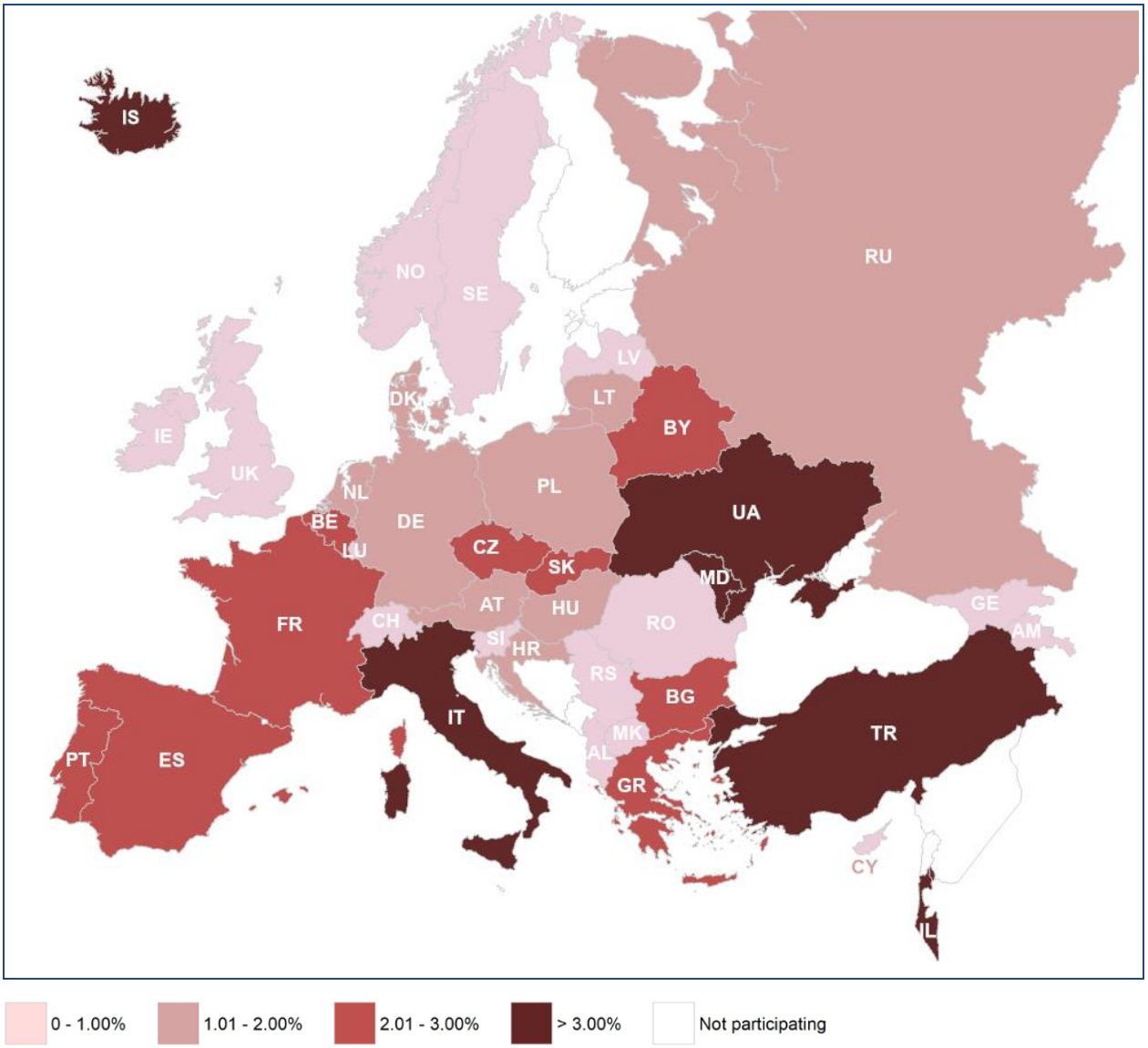
Although this mutation is the most common in all countries, the highest frequency occurs in Albania (82.9%) and Croatia (81.4%), and in the north of Europe, in Denmark (82.7%).

Figure 3.4 Geographical distribution of mutation G542X.



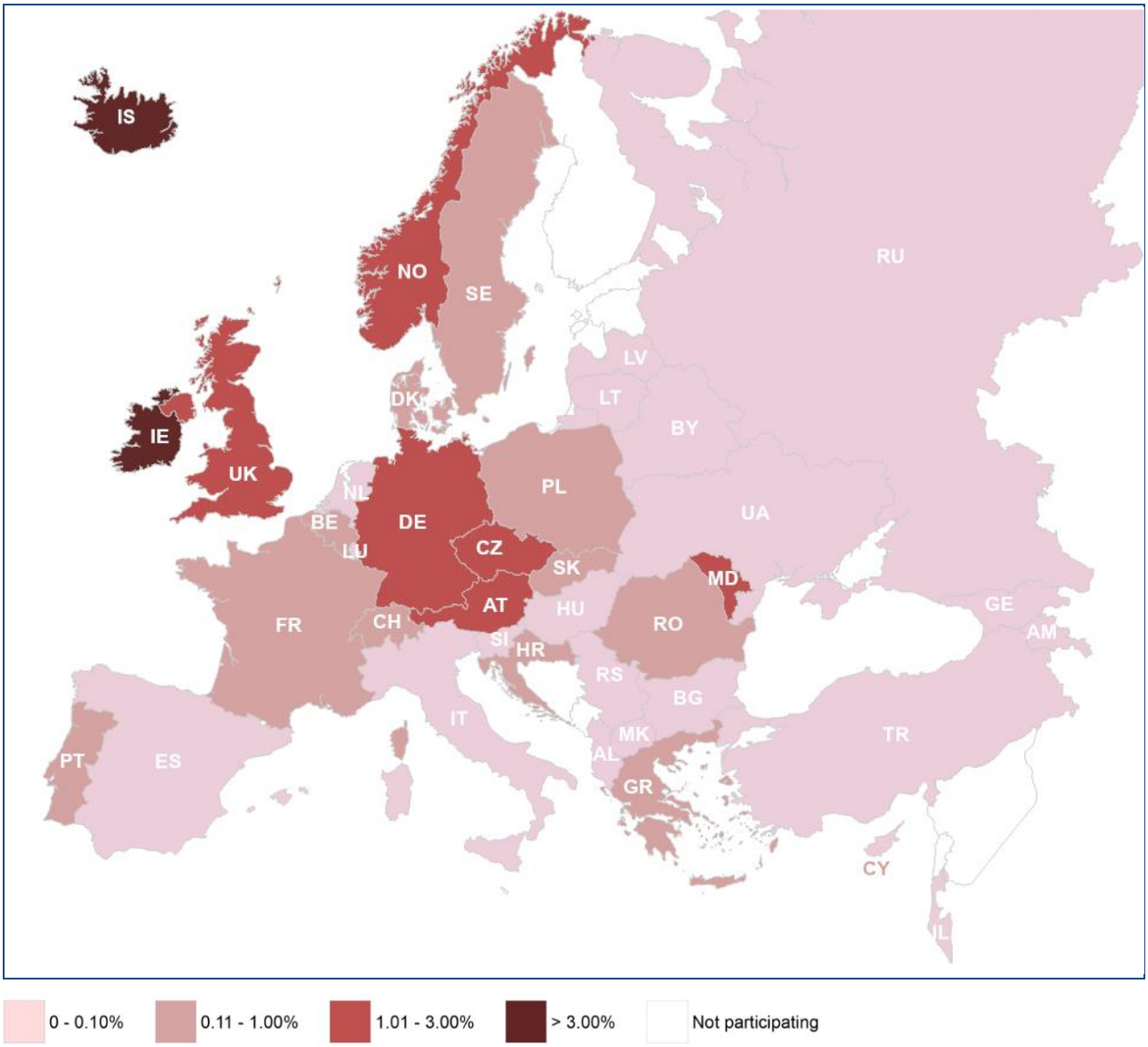
This mutation is most frequent in Southern Europe, with the highest allele frequency in Armenia (8.0%), whereas it is very rarely found in Ireland, Scandinavia, and the Russian Federation.

Figure 3.5 Geographical distribution of mutation N1303K.



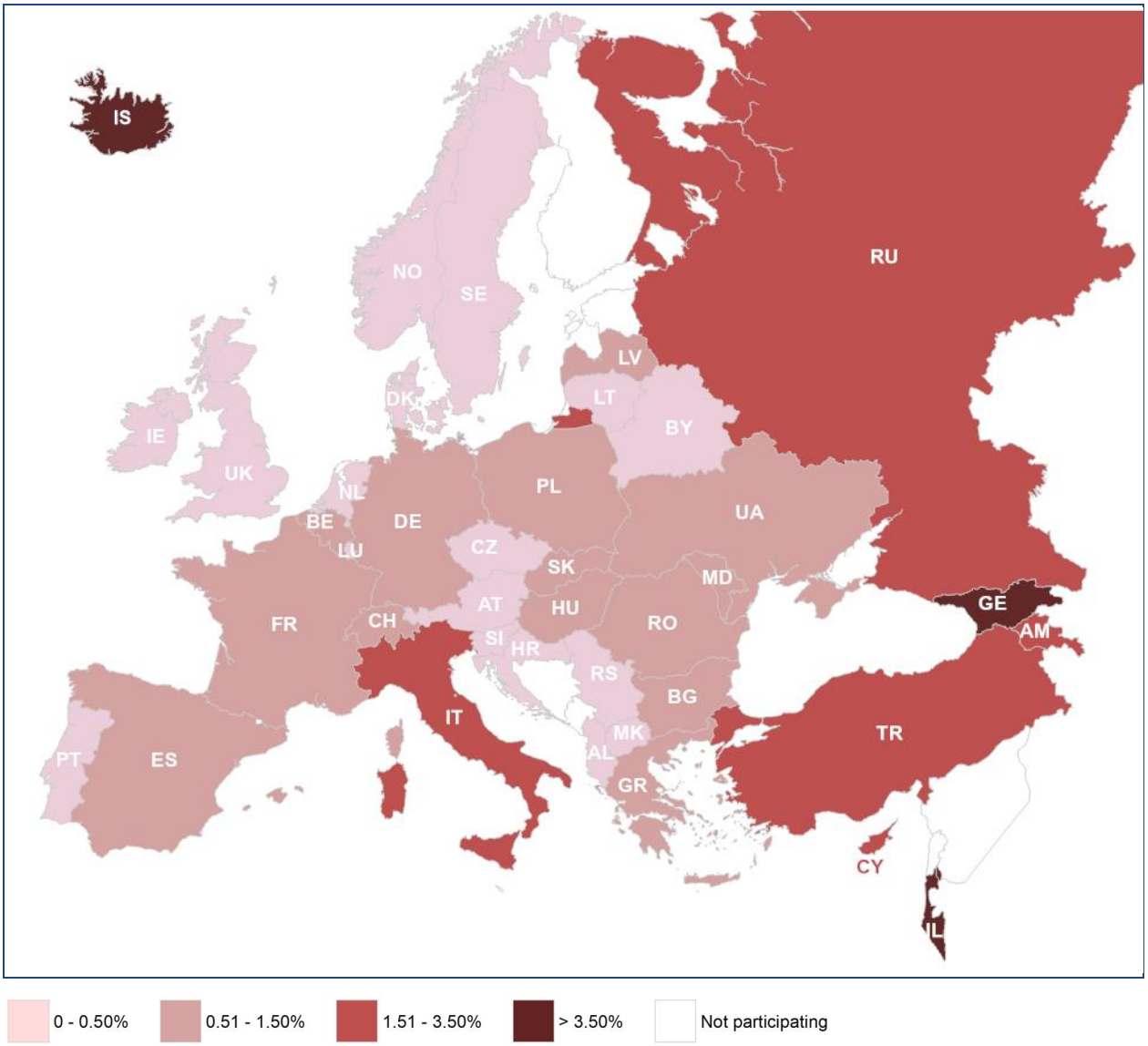
This mutation is most frequent in Iceland (46.4%). This is an exception in the Northern Europe where it is rare, while it is more frequent in countries in Southern and Eastern Europe.

Figure 3.6 Geographical distribution of mutation G551D.



This mutation is most frequent in Ireland (8.3%) and in the north of Europe whereas it is rare in Southern and Eastern Europe.

Figure 3.7 Geographical distribution of mutation W1282X.



This mutation, of Middle Eastern origin, is by far most frequent in Israel (22.6%) with a very high allele frequency in Ashkenazi Jews, and frequent in Georgia (10.2%).

4. Lung function

FEV_1 is measured in litres but it is normally expressed as a percentage of the expected (i.e. predicted) value (FEV_1%). The predicted value is computed from healthy individuals of the same sex, height and age and is termed the reference population.

We used the Global Lung Function Initiative equations described by Quanjer PH et al. for this report (for the full reference we refer you to Appendix 3, page 152). This is the global reference for spirometry and it has been agreed, as part of the CF global harmonisation project, that this is the best way to present lung function.

A FEV_1% of 100 means that the lung function measurement is equal to the mean lung function measurement of people of the same age, sex and height of the healthy reference population.

Spirometry, the test that measures FEV_1, requires a certain amount of coordination, and usually cannot be performed reliably until a person with CF is about four to six years of age. We have therefore computed FEV_1% values only for patients aged 6 years or older.

We asked the countries to report the best FEV_1 recorded throughout the year (relative to the best FEV_1% computed at the CF centres) to the ECFSPR.

We excluded patients from the analyses on FEV_1 who have had one or more lung transplants, since their lung function does not reflect the severity of their CF lung disease. Moreover, we also excluded patients who had a liver or other transplantation since the follow-up data of those patients is sometimes missing.

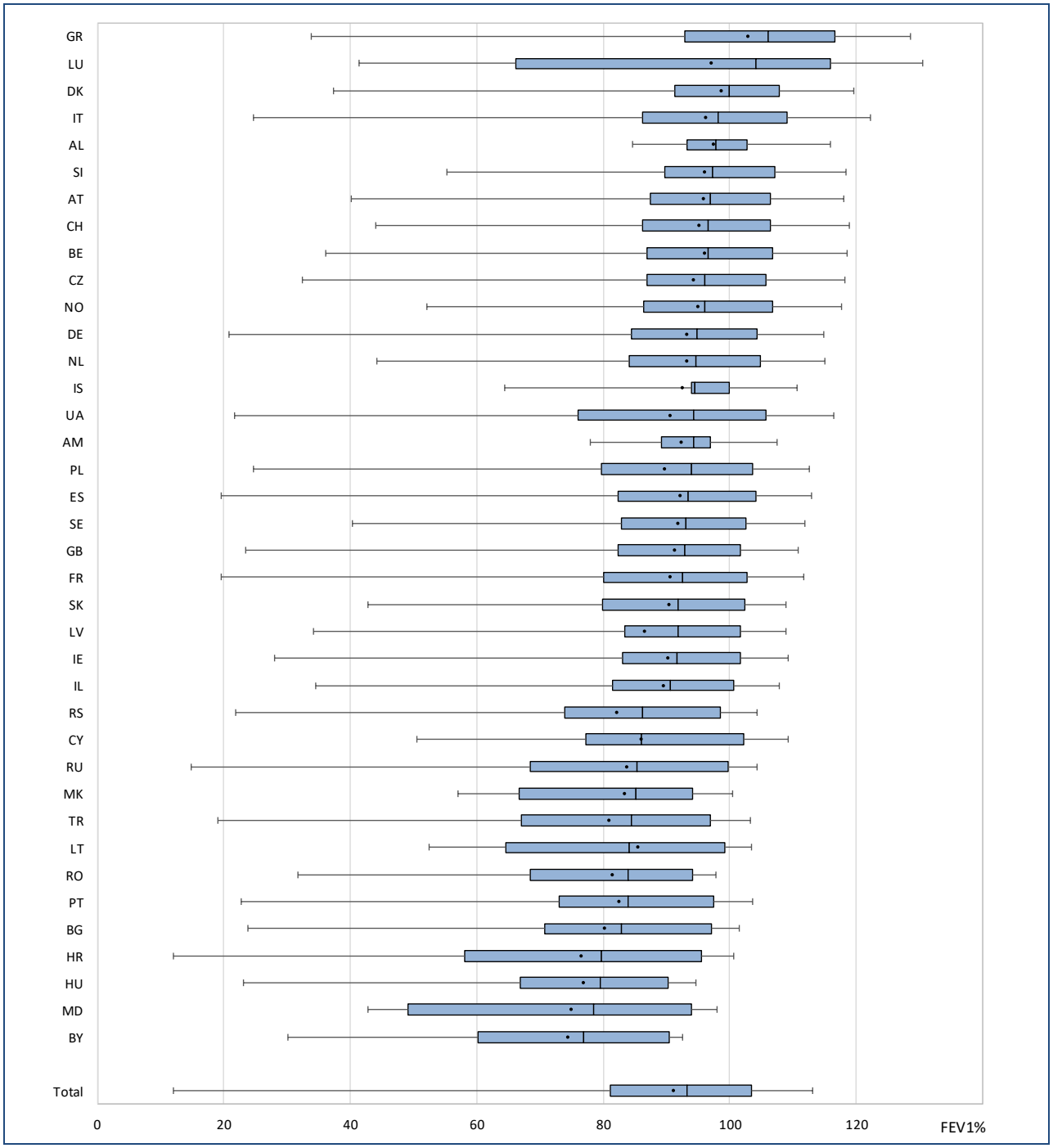
Table 4.1 FEV_1% of predicted: descriptive statistics, by country. Patients aged 6-17 years who have never had a transplant.

Country	N	N Miss	Mean (average FEV_1%)	Min	25th pctl (25% of patients have FEV_1% below this value)	Median (50% of patients have FEV_1% below this value)	75th pctl (75% of patients have FEV_1% below this value)	Max
Albania	41	11	97.5	84.7	93.2	97.8	102.7	107.1
Armenia	10	8	92.4	77.9	89.3	94.3	97.0	102.6
Austria	261	2	95.9	40.1	87.5	97.0	106.5	129.6
Belarus	46	19	74.5	30.1	60.2	77.0	90.4	120.8
Belgium	331	8	96.1	36.1	87.0	96.6	106.8	151.1
Bulgaria	66	6	80.2	23.8	70.7	82.9	97.2	122.8
Croatia	47	7	76.5	12.0	58.1	79.7	95.5	121.8
Cyprus	8	0	86.0	50.5	77.2	86.1	102.2	106.3
Czech Republic	205	3	94.4	32.4	87.0	96.1	105.7	125.7
Denmark	127	0	98.7	37.4	91.3	99.9	107.9	130.5
France	1844	110	90.7	19.5	80.1	92.6	102.7	167.8
Germany	1730	39	93.2	20.8	84.4	94.9	104.3	163.8
Greece	61	2	102.9	33.8	92.9	106.1	116.6	142.1
Hungary	148	22	76.9	23.1	66.9	79.5	90.3	130.8
Iceland	5	0	92.6	64.4	94.0	94.5	100.0	110.0
Ireland	296	88	90.3	28.1	83.0	91.7	101.7	126.9
Israel	157	1	89.6	34.5	81.5	90.7	100.6	130.0
Italy	1387	121	96.3	24.7	86.3	98.2	109.1	165.7
Latvia	19	1	86.5	34.1	83.5	91.8	101.7	114.8
Lithuania	6	1	85.6	52.5	64.6	84.1	99.3	129.3
Luxembourg	7	1	97.2	41.4	66.2	104.2	116.0	134.1
Rep of Moldova	7	22	75.0	42.8	49.1	78.5	93.9	108.3
The Netherlands	394	2	93.3	44.2	84.1	94.7	104.8	130.9
North Macedonia	43	9	83.5	57.1	66.8	85.1	94.2	126.2
Norway	73	3	95.1	52.1	86.4	96.0	106.9	118.4
Poland	500	56	89.8	24.7	79.7	93.9	103.6	136.3
Portugal	105	24	82.5	22.8	73.0	84.0	97.5	128.1
Romania	80	54	81.5	31.7	68.4	84.0	94.1	122.9
Russian Federation	724	388	83.7	14.9	68.5	85.4	99.7	165.3
Serbia	67	1	82.2	21.9	74.0	86.2	98.6	108.8
Slovak Republic	81	2	90.5	42.8	79.9	91.8	102.4	128.9
Slovenia	40	0	96.1	55.2	89.8	97.3	107.1	125.3
Spain	739	33	92.2	19.6	82.4	93.5	104.1	146.3
Sweden	193	5	91.9	40.3	82.9	93.1	102.6	169.3
Switzerland	288	9	95.2	44.1	86.3	96.7	106.5	133.0
Turkey	581	445	81.0	19.1	67.0	84.4	96.9	144.8
Ukraine	79	11	90.7	21.7	76.1	94.4	105.8	158.4
United Kingdom	2795	154	91.3	23.5	82.4	93.0	101.8	155.2
Total	13591	1710	91.1	12.0	81.2	93.3	103.4	169.3

Note: Georgia has <5 patients aged 6-17 years at FEV_1 measurement and is excluded from the table.
Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

This table shows some descriptive statistics for FEV_1 in children, expressed as % of predicted. Note that patients who have had a transplant and children below 6 years of age have been excluded from the analyses.

Figure 4.1 FEV_1% of predicted: box-plot, by country and overall. Patients aged 6-17 years who have never had a transplant.



Note: Georgia has <5 patients aged 6-17 years at FEV_1 measurement and is excluded from the graph.

Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

This boxplot is a graphic representation of the FEV_1 in children, expressed as % of predicted, detailed in table 4.1. For each country, the borders of the box are the first and third quartile, the dash (black line crossing the blue box) is the median, the black dot is the mean and the whiskers (vertical lines with a T-shaped end) are the minimum and the maximum.

Table 4.2 FEV_1% of predicted: descriptive statistics, by country. Patients aged 18 years or older who have never had a transplant.

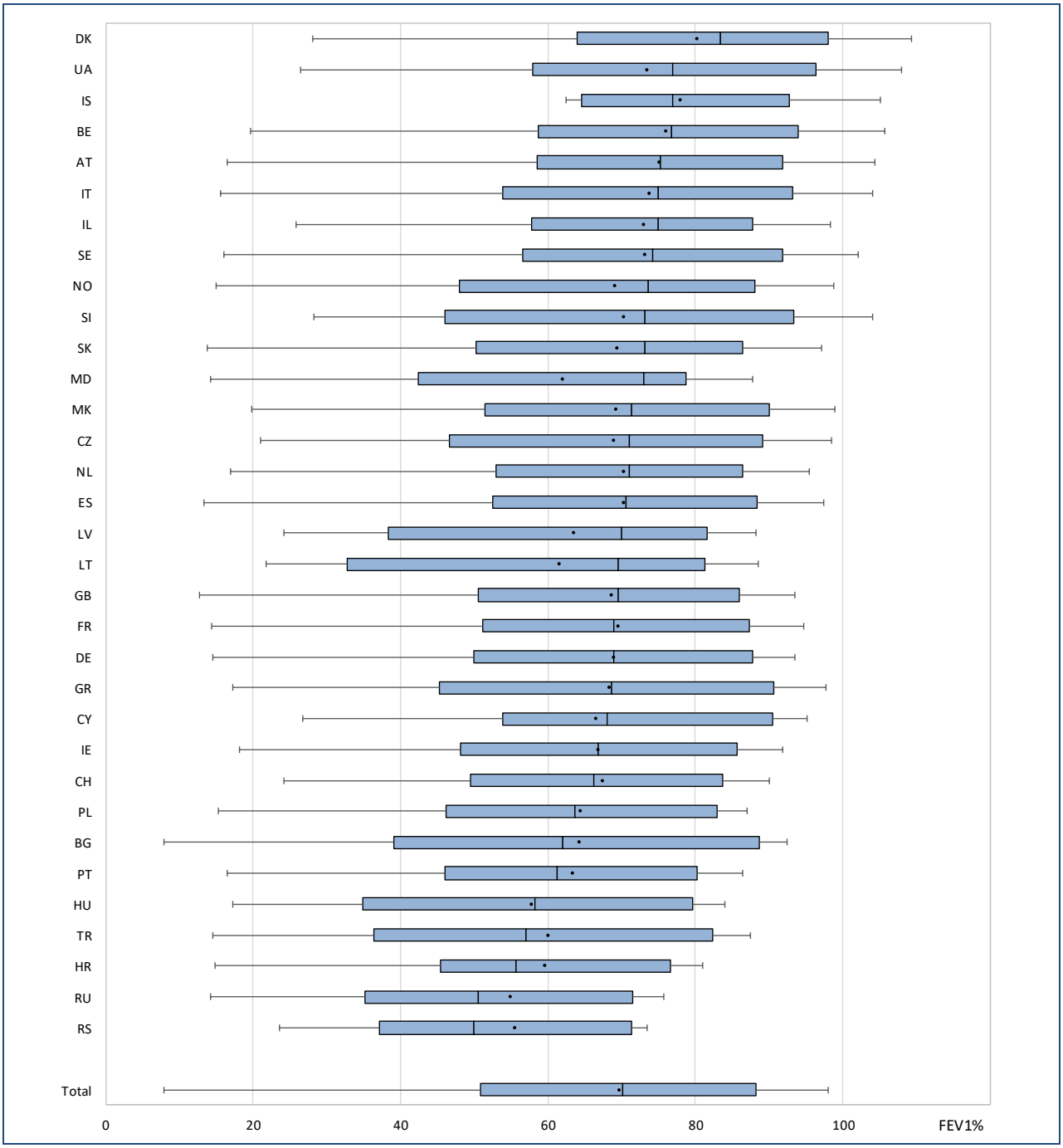
Country	N	N Miss	Mean (average FEV_1%)	Min	25th pctl (25% of patients have FEV_1% below this value)	Median (50% of patients have FEV_1% below this value)	75th pctl (75% of patients have FEV_1% below this value)	Max
Austria	343	3	75.1	16.5	58.6	75.2	91.9	126.9
Belgium	647	8	76.1	19.6	58.7	76.8	94.0	145.6
Bulgaria	75	3	64.2	7.9	39.1	62.0	88.7	110.8
Croatia	37	0	59.6	14.8	45.4	55.7	76.7	102.5
Cyprus	10	1	66.6	26.8	53.9	68.0	90.5	96.0
Czech Republic	242	6	68.9	21.0	46.6	71.1	89.1	122.3
Denmark	261	0	80.2	28.1	63.9	83.4	98.0	134.7
France	3115	74	69.5	14.3	51.1	69.0	87.4	134.0
Germany	3309	84	69.0	14.5	49.9	68.9	87.8	133.2
Greece	235	8	68.3	17.3	45.3	68.6	90.7	148.2
Hungary	148	15	57.8	17.3	34.8	58.2	79.6	110.6
Iceland	6	0	78.0	62.4	64.6	76.9	92.7	94.8
Ireland	552	69	66.9	18.2	48.1	66.9	85.7	132.5
Israel	314	3	73.0	25.9	57.8	75.0	87.8	133.7
Italy	2591	186	73.8	15.6	53.9	75.0	93.2	136.1
Latvia	12	1	63.5	24.2	38.4	70.0	81.6	99.4
Lithuania	14	0	61.5	21.8	32.7	69.5	81.3	96.8
Rep of Moldova	6	4	62.0	14.2	42.4	73.0	78.7	90.7
The Netherlands	832	4	70.3	16.9	53.0	71.0	86.4	128.8
North Macedonia	35	2	69.3	19.8	51.5	71.4	90.1	109.4
Norway	156	3	69.1	15.0	48.0	73.6	88.1	131.2
Poland	251	24	64.4	15.3	46.2	63.7	82.9	130.4
Portugal	120	16	63.4	16.5	46.0	61.2	80.3	118.7
Russian Federation	295	320	54.9	14.2	35.2	50.6	71.5	112.0
Serbia	50	0	55.5	23.5	37.2	49.9	71.3	115.3
Slovak Republic	122	2	69.4	13.7	50.2	73.1	86.5	133.0
Slovenia	39	0	70.3	28.2	46.1	73.2	93.4	111.5
Spain	953	19	70.3	13.3	52.5	70.6	88.4	136.8
Sweden	327	17	73.1	16.1	56.6	74.2	91.8	128.9
Switzerland	491	1	67.5	24.1	49.5	66.2	83.7	125.7
Turkey	146	82	60.1	14.5	36.4	57.0	82.3	112.2
Ukraine	26	3	73.5	26.5	58.0	77.0	96.4	112.6
United Kingdom	4991	223	68.7	12.7	50.6	69.5	86.0	171.8
Total	20761	1182	69.7	7.9	50.8	70.2	88.2	171.8

Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia, Luxembourg, Romania have <5 patients aged 18 years or more at FEV_1 measurement and are excluded from the table.

Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

This table shows some descriptive statistics for FEV_1 in adults, expressed as % of predicted. Note that patients who have had a transplant have been excluded from the analyses.

Figure 4.2 FEV_1% of predicted: boxplot, by country and overall. Patients aged 18 years or older who have never had a transplant.



Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia, Luxembourg, Romania have <5 patients aged 18 years or more at FEV_1 measurement and are excluded from the graph.

Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

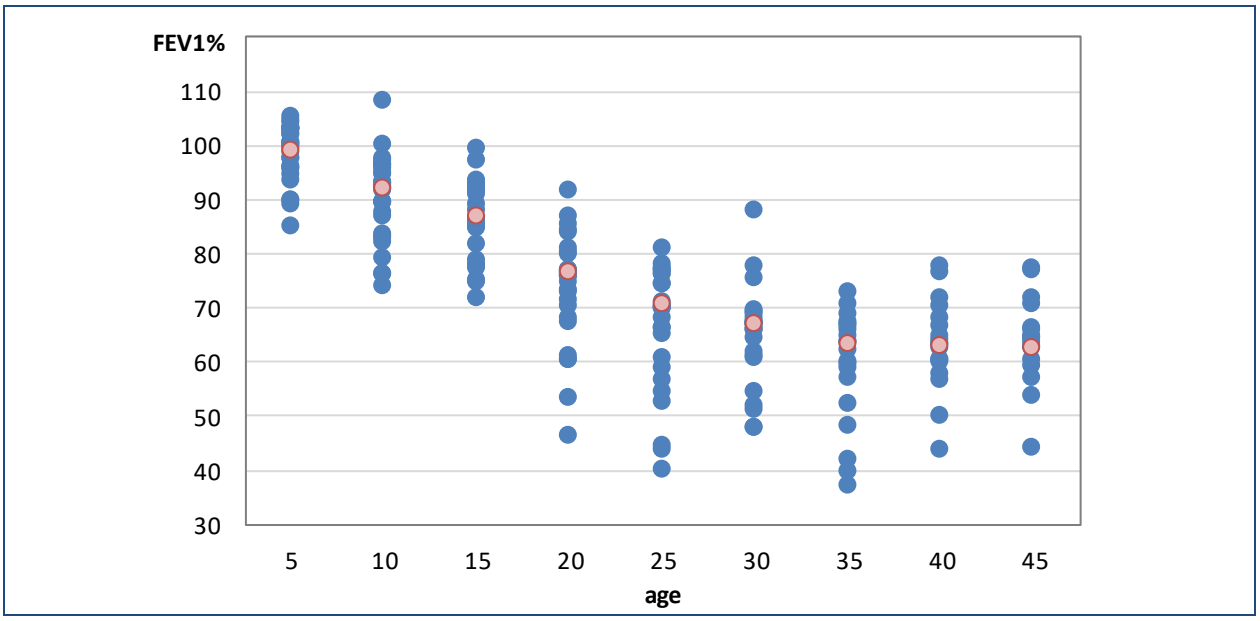
This boxplot is a graphic representation of the FEV_1 in adults, expressed as % of predicted detailed in table 4.2. For each country the borders of the box are first and third quartile, dash (black line crossing the blue box) is the median, the black dot is the mean and the whiskers (vertical lines with a T-shaped end) are the minimum and the maximum.

Table 4.3 FEV_1% of predicted: descriptive statistics by age group (patients aged 6 years or older) who have never had a transplant.

Age at FEV_1 measurement	N	N Miss	Mean	Min	25th pctl	Median	75th pctl	Max
6-9	4470	835	97.4	23.5	88.5	98.7	108.0	169.3
10-14	5854	604	89.6	19.2	80.3	91.8	101.7	165.3
15-19	5203	396	83.4	12.0	71.2	86.8	97.9	164.2
20-24	4653	269	74.4	13.2	58.2	76.5	91.4	136.8
25-29	4055	220	70.3	13.7	52.1	70.6	88.3	134.0
30-34	3291	193	67.1	7.9	49.0	66.6	84.7	135.2
35-39	2330	131	64.2	14.3	45.4	63.0	82.2	135.5
40-44	1642	94	64.6	12.7	45.9	62.6	82.4	145.6
45+	2854	150	64.4	12.7	45.8	62.5	81.7	171.8

This table shows FEV_1% by age group for the total dataset. The median values reported in this table are shown as red dots in Figure 4.3.

Figure 4.3 Median FEV_1% of predicted by age group and by country. Patients aged 6 years or older who have never had a transplant.



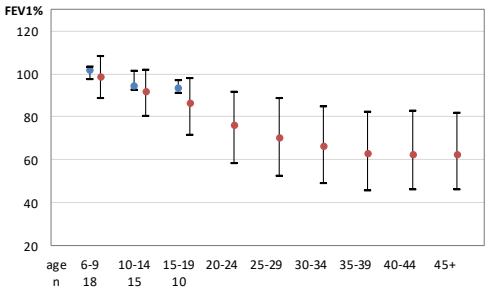
Note: We excluded from the analyses those age groups where the number of patients was <10.

This graph shows the median FEV_1% (the value that separates the highest and lowest half of the patients) by age group. Each country is represented by a dot (in blue) and the overall estimate is in red. The general pattern shows that the FEV_1% slowly decreases until the age of 35-39, and then levels out. The patients in the oldest age groups are patients that survived and may therefore represent the patients with less disease severity. There is considerable variability between countries.

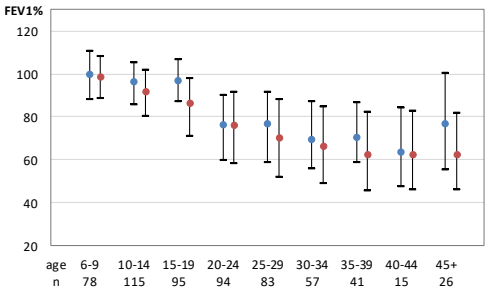
Figure 4.4 Quartiles of FEV_1% of predicted by age group and by country. Patients aged 6 years or older and who have never had a transplant.

The figures below show the FEV_1% in different age groups, separately for each country. The dot shows the median, and the whiskers show the 25th and 75th percentiles (the median, the 25th percentile and the 75th percentile are collectively named "quartiles"). In blue are the quartiles for the country, in red are the pooled quartiles computed on all other countries (i.e. excluding that country). We did not compute quartiles where the number of patients is <10 in an age group, so there are no blue dots for those age groups (the number of patients in each age group is shown below the horizontal axis). We therefore excluded Armenia, Cyprus, Georgia, Iceland, Latvia, Lithuania, Luxembourg and Republic of Moldova from the graphs because none of the age groups had more than 10 patients.

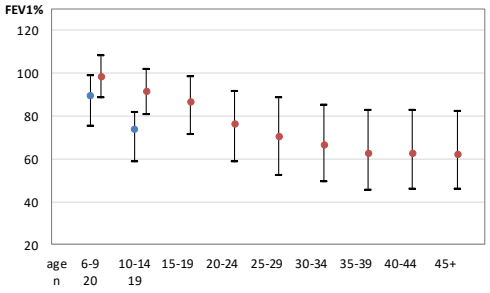
Quartiles of FEV_1%: Albania



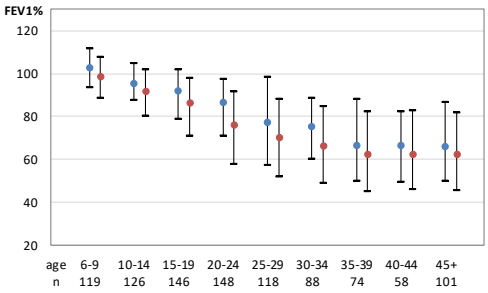
Quartiles of FEV_1%: Austria



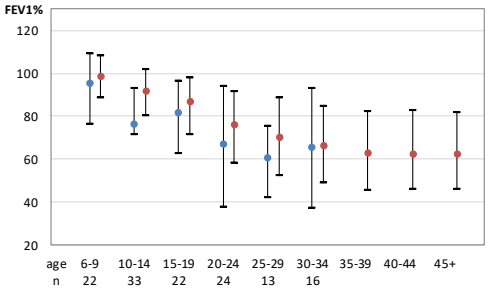
Quartiles of FEV_1%: Belarus



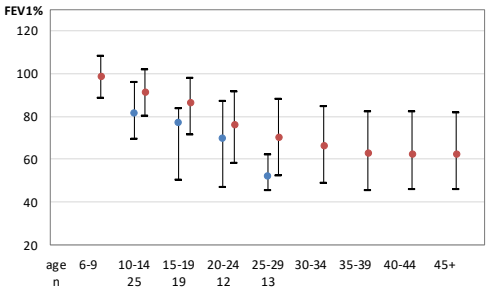
Quartiles of FEV_1%: Belgium



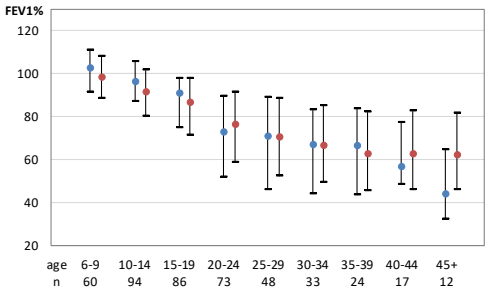
Quartiles of FEV_1%: Bulgaria



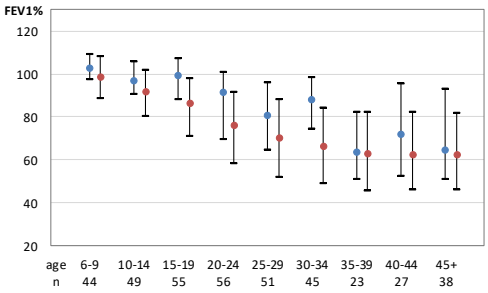
Quartiles of FEV_1%: Croatia



Quartiles of FEV1%: Czech Republic

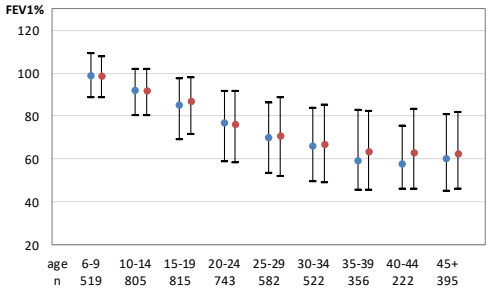


Quartiles of FEV1%: Denmark

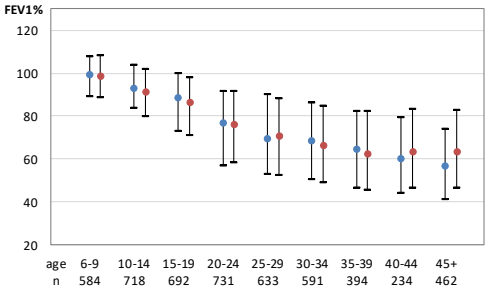


[figure 4.4 continued]

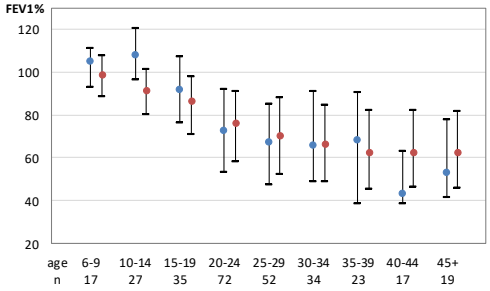
Quartiles of FEV_1%: France



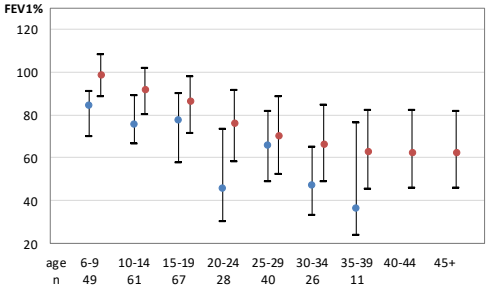
Quartiles of FEV_1%: Germany



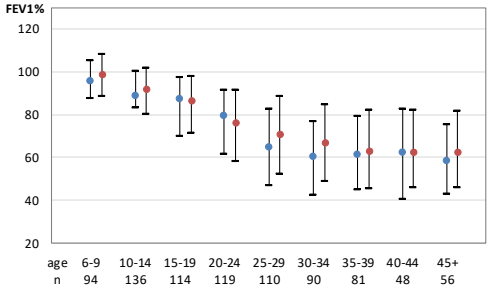
Quartiles of FEV_1%: Greece



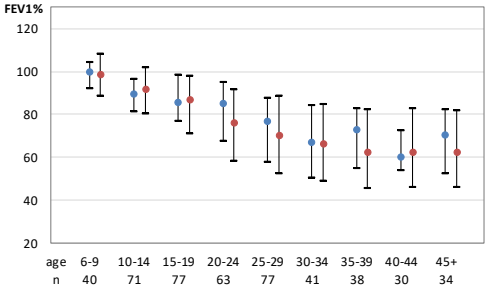
Quartiles of FEV_1%: Hungary



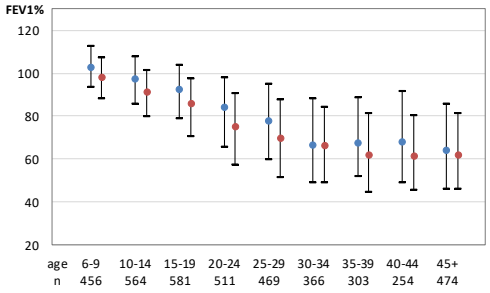
Quartiles of FEV_1%: Ireland



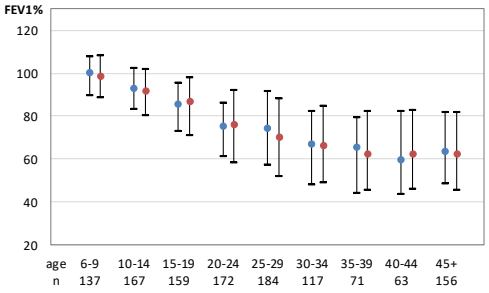
Quartiles of FEV_1%: Israel



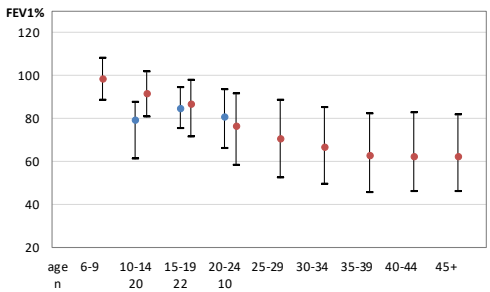
Quartiles of FEV_1%: Italy



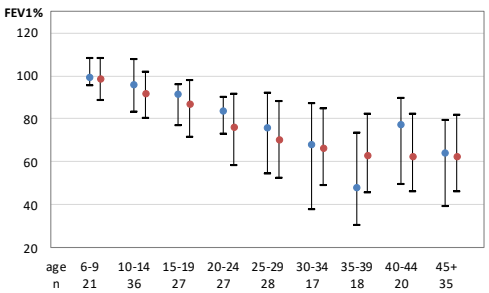
Quartiles of FEV_1%: The Netherlands



Quartiles of FEV_1%: North Macedonia

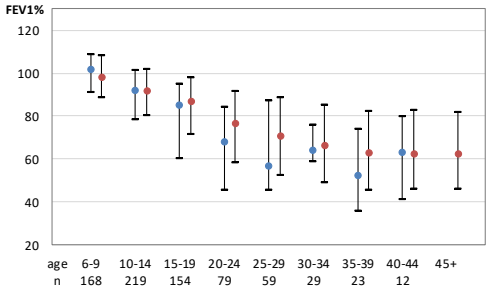


Quartiles of FEV_1%: Norway

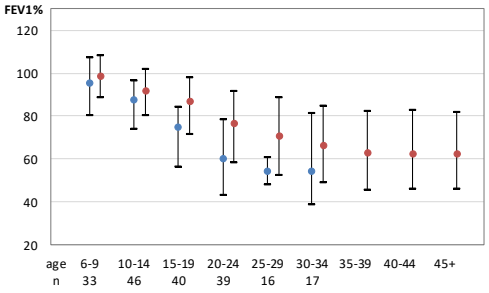


[figure 4.4 continued]

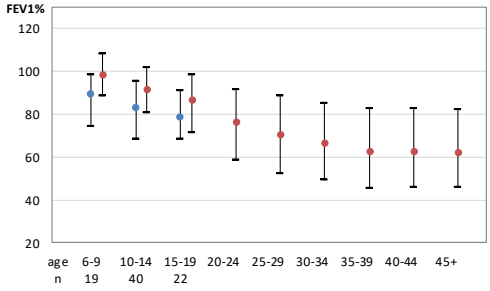
Quartiles of FEV_1%: Poland



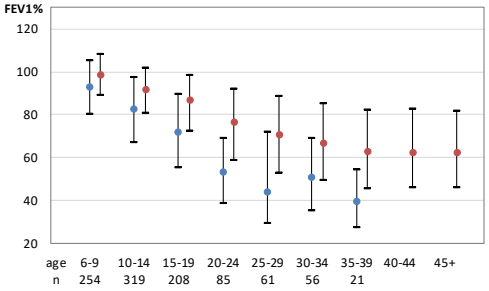
Quartiles of FEV_1%: Portugal



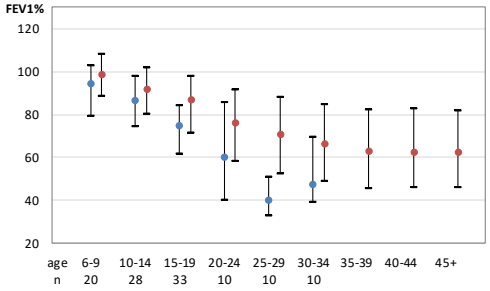
Quartiles of FEV_1%: Romania



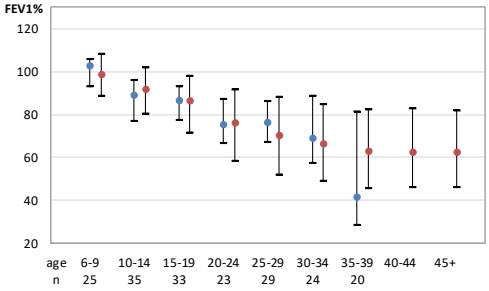
Quartiles of FEV1%: Russian Federation



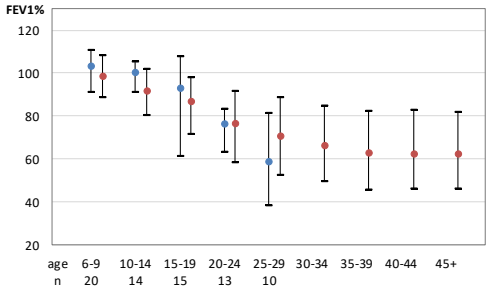
Quartiles of FEV_1%: Serbia



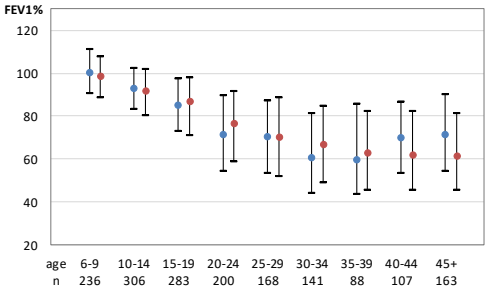
Quartiles of FEV_1%: Slovak Republic



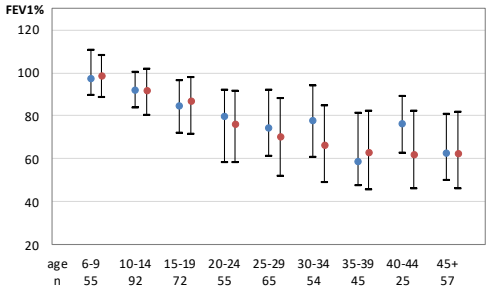
Quartiles of FEV_1%: Slovenia



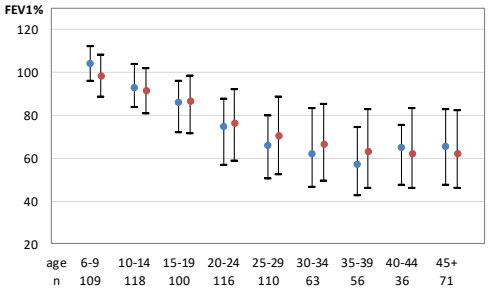
Quartiles of FEV_1%: Spain



Quartiles of FEV_1%: Sweden

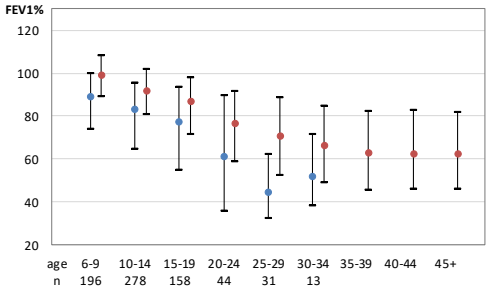


Quartiles of FEV_1%: Switzerland

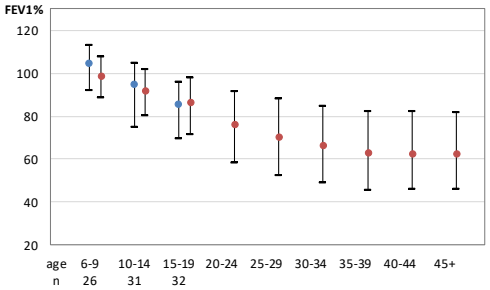


[figure 4.4 continued]

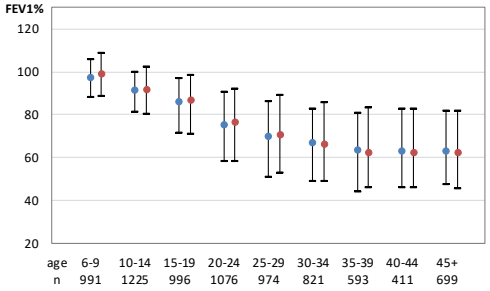
Quartiles of FEV_1%: Turkey



Quartiles of FEV_1%: Ukraine

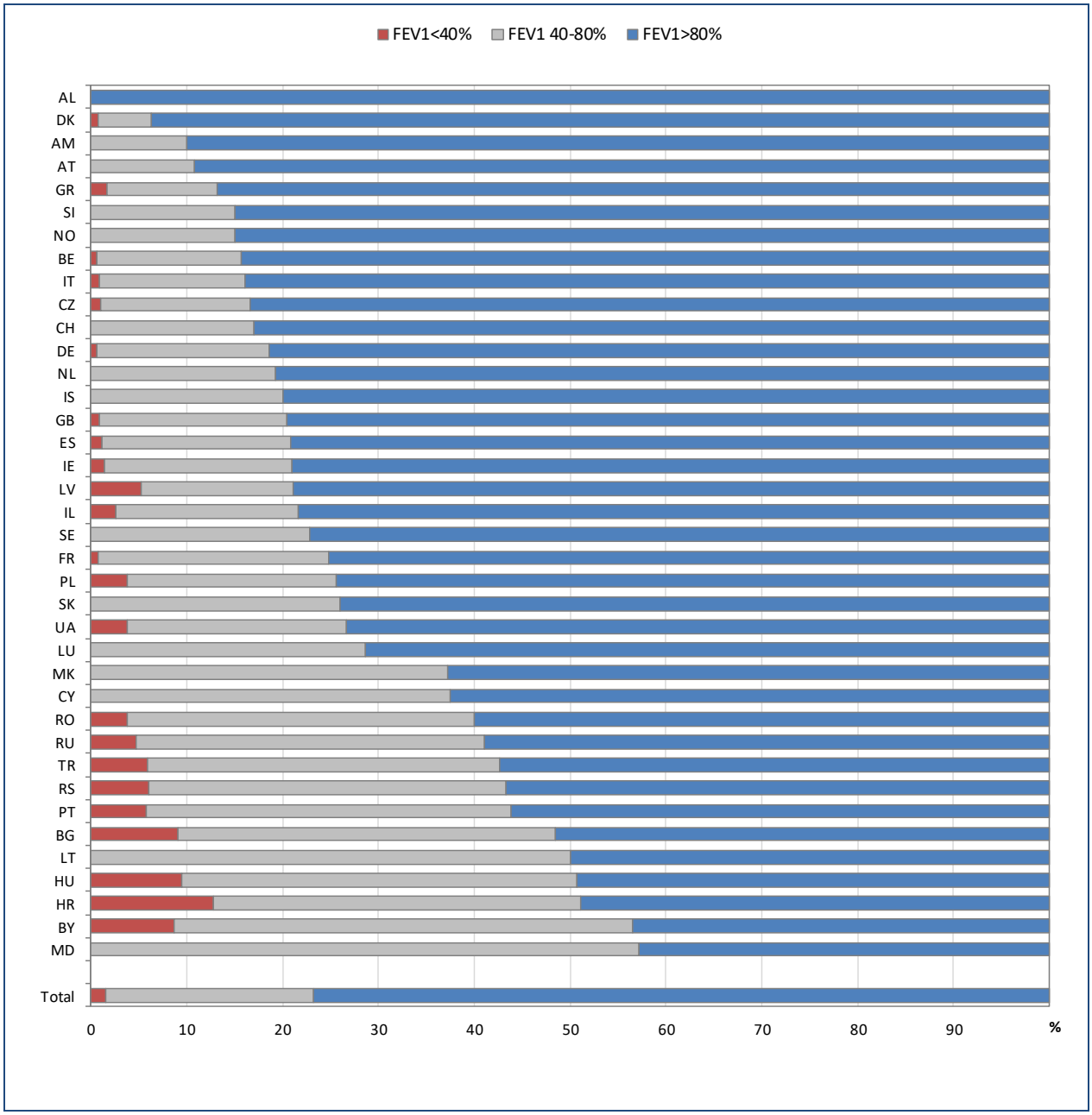


Quartiles of FEV_1%: United Kingdom



Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

Figure 4.5 FEV_1% of predicted according to severity group and age group, by country and overall. Patients aged 6-17 years who have never had a transplant.

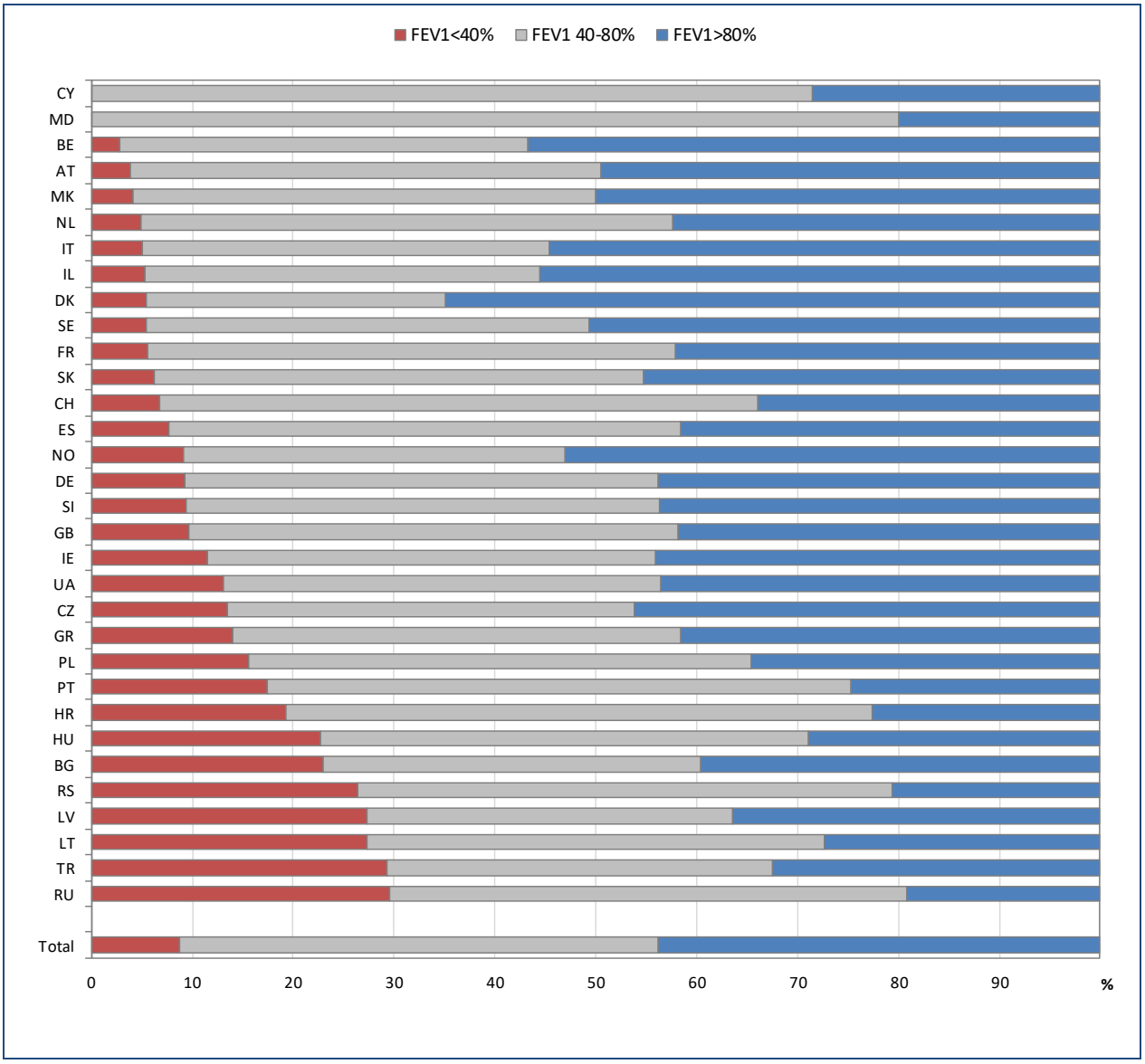


Note: Georgia has < 5 patients aged 6-17 years at FEV_1 measurement and is excluded from the graph.

Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

Figures 4.5, 4.6 and 4.7 show the FEV_1% by severity group, by country and overall. Patients with an FEV_1% higher than 80% are generally considered to have mild lung disease, patients with FEV_1% between 80% and 40% moderate lung disease, and patients with FEV_1 <40% severe lung disease. However, since a 10-year-old child with a lung function of 50% has considerably worse lung disease than a 50-year-old patient with the same FEV_1%, and the age distribution is not the same in all countries, we have chosen to present children (Figure 4.5) and adults (Figure 4.6 and 4.7) separately.

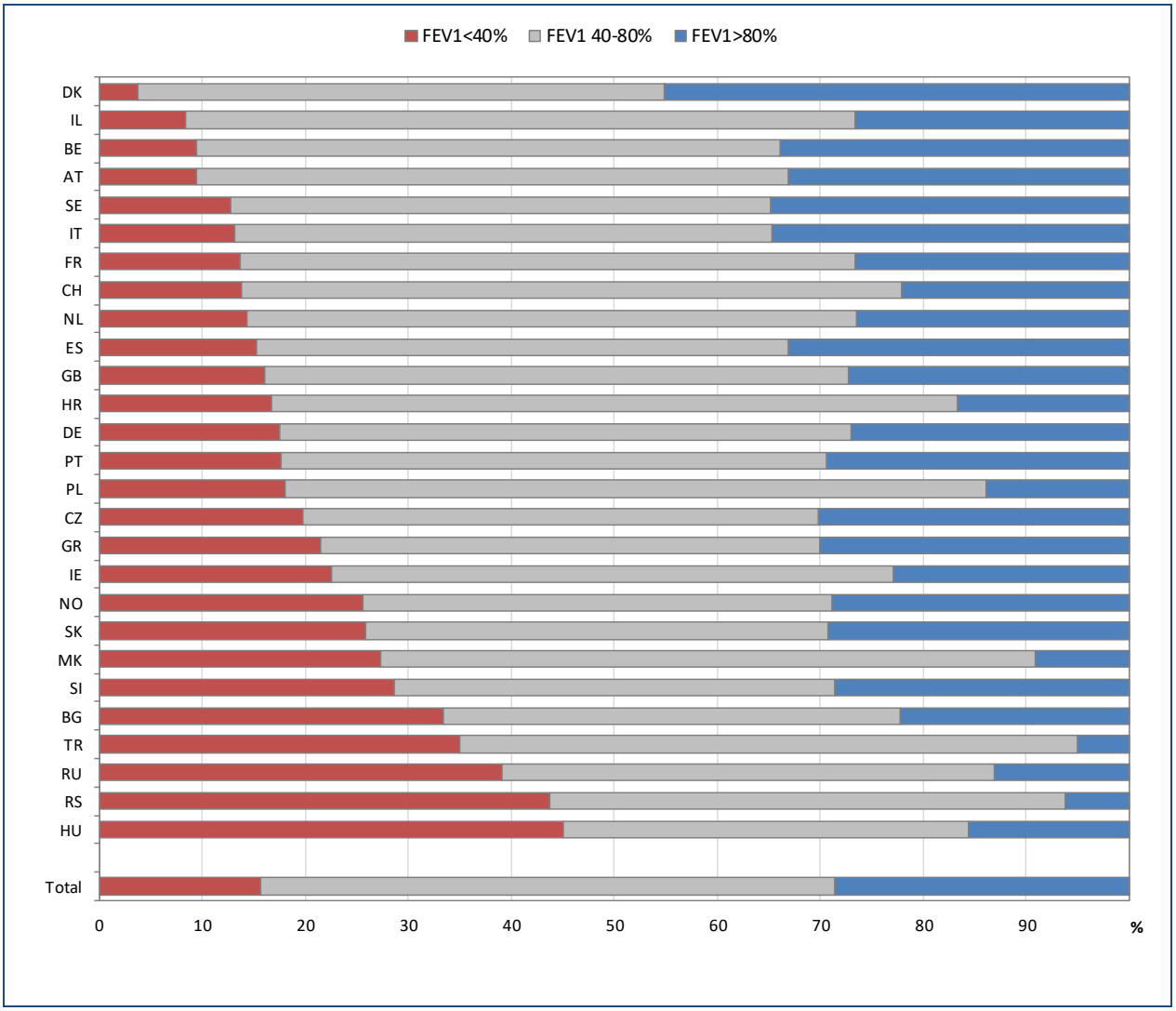
Figure 4.6 FEV_1% of predicted according to severity group and age group, by country and overall. Patients aged 18-29 years who have never had a transplant.



Note: Belarus and Georgia have 0% coverage for adults and are excluded from the graph.
Albania, Armenia, Iceland, Luxembourg, Romania have < 5 patients aged 18-29 years at FEV_1 measurement and are excluded from the graph.

Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

Figure 4.7 FEV_1% of predicted according to severity group and age group, by country and overall. Patients aged 30 years or older who have never had a transplant.



Note: Belarus and Georgia have 0% coverage for adults and are excluded from the graph.
Albania, Armenia, Cyprus, Iceland, Latvia, Lithuania, Luxembourg, Rep of Moldova, Romania and Ukraine have < 5 patients aged 30 years or more at FEV_1 measurement and are excluded from the graph.

Note: The United Kingdom reports best FEV_1 from the annual review, which is the time period between data sets and is not necessarily a calendar year. Therefore, in some cases measurement of FEV_1 could be from the previous calendar year.

5. Microbiology

We collect data on three chronic infections *Pseudomonas aeruginosa*, *Burkholderia cepacia complex species* and *Staphylococcus aureus* as well as the occurrence of *non-tuberculous mycobacteria (NTM)*, *Stenotrophomonas maltophilia, Achromobacter species, Haemophilus Influenzae* and methicillin-resistant *Staphylococcus aureus (MRSA)*.

In the microbiology category, discrepancies exist between the ECFSPR definition of chronicity and those of the national registries. The ECFSPR definition of chronic infection (see Appendix 3, page 152) is the following:

Patient should be defined as chronically infected if he/she fulfils the criteria now or has done in recent years and the physician has no reason to think the status has changed, when:

a. >50% of respiratory samples collected during the last 12 months are positive; at least 4 samples collected during that period (modified Leeds criteria for chronic infection);

   and/or

b. significantly raised bacteria-specific antibodies according to local laboratories are present.

When minor differences exist, the alternative definition is in a footnote; when differences are major, or if the variable is not collected at all, the variable has been set to missing for that country.

Table 5.1 Prevalence of bacterial infection in children seen in 2020 who have never had a transplant, by country and overall.

Country	Chronic *Pseudomonas aeruginosa* number (%)			Chronic *Burkholderia cepacia complex species* number (%)			*Haemophilus influenzae* number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	1 (1.30)	53 (68.83)	23 (29.87)	2 (2.60)	75 (97.40)	0 (0.00)	3 (3.90)	72 (93.51)	2 (2.60)
Armenia	0 (0.00)	14 (58.33)	10 (41.67)	4 (16.67)	20 (83.33)	0 (0.00)	3 (12.50)	20 (83.33)	1 (4.17)
Austria	2 (0.53)	351 (92.61)	26 (6.86)	1 (0.26)	376 (99.21)	2 (0.53)	2 (0.53)	270 (71.24)	107 (28.23)
Belarus	0 (0.00)	116 (77.33)	34 (22.67)	0 (0.00)	146 (97.33)	4 (2.67)	0 (0.00)	140 (93.33)	10 (6.67)
Belgium	1 (0.22)	435 (93.55)	29 (6.24)	1 (0.22)	460 (98.92)	4 (0.86)	0 (0.00)	348 (74.84)	117 (25.16)
Bulgaria	0 (0.00)	74 (66.07)	38 (33.93)	0 (0)	112 (100)	0 (0)	1 (0.89)	107 (95.54)	4 (3.57)
Croatia	9 (11.25)	59 (73.75)	12 (15.00)	9 (11.25)	71 (88.75)	0 (0.00)	6 (7.50)	69 (86.25)	5 (6.25)
Cyprus	2 (20.00)	5 (50.00)	3 (30.00)	2 (20.00)	8 (80.00)	0 (0.00)	0 (0.00)	4 (40.00)	6 (60.00)
Czech Republic	5 (1.52)	302 (91.79)	22 (6.69)	5 (1.52)	322 (97.87)	2 (0.61)	5 (1.52)	281 (85.41)	43 (13.07)
Denmark	0 (0.00)	189 (92.65)	15 (7.35)	0 (0.00)	202 (99.02)	2 (0.98)	0 (0.00)	114 (55.88)	90 (44.12)
France	0 (0.00)	2502 (91.75)	225 (8.25)	0 (0.00)	2708 (99.30)	19 (0.70)	0 (0.00)	2295 (84.16)	432 (15.84)
Georgia	4 (5.56)	44 (61.11)	24 (33.33)	3 (4.17)	69 (95.83)	0 (0.00)	1 (1.39)	71 (98.61)	0 (0.00)
Germany	35 (1.32)	2373 (89.18)	253 (9.51)	31 (1.16)	2610 (98.08)	20 (0.75)	24 (0.90)	2076 (78.02)	561 (21.08)
Greece	0 (0.00)	87 (91.58)	8 (8.42)	1 (1.05)	94 (98.95)	0 (0.00)	1 (1.05)	94 (98.95)	0 (0.00)
Hungary	0 (0.00)	166 (66.94)	82 (33.06)	0 (0.00)	246 (99.19)	2 (0.81)	248 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	7 (87.50)	1 (12.50)	0 (0)	8 (100)	0 (0)	0 (0.00)	6 (75.00)	2 (25.00)
Ireland[1]	0 (0.00)	466 (93.95)	30 (6.05)	0 (0.00)	490 (98.79)	6 (1.21)	0 (0.00)	415 (83.67)	81 (16.33)
Israel	7 (4.12)	129 (75.88)	34 (20.00)	7 (4.12)	163 (95.88)	0 (0.00)	7 (4.12)	140 (82.35)	23 (13.53)
Italy	1 (0.04)	2109 (92.74)	164 (7.21)	2 (0.09)	2270 (99.82)	2 (0.09)	2 (0.09)	1972 (86.72)	300 (13.19)
Latvia	4 (12.12)	24 (72.73)	5 (15.15)	4 (12.12)	29 (87.88)	0 (0.00)	5 (15.15)	17 (51.52)	11 (33.33)
Lithuania	2 (14.29)	9 (64.29)	3 (21.43)	2 (14.29)	11 (78.57)	1 (7.14)	2 (14.29)	11 (78.57)	1 (7.14)
Luxembourg	0 (0.00)	19 (90.48)	2 (9.52)	1 (4.76)	20 (95.24)	0 (0.00)	0 (0.00)	15 (71.43)	6 (28.57)

[1] Ireland: chronicity for *Pseudomonas aeruginosa* and *Burkholderia* cepacia *complex species* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.

[table 5.1 continued]

Country	Chronic *Pseudomonas aeruginosa* number (%)			Chronic *Burkholderia cepacia complex species* number (%)			*Haemophilus influenzae* number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	21 (55.26)	17 (44.74)	38 (100)	0 (0)	0 (0)	0 (0)	38 (100)	0 (0)
The Netherlands	14 (2.62)	473 (88.41)	48 (8.97)	9 (1.68)	521 (97.38)	5 (0.93)	43 (8.04)	407 (76.07)	85 (15.89)
North Macedonia	0 (0.00)	61 (77.22)	18 (22.78)	0 (0.00)	77 (97.47)	2 (2.53)	0 (0.00)	77 (97.47)	2 (2.53)
Norway	1 (0.83)	115 (95.83)	4 (3.33)	1 (0.83)	118 (98.33)	1 (0.83)	1 (0.83)	84 (70.00)	35 (29.17)
Poland	8 (0.97)	723 (87.32)	97 (11.71)	11 (1.33)	809 (97.71)	8 (0.97)	10 (1.21)	689 (83.21)	129 (15.58)
Portugal	3 (1.69)	140 (78.65)	35 (19.66)	2 (1.12)	172 (96.63)	4 (2.25)	2 (1.12)	133 (74.72)	43 (24.16)
Romania	2 (0.91)	147 (67.12)	70 (31.96)	4 (1.83)	214 (97.72)	1 (0.46)	26 (11.87)	188 (85.84)	5 (2.28)
Russian Federation	32 (1.88)	1183 (69.47)	488 (28.66)	42 (2.47)	1597 (93.78)	64 (3.76)	37 (2.17)	1595 (93.66)	71 (4.17)
Serbia	0 (0.00)	72 (72.73)	27 (27.27)	0 (0.00)	92 (92.93)	7 (7.07)	0 (0.00)	44 (44.44)	55 (55.56)
Slovak Republic	0 (0.00)	94 (76.42)	29 (23.58)	0 (0.00)	122 (99.19)	1 (0.81)	1 (0.81)	107 (86.99)	15 (12.20)
Slovenia	0 (0.00)	48 (92.31)	4 (7.69)	0 (0)	52 (100)	0 (0)	0 (0.00)	28 (53.85)	24 (46.15)
Spain	11 (1.02)	938 (87.26)	126 (11.72)	9 (0.84)	1048 (97.49)	18 (1.67)	4 (0.37)	894 (83.16)	177 (16.47)
Sweden	0 (0.00)	236 (89.06)	29 (10.94)	0 (0.00)	264 (99.62)	1 (0.38)	3 (1.13)	190 (71.70)	72 (27.17)
Switzerland	4 (0.94)	382 (90.09)	38 (8.96)	3 (0.71)	417 (98.35)	4 (0.94)	1 (0.24)	323 (76.18)	100 (23.58)
Turkey	25 (1.38)	1507 (83.40)	275 (15.22)	34 (1.88)	1768 (97.84)	5 (0.28)	0 (0.00)	1732 (95.85)	75 (4.15)
Ukraine	7 (5.26)	80 (60.15)	46 (34.59)	9 (6.77)	118 (88.72)	6 (4.51)	7 (5.26)	114 (85.71)	12 (9.02)
United Kingdom[2]	5 (0.12)	3980 (94.20)	240 (5.68)	5 (0.12)	4153 (98.30)	67 (1.59)	5 (0.12)	3405 (80.59)	815 (19.29)
Total	185 (0.82)	19733 (87.50)	2634 (11.68)	242 (1.07)	22052 (97.78)	258 (1.14)	450 (2.00)	18585 (82.41)	3517 (15.60)

[2] United Kingdom: chronicity for *Pseudomonas aeruginosa* and *Burkholderia cepacia complex species* is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

Table 5.1 shows, separately by country, the frequency of chronic *Pseudomonas aeruginosa*, chronic *Burkholderia cepacia complex species* and *Haemophilus influenzae* in children. The number of missing values is also included. The identification rate of *Burkholderia cepacia complex species* in particular may also be influenced by differences in culture techniques employed.

Table 5.2 Prevalence of bacterial infection in adults seen in 2020 who have never had a transplant, by country and overall.

Country	Chronic *Pseudomonas aeruginosa* number (%)			Chronic *Burkholderia cepacia complex species* number (%)			*Haemophilus influenzae* number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	2 (0.56)	202 (56.58)	153 (42.86)	3 (0.84)	334 (93.56)	20 (5.60)	6 (1.68)	304 (85.15)	47 (13.17)
Belgium	10 (1.49)	438 (65.47)	221 (33.03)	6 (0.90)	643 (96.11)	20 (2.99)	0 (0.00)	598 (89.39)	71 (10.61)
Bulgaria	0 (0.00)	27 (33.33)	54 (66.67)	0 (0)	81 (100)	0 (0)	0 (0.00)	79 (97.53)	2 (2.47)
Croatia	2 (4.55)	10 (22.73)	32 (72.73)	2 (4.55)	42 (95.45)	0 (0.00)	2 (4.55)	41 (93.18)	1 (2.27)
Cyprus	5 (41.67)	3 (25.00)	4 (33.33)	5 (41.67)	7 (58.33)	0 (0.00)	1 (8.33)	4 (33.33)	7 (58.33)
Czech Republic	8 (3.15)	165 (64.96)	81 (31.89)	9 (3.54)	212 (83.46)	33 (12.99)	8 (3.15)	233 (91.73)	13 (5.12)
Denmark	0 (0.00)	146 (55.09)	119 (44.91)	0 (0.00)	242 (91.32)	23 (8.68)	0 (0.00)	225 (84.91)	40 (15.09)
France	0 (0.00)	2187 (66.05)	1124 (33.95)	0 (0.00)	3231 (97.58)	80 (2.42)	0 (0.00)	2961 (89.43)	350 (10.57)
Germany	170 (4.89)	1559 (44.84)	1748 (50.27)	170 (4.89)	3198 (91.98)	109 (3.13)	179 (5.15)	3067 (88.21)	231 (6.64)
Greece	16 (5.63)	73 (25.7)	195 (68.66)	17 (5.99)	266 (93.66)	1 (0.35)	17 (5.99)	266 (93.66)	1 (0.35)
Hungary	3 (1.62)	80 (43.24)	102 (55.14)	5 (2.70)	173 (93.51)	7 (3.78)	185 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	4 (66.67)	2 (33.33)	0 (0)	6 (100)	0 (0)	0 (0)	6 (100)	0 (0)
Ireland[1]	0 (0.00)	410 (64.57)	225 (35.43)	0 (0.00)	619 (97.48)	16 (2.52)	0 (0.00)	606 (95.43)	29 (4.57)
Israel	17 (5.04)	145 (43.03)	175 (51.93)	17 (5.04)	315 (93.47)	5 (1.48)	18 (5.34)	300 (89.02)	19 (5.64)
Italy	6 (0.19)	1951 (60.87)	1248 (38.94)	6 (0.19)	3111 (97.07)	88 (2.75)	6 (0.19)	3095 (96.57)	104 (3.24)
Latvia	0 (0.00)	6 (46.15)	7 (53.85)	0 (0.00)	12 (92.31)	1 (7.69)	1 (7.69)	12 (92.31)	0 (0.00)
Lithuania	0 (0.00)	18 (90.00)	2 (10.00)	0 (0.00)	17 (85.00)	3 (15.00)	0 (0.00)	19 (95.00)	1 (5.00)

Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia, Luxembourg have < 5 patients aged 18 years or more at 31/12/2020 and are not shown in this table but are considered in the total.

[1] Ireland: chronicity for *Pseudomonas aeruginosa* and *Burkholderia cepacia complex species* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.

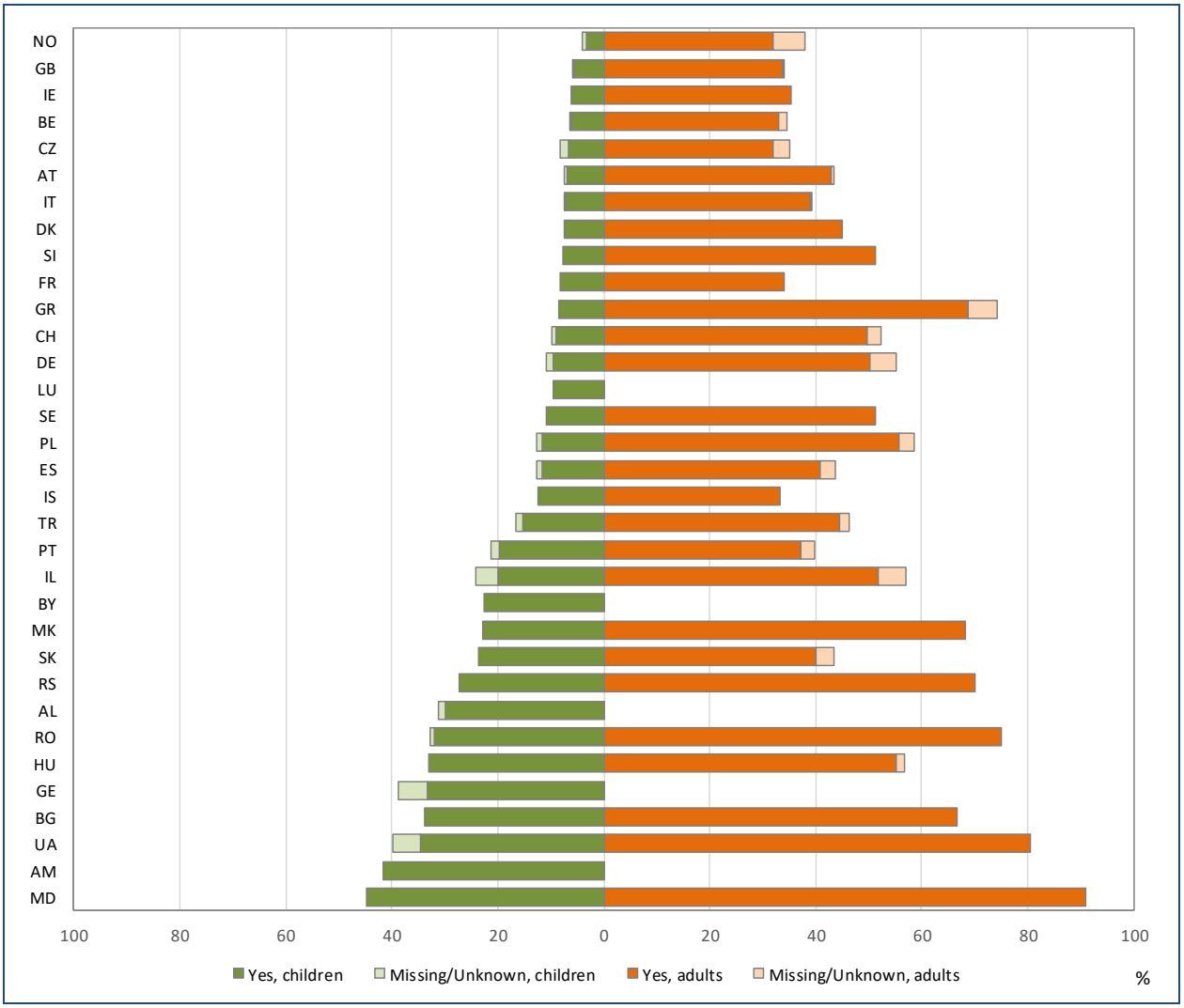
[table 5.2 continued]

Country	Chronic *Pseudomonas aeruginosa* number (%)			Chronic *Burkholderia cepacia complex species* number (%)			*Haemophilus influenzae* number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	1 (9.09)	10 (90.91)	11 (100)	0 (0)	0 (0)	1 (9.09)	10 (90.91)	0 (0.00)
The Netherlands	97 (10.79)	395 (43.94)	407 (45.27)	95 (10.57)	784 (87.21)	20 (2.22)	71 (7.90)	736 (81.87)	92 (10.23)
North Macedonia	0 (0.00)	13 (31.71)	28 (68.29)	0 (0)	41 (100)	0 (0)	0 (0)	41 (100)	0 (0)
Norway	10 (5.92)	105 (62.13)	54 (31.95)	11 (6.51)	150 (88.76)	8 (4.73)	7 (4.14)	143 (84.62)	19 (11.24)
Poland	9 (2.76)	135 (41.41)	182 (55.83)	9 (2.76)	300 (92.02)	17 (5.21)	10 (3.07)	296 (90.80)	20 (6.13)
Portugal	4 (2.61)	92 (60.13)	57 (37.25)	5 (3.27)	138 (90.20)	10 (6.54)	5 (3.27)	128 (83.66)	20 (13.07)
Romania	0 (0.00)	2 (25.00)	6 (75.00)	0 (0.00)	7 (87.50)	1 (12.50)	0 (0)	8 (100)	0 (0)
Russian Federation	220 (33.74)	70 (10.74)	362 (55.52)	403 (61.81)	169 (25.92)	80 (12.27)	451 (69.17)	190 (29.14)	11 (1.69)
Serbia	0 (0.00)	17 (29.82)	40 (70.18)	0 (0.00)	47 (82.46)	10 (17.54)	0 (0.00)	37 (64.91)	20 (35.09)
Slovak Republic	5 (3.57)	79 (56.43)	56 (40.00)	5 (3.57)	124 (88.57)	11 (7.86)	5 (3.57)	125 (89.29)	10 (7.14)
Slovenia	0 (0.00)	20 (48.78)	21 (51.22)	0 (0.00)	40 (97.56)	1 (2.44)	4 (9.76)	36 (87.80)	1 (2.44)
Spain	32 (2.98)	604 (56.29)	437 (40.73)	41 (3.82)	954 (88.91)	78 (7.27)	34 (3.17)	976 (90.96)	63 (5.87)
Sweden	0 (0.00)	170 (48.71)	179 (51.29)	0 (0.00)	341 (97.71)	8 (2.29)	18 (5.16)	287 (82.23)	44 (12.61)
Switzerland	13 (2.59)	239 (47.61)	250 (49.80)	15 (2.99)	466 (92.83)	21 (4.18)	16 (3.19)	418 (83.27)	68 (13.55)
Turkey	4 (1.59)	135 (53.78)	112 (44.62)	2 (0.80)	247 (98.41)	2 (0.80)	0 (0.00)	238 (94.82)	13 (5.18)
Ukraine	0 (0.00)	7 (19.44)	29 (80.56)	2 (5.56)	32 (88.89)	2 (5.56)	2 (5.56)	33 (91.67)	1 (2.78)
United Kingdom[2]	3 (0.06)	3551 (66.21)	1809 (33.73)	3 (0.06)	5106 (95.21)	254 (4.74)	3 (0.06)	5061 (94.37)	299 (5.58)
Total	636 (2.74)	13062 (56.22)	9536 (41.04)	843 (3.63)	21462 (92.37)	929 (4.00)	1051 (4.52)	20586 (88.60)	1597 (6.87)

[2] United Kingdom: chronicity for *Pseudomonas aeruginosa* and *Burkholderia cepacia complex species* is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

Table 5.2 shows, separately by country, the frequency of chronic *Pseudomonas aeruginosa*, chronic *Burkholderia cepacia complex species* and *Haemophilus influenza* in adults. The number of missing values is also included.

Figure 5.1 Prevalence of chronic Pseudomonas aeruginosa infection in children and adults seen in 2020 who have never had a transplant, by country.

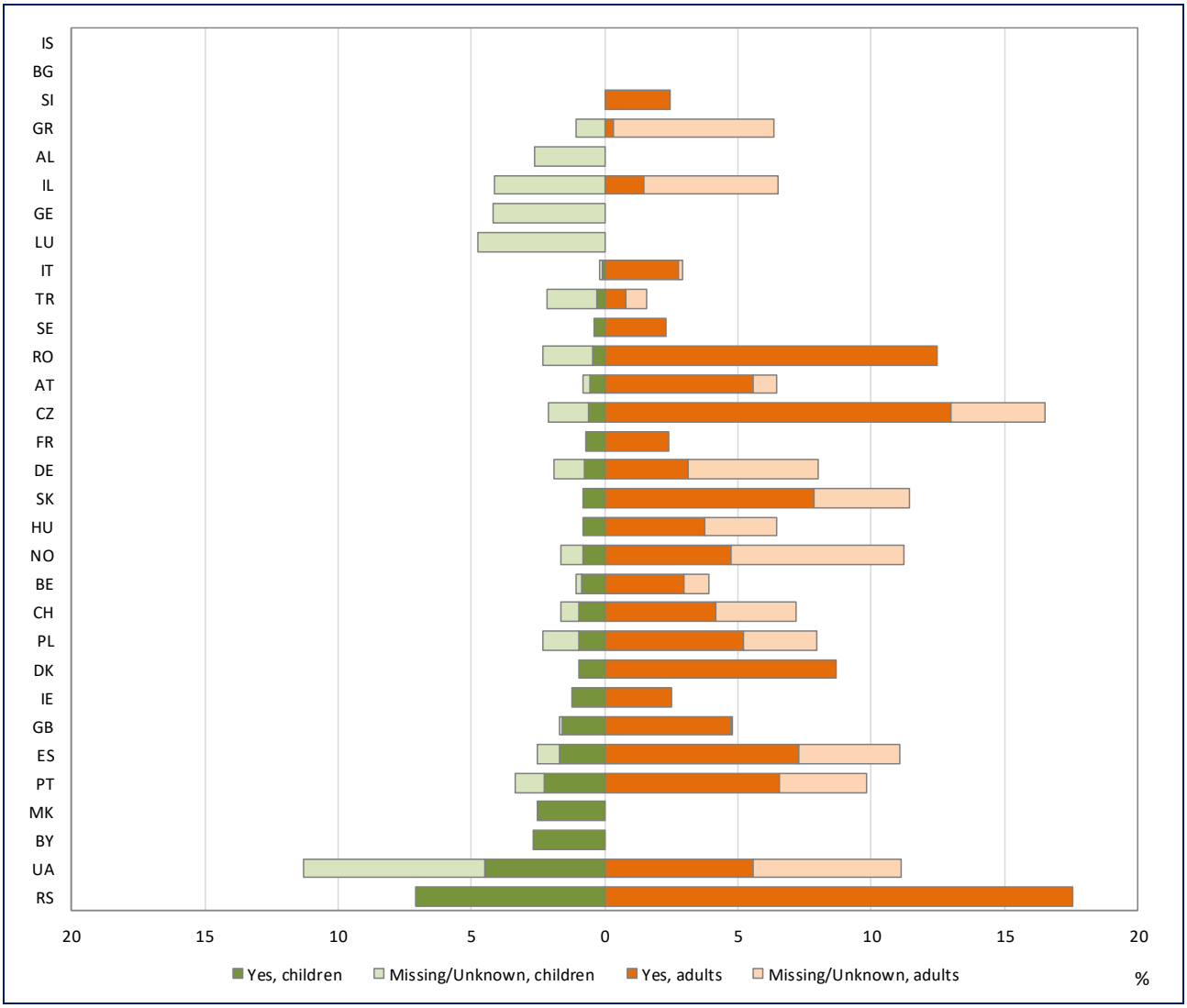


Note: We excluded from the graph the countries for which the information on *Pseudomonas aeruginosa* is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

Note: Ireland: chronicity for *Pseudomonas aeruginosa* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.
United Kingdom: chronicity for *Pseudomonas aeruginosa* is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

This graph represents the percentage of people with chronic *Pseudomonas aeruginosa* infection (in dark colours) and the percentage of people where information on chronic *Pseudomonas aeruginosa* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults. This is a frequent infection, but prevalence varies considerably between countries.

Figure 5.2 Prevalence of chronic Burkholderia cepacia complex species infection in children and adults seen in 2020 who have never had a transplant, by country.

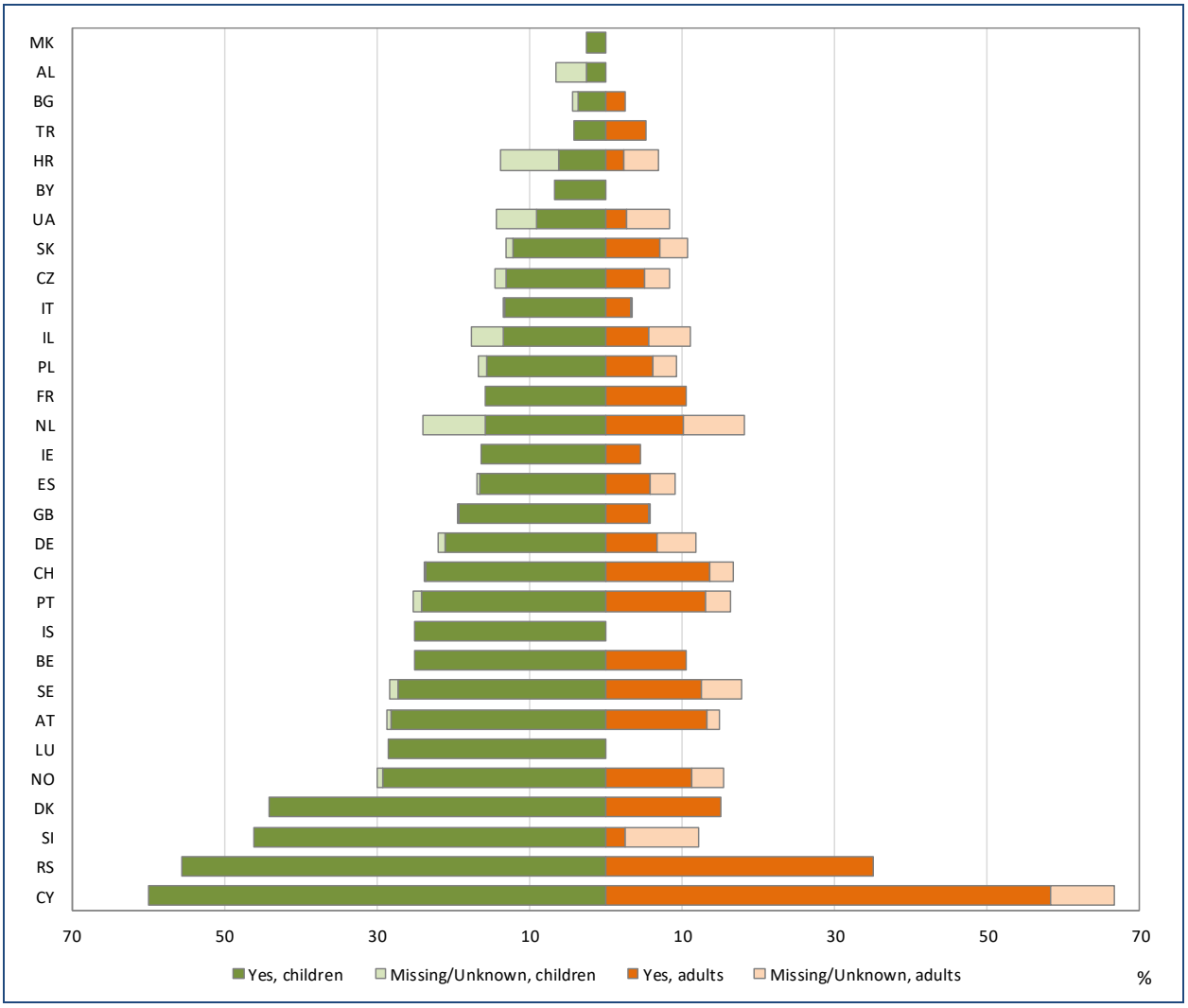


Note: We excluded from the graph the countries for which the information on *Burkholderia cepacia complex species* is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

Note: Ireland: chronicity for *Burkholderia cepacia complex species* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.
United Kingdom: chronicity for *Burkholderia cepacia complex species* is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

This graph represents the percentage of people with chronic *Burkholderia cepacia complex species* infection (in dark colours) and the percentage of people where information on chronic *Burkholderia cepacia complex species* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults. This infection is much less frequent than *Pseudomonas aeruginosa* (note the different scale on the horizontal axis), and there is also some variation among countries.

Figure 5.3 Prevalence of Haemophilus influenzae infection in children and adults seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on *Haemophilus influenzae* is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

This graph represents the percentage of people with *Haemophilus influenzae* infection (in dark colours) and the percentage of people where information on *Haemophilus influenzae* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults. This infection is as frequent as chronic *Pseudomonas aeruginosa* infection and a similar degree of variation between the countries can be observed.

Table 5.3 Prevalence of chronic Staphylococcus aureus and methicillin-resistant Staphylococcus aureus (MRSA) in children seen in 2020 who have never had a transplant, by country and overall.

Country	Chronic *Staphylococcus aureus* number (%)			MRSA number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	0 (0.00)	58 (75.32)	19 (24.68)	3 (3.90)	72 (93.51)	2 (2.60)
Armenia	0 (0.00)	3 (12.50)	21 (87.50)	18 (75.00)	6 (25.00)	0 (0.00)
Austria	1 (0.26)	155 (40.90)	223 (58.84)	2 (0.53)	368 (97.10)	9 (2.37)
Belarus	0 (0.00)	77 (51.33)	73 (48.67)	0 (0.00)	149 (99.33)	1 (0.67)
Belgium[1]	291 (62.58)	172 (36.99)	2 (0.43)	0 (0.00)	447 (96.13)	18 (3.87)
Bulgaria	0 (0.00)	81 (72.32)	31 (27.68)	0 (0.00)	111 (99.11)	1 (0.89)
Croatia	9 (11.25)	43 (53.75)	28 (35.00)	6 (7.50)	71 (88.75)	3 (3.75)
Cyprus	2 (20.00)	5 (50.00)	3 (30.00)	0 (0.00)	7 (70.00)	3 (30.00)
Czech Republic	5 (1.52)	181 (55.02)	143 (43.47)	5 (1.52)	320 (97.26)	4 (1.22)
Denmark	0 (0.00)	140 (68.63)	64 (31.37)	0 (0.00)	203 (99.51)	1 (0.49)
France	0 (0.00)	1546 (56.69)	1181 (43.31)	0 (0.00)	2636 (96.66)	91 (3.34)
Georgia	6 (8.33)	42 (58.33)	24 (33.33)	1 (1.39)	71 (98.61)	0 (0.00)
Germany	32 (1.20)	1571 (59.04)	1058 (39.76)	24 (0.90)	2551 (95.87)	86 (3.23)
Greece	0 (0.00)	49 (51.58)	46 (48.42)	3 (3.16)	75 (78.95)	17 (17.89)
Hungary	0 (0.00)	109 (43.95)	139 (56.05)	0 (0.00)	231 (93.15)	17 (6.85)
Iceland	0 (0.00)	4 (50.00)	4 (50.00)	0 (0)	8 (100)	0 (0)
Ireland[2]	0 (0.00)	310 (62.50)	186 (37.50)	0 (0.00)	481 (96.98)	15 (3.02)
Israel	7 (4.12)	80 (47.06)	83 (48.82)	11 (6.47)	155 (91.18)	4 (2.35)
Italy	1 (0.04)	1480 (65.08)	793 (34.87)	2 (0.09)	2076 (91.29)	196 (8.62)
Latvia	5 (15.15)	5 (15.15)	23 (69.70)	7 (21.21)	26 (78.79)	0 (0.00)
Lithuania	3 (21.43)	4 (28.57)	7 (50.00)	2 (14.29)	12 885.71)	0 (0.00)
Luxembourg	0 (0.00)	9 (42.86)	12 (57.14)	0 (0)	21 (100)	0 (0)

[1] Belgium: chronic *Staphylococcus Aureus*: Variable is not collected as such, but derived as chronic MRSA = chronic SA, and no SA during the year = no chronic SA. Yes is sure, based on chronic MRSA; No is an assumption if no SA was detected in the year.

[2] Ireland: chronicity for *Staphylococcus aureus* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.

[table 5.3 continued]

Country	Chronic *Staphylococcus aureus* number (%)			MRSA number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	1 (2.63)	37 (97.37)	1 (2.63)	36 (94.74)	1 (2.63)
The Netherlands	10 (1.87)	275 (51.40)	250 (46.73)	24 (4.49)	505 (94.39)	6 (1.12)
North Macedonia	0 (0.00)	59 (74.68)	20 (25.32)	0 (0.00)	61 (77.22)	18 (22.78)
Norway	1 (0.83)	60 (50.00)	59 (49.17)	1 (0.83)	119 (99.17)	0 (0.00)
Poland	9 (1.09)	278 (33.57)	541 (65.34)	11 (1.33)	794 (95.89)	23 (2.78)
Portugal	3 (1.69)	102 (57.30)	73 (41.01)	2 (1.12)	163 (91.57)	13 (7.30)
Romania	3 (1.37)	181 (82.65)	35 (15.98)	4 (1.83)	176 (80.37)	39 (17.81)
Russian Federation	38 (2.23)	573 (33.65)	1092 (64.12)	45 (2.64)	1611 (94.60)	47 (2.76)
Serbia	0 (0.00)	30 (30.30)	69 (69.70)	0 (0.00)	86 (86.87)	13 (13.13)
Slovak Republic	0 (0.00)	40 (32.52)	83 (67.48)	1 (0.81)	118 (95.93)	4 (3.25)
Slovenia	0 (0.00)	2 (3.85)	50 (96.15)	0 (0.00)	48 (92.31)	4 (7.69)
Spain	9 (0.84)	646 (60.09)	420 (39.07)	5 (0.47)	1024 (95.26)	46 (4.28)
Sweden	6 (2.26)	178 (67.17)	81 (30.57)	0 (0.00)	261 (98.49)	4 (1.51)
Switzerland	1 (0.24)	155 (36.56)	268 (63.21)	1 (0.24)	416 (98.11)	7 (1.65)
Turkey	26 (1.44)	1372 (75.93)	409 (22.63)	0 (0.00)	1585 (87.71)	222 (12.29)
Ukraine	7 (5.26)	55 (41.35)	71 (53.38)	7 (5.26)	117 (87.97)	9 (6.77)
United Kingdom[3]	5 (0.12)	3735 (88.40)	485 (11.48)	5 (0.12)	4116 (97.42)	104 (2.46)
Total	480 (2.13)	13866 (61.48)	8206 (36.39)	191 (0.85)	21333 (94.59)	1028 (4.56)

[3] United Kingdom: chronicity for Staphylococcus aureus is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

Table 5.3 shows, separately by country, the frequency of chronic *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) in children. The number of missing values is also included.

Table 5.4 Prevalence of chronic Staphylococcus aureus, methicillin-resistant Staphylococcus aureus (MRSA) in adults seen in 2020 who have never had a transplant, by country and overall.

Country	Chronic *Staphylococcus aureus* number (%)			MRSA number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	3 (0.84)	130 (36.41)	224 (62.75)	8 (2.24)	341 (95.52)	8 (2.24)
Belgium[1]	384 (57.40)	249 (37.22)	36 (5.38)	0 (0.00)	614 (91.78)	55 (8.22)
Bulgaria	0 (0.00)	67 (82.72)	14 (17.28)	0 (0)	81 (100)	0 (0)
Croatia	2 (4.55)	18 (40.91)	24 (54.55)	2 (4.55)	41 (93.18)	1 (2.27)
Cyprus	6 (50.00)	3 (25.00)	3 (25.00)	1 (8.33)	10 (83.33)	1 (8.33)
Czech Republic	9 (3.54)	115 (45.28)	130 (51.18)	9 (3.54)	230 (90.55)	15 (5.91)
Denmark	0 (0.00)	197 (74.34)	68 (25.66)	0 (0)	265 (100)	0 (0)
France	0 (0.00)	1970 (59.50)	1341 (40.50)	0 (0.00)	3038 (91.75)	273 (8.25)
Germany	170 (4.89)	1506 (43.31)	1801 (51.80)	179 (5.15)	3096 (89.04)	202 (5.81)
Greece	17 (5.99)	142 (50.00)	125 (44.01)	19 (6.69)	226 (79.58)	39 (13.73)
Hungary	3 (1.62)	74 (40.00)	108 (58.38)	4 (2.16)	166 (89.73)	15 (8.11)
Iceland	0 (0)	0 (0)	6 (100)	0 (0.00)	5 (83.33)	1 (16.67)
Ireland[2]	0 (0.00)	450 (70.87)	185 (29.13)	0 (0.00)	600 (94.49)	35 (5.51)
Israel	16 (4.75)	211 (62.61)	110 (32.64)	20 (5.93)	301 (89.32)	16 (4.75)
Italy	7 (0.22)	1995 (62.25)	1203 (37.54)	6 (0.19)	2945 (91.89)	254 (7.93)
Latvia	0 (0.00)	2 (15.38)	11 (84.62)	2 (15.38)	11 (84.62)	0 (0.00)
Lithuania	0 (0.00)	9 (45.00)	11 (55.00)	0 (0)	20 (100)	0 (0)

Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and are not shown in this table but are considered in the total.

[1] Belgium: chronic *Staphylococcus Aureus*: Variable is not collected as such, but derived as chronic MRSA = chronic SA, and no SA during the year = no chronic SA. Yes is sure, based on chronic MRSA; No is an assumption if no SA was detected in the year.

[2] Ireland: chronicity for *Staphylococcus aureus* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.

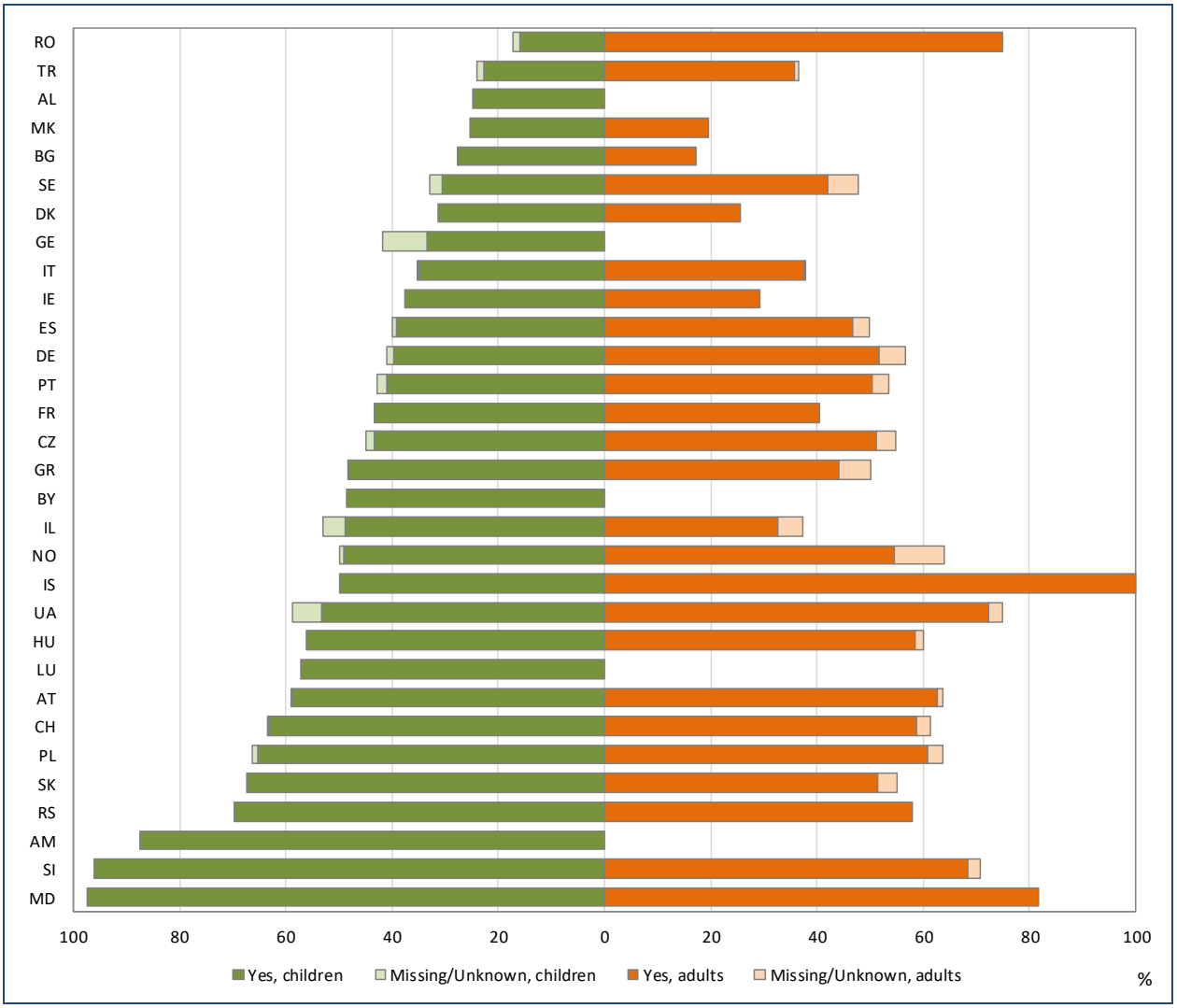
[table 5.4 continued]

Country	Chronic *Staphylococcus aureus* number (%)			MRSA number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	2 (18.18)	9 (81.82)	0 (0.00)	10 (90.91)	1 (9.09)
The Netherlands	93 (10.34)	398 (44.27)	408 (45.38)	71 (7.90)	818 (90.99)	10 (1.11)
North Macedonia	0 (0.00)	33 (80.49)	8 (19.51)	0 (0.00)	30 (73.17)	11 (26.83)
Norway	16 (9.47)	61 (36.09)	92 (54.44)	7 (4.14)	160 (94.67)	2 (1.18)
Poland	10 (3.07)	118 (36.20)	198 (60.74)	10 (3.07)	294 (90.18)	22 (6.75)
Portugal	5 (3.27)	71 (46.41)	77 (50.33)	5 (3.27)	136 (88.89)	12 (7.84)
Romania	0 (0.00)	2 (25.00)	6 (75.00)	0 (0.00)	5 (62.50)	3 (37.50)
Russian Federation	460 (70.55)	90 (13.80)	102 (15.64)	461 (70.71)	185 (28.37)	6 (0.92)
Serbia	0 (0.00)	24 (42.11)	33 (57.89)	0 (0.00)	51 (89.47)	6 (10.53)
Slovak Republic	5 (3.57)	63 (45.00)	72 (51.43)	6 (4.29)	125 (89.29)	9 (6.43)
Slovenia	1 (2.44)	12 (29.27)	28 (68.29)	5 (12.20)	34 (82.93)	2 (4.88)
Spain	34 (3.17)	538 (50.14)	501 (46.69)	41 (3.82)	964 (89.84)	68 (6.34)
Sweden	20 (5.73)	182 (52.15)	147 (42.12)	0 (0.00)	345 (98.85)	4 (1.15)
Switzerland	13 (2.59)	194 (38.65)	295 (58.76)	18 (3.59)	476 (94.82)	8 (1.59)
Turkey	2 (0.80)	159 (63.35)	90 (35.86)	0 (0.00)	234 (93.23)	17 (6.77)
Ukraine	1 (2.78)	9 (25.00)	26 (72.22)	1 (2.78)	31 (86.11)	4 (11.11)
United Kingdom[3]	3 (0.06)	4497 (83.85)	863 (16.09)	3 (0.06)	5172 (96.44)	188 (3.51)
Total	1280 (5.51)	13594 (58.51)	8360 (35.98)	879 (3.78)	21066 (90.67)	1289 (5.55)

[3] United Kingdom: chronicity for Staphylococcus aureus is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

Table 5.4 shows, separately by country, the frequency of chronic *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) in adults. The number of missing values is also included.

Figure 5.4 Prevalence of chronic Staphylococcus aureus infection in children and adults seen in 2020 who have never had a transplant, by country.

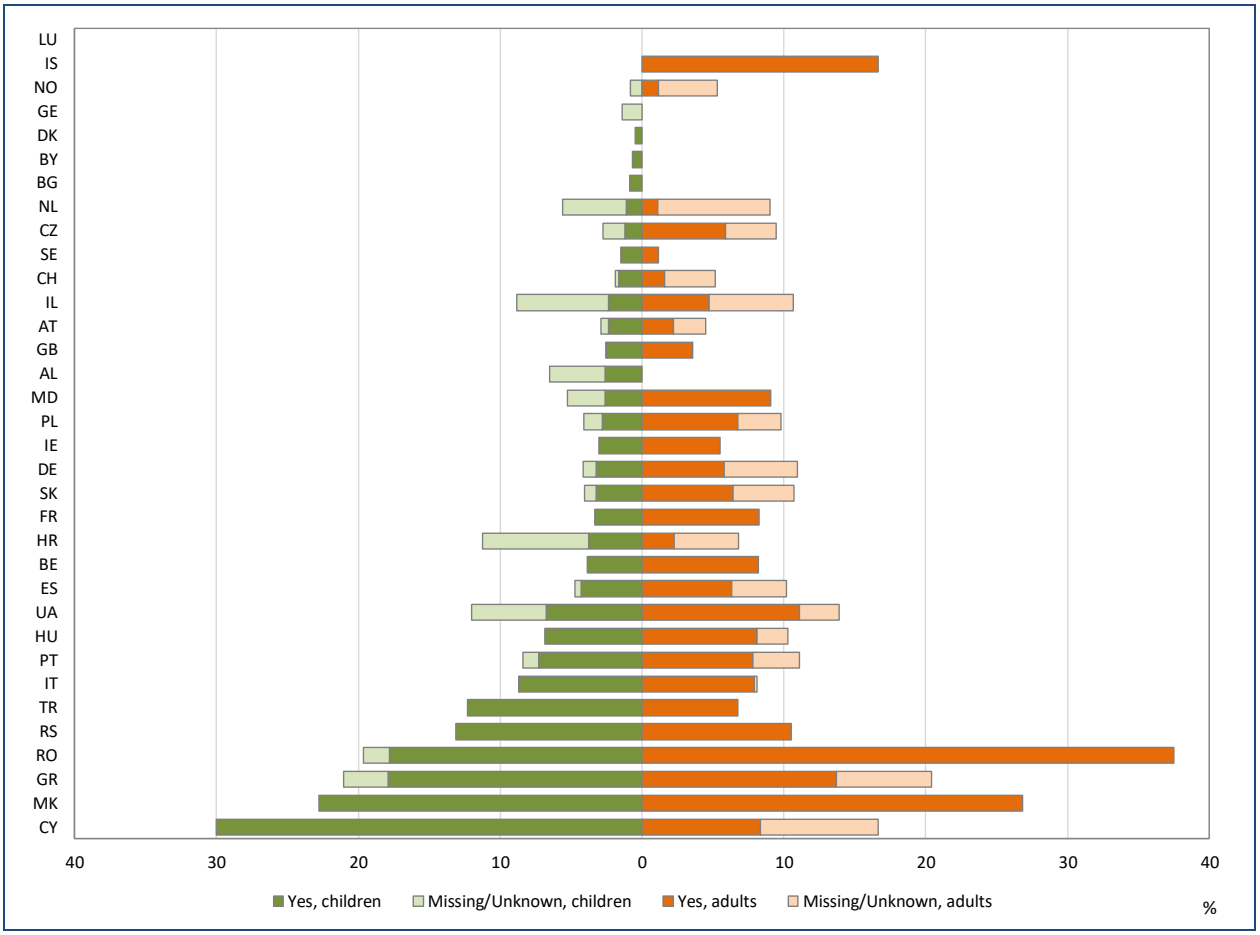


Note: We excluded from the graph the countries for which the information on *Staphylococcus aureus* is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

Note: Belgium: chronic *Staphylococcus Aureus*: Variable is not collected as such, but derived from chronic MRSA = chronic SA, and no SA during the year = no chronic SA. Yes is sure, based on chronic MRSA ; No is an assumption if no SA was detected in the year.
Ireland: chronicity for *Staphylococcus aureus* is defined as: at least 3 or more positive isolates during the last 12 months preceding the last reported culture in 2020.
United Kingdom: chronicity for Staphylococcus aureus is defined as: 3 or more positive isolates during the 12 months preceding last annual review.

This graph represents the percentage of people with chronic *Staphylococcus aureus* infection (in dark colours) and the percentage of people where information on chronic *Staphylococcus aureus* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults. This infection is as frequent as chronic *Pseudomonas aeruginosa* infection and a similar degree of variation between the countries can be observed.

Figure 5.5 Prevalence of methicillin-resistant Staphylococcus aureus (MRSA) infection in children and adults seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on MRSA is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

This graph represents the percentage of people with methicillin-resistant *Staphylococcus aureus* (MRSA) infection (in dark colours) and the percentage of people where information on methicillin-resistant *Staphylococcus aureus* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults. Prevalence of MRSA varies considerably between countries.

Table 5.5 Prevalence of non-tuberculous mycobacteria, Stenotrophomonas maltophilia and Achromobacter species infection in children seen in 2020 who have never had a transplant, by country and overall.

Country	Non-tuberculous mycobacteria (NTM) infection this year number (%)			*Stenotrophomonas maltophilia* infection this year number (%)			*Achromobacter species* infection this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	77 (100)	0 (0)	0 (0)	0 (0.00)	76 (98.70)	1 (1.30)	0 (0)	77 (100)	0 (0)
Armenia	20 (83.33)	4 (16.67)	0 (0.00)	20 (83.33)	4 (16.67)	0 (0.00)	20 (83.33)	4 (16.67)	0 (0.00)
Austria	7 (1.85)	366 (96.57)	6 (1.58)	1 (0.26)	343 (90.50)	35 (9.23)	2 (0.53)	369 (97.36)	8 (2.11)
Belarus	150 (100)	0 (0)	0 (0)	0 (0.00)	146 (97.33)	4 (2.67)	0 (0.00)	145 (96.67)	5 (3.33)
Belgium[1]	0 (0.00)	462 (99.35)	3 (0.65)	0 (0.00)	416 (89.46)	49 (10.54)	0 (0.00)	442 (95.05)	23 (4.95)
Bulgaria	109 (97.32)	3 (2.68)	0 (0.00)	0 (0)	112 (100)	0 (0)	0 (0.00)	108 (96.43)	4 (3.57)
Croatia	38 (47.50)	41 (51.25)	1 (1.25)	6 (7.50)	70 (87.50)	4 (5.00)	6 (7.50)	69 (86.25)	5 (6.25)
Cyprus	0 (0)	10 (100)	0 (0)	0 (0.00)	8 (80.00)	2 (20.00)	0 (0)	10 (100)	0 (0)
Czech Republic	253 (76.90)	67 (20.36)	9 (2.74)	5 (1.52)	310 (94.22)	14 (4.26)	5 (1.52)	320 (97.26)	4 (1.22)
Denmark	0 (0.00)	203 (99.51)	1 (0.49)	0 (0.00)	165 (80.88)	39 (19.12)	0 (0.00)	189 (92.65)	15 (7.35)
France	0 (0.00)	2669 (97.87)	58 (2.13)	0 (0.00)	2425 (88.93)	302 (11.07)	0 (0.00)	2582 (94.68)	145 (5.32)
Georgia	72 (100)	0 (0)	0 (0)	2 (2.78)	70 (97.22)	0 (0.00)	1 (1.39)	71 (98.61)	0 (0.00)
Germany	2007 (75.42)	620 (23.30)	34 (1.28)	24 (0.90)	2433 (91.43)	204 (7.67)	24 (0.90)	2564 (96.35)	73 (2.74)
Greece	0 (0)	95 (100)	0 (0)	1 (1.05)	88 (92.63)	6 (6.32)	1 (1.05)	93 (97.89)	1 (1.05)
Hungary	6 (2.42)	240 (96.77)	2 (0.81)	0 (0.00)	236 (95.16)	12 (4.84)	248 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	7 (87.50)	1 (12.50)	0 (0.00)	6 (75.00)	2 (25.00)	0 (0.00)	7 (87.50)	1 (12.50)
Ireland	0 (0.00)	494 (99.60)	<5 (0.40)	0 (0.00)	462 (93.15)	34 (6.85)	0 (0.00)	486 (97.98)	10 (2.02)
Israel	14 (8.24)	143 (84.12)	13 (7.65)	8 (4.71)	154 (90.59)	8 (4.71)	9 (5.29)	154 (90.59)	7 (4.12)
Italy	2 (0.09)	2267 (99.69)	5 (0.22)	2 (0.09)	2078 (91.38)	194 (8.53)	2 (0.09)	2172 (95.51)	100 (4.40)
Latvia	5 (15.15)	28 (84.85)	0 (0.00)	6 (18.18)	21 (63.64)	6 (18.18)	5 (15.15)	27 (81.82)	1 (3.03)
Lithuania	2 (14.29)	12 (85.71)	0 (0.00)	2 (14.29)	11 (78.57)	1 (7.14)	3 (21.43)	10 (71.43)	1 (7.14)
Luxembourg	1 (4.76)	20 (95.24)	0 (0.00)	0 (0.00)	18 (85.71)	3 (14.29)	0 (0.00)	20 (95.24)	1 (4.76)

[1] Belgium: Achromobacter xylosoxidans (Alcaligenes) rather than Achromobacter species are collected.

[table 5.5 continued]

Country	Non-tuberculous mycobacteria (NTM) infection this year number (%)			*Stenotrophomonas maltophilia* infection this year number (%)			*Achromobacter species* infection this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	38 (100)	0 (0)	0 (0)	38 (100)	0 (0)	0 (0)	38 (100)	0 (0)	0 (0)
The Netherlands	224 (41.87)	298 (55.70)	13 (2.43)	22 (4.11)	466 (87.10)	47 (8.79)	116 (21.68)	409 (76.45)	10 (1.87)
North Macedonia	0 (0)	79 (100)	0 (0)	0 (0)	79 (100)	0 (0)	0 (0)	79 (100)	0 (0)
Norway	33 (27.50)	85 (70.83)	2 (1.67)	1 (0.83)	98 (81.67)	21 (17.50)	2 (1.67)	117 (97.50)	1 (0.83)
Poland	226 (27.29)	599 (72.34)	3 (0.36)	9 (1.09)	781 (94.32)	38 (4.59)	11 (1.33)	799 (96.50)	18 (2.17)
Portugal	2 (1.12)	174 (97.75)	2 (1.12)	2 (1.12)	161 (90.45)	15 (8.43)	2 (1.12)	169 (94.94)	7 (3.93)
Romania	27 (12.33)	192 (87.67)	0 (0.00)	3 (1.37)	210 (95.89)	6 (2.74)	3 (1.37)	215 (98.17)	1 (0.46)
Russian Federation	249 (14.62)	1433 (84.15)	21 (1.23)	50 (2.94)	1559 (91.54)	94 (5.52)	46 (2.70)	1553 (91.19)	104 (6.11)
Serbia	0 (0.00)	98 (98.99)	1 (1.01)	0 (0.00)	88 (88.89)	11 (11.11)	0 (0.00)	94 (94.95)	5 (5.05)
Slovak Republic	1 (0.81)	122 (99.19)	0 (0.00)	1 (0.81)	117 (95.12)	5 (4.07)	1 (0.81)	118 (95.93)	4 (3.25)
Slovenia	0 (0)	52 (100)	0 (0)	0 (0.00)	48 (92.31)	4 (7.69)	0 (0.00)	51 (98.08)	1 (1.92)
Spain	193 (17.95)	863 (80.28)	19 (1.77)	3 (0.28)	1008 (93.77)	64 (5.95)	4 (0.37)	1027 (95.53)	44 (4.09)
Sweden	0 (0.0)	257 (96.98)	8 (3.02)	0 (0.00)	245 (92.45)	20 (7.55)	0 (0.00)	259 (97.74)	6 (2.26)
Switzerland	1 (0.24)	420 (99.06)	3 (0.71)	2 (0.47)	385 (90.80)	37 (8.73)	4 (0.94)	407 (95.99)	13 (3.07)
Turkey	1500 (83.01)	303 (16.77)	4 (0.22)	31 (1.72)	1745 (96.57)	31 (1.72)	0 (0.00)	1778 (98.40)	29 (1.60)
Ukraine	129 (96.99)	3 (2.26)	1 (0.75)	7 (5.26)	113 (84.96)	13 (9.77)	7 (5.26)	125 (93.98)	1 (0.75)
United Kingdom	5 (0.12)	4061 (96.12)	159 (3.76)	5 (0.12)	3950 (93.49)	270 (6.39)	5 (0.12)	4144 (98.08)	76 (1.80)
Total				251 (1.11)	20705 (91.81)	1596 (7.08)	565 (2.51)	21263 (94.28)	724 (3.21)

Note: For non-tuberculous mycobacteria (NTM) the total percentage of missing information is higher than 10%, therefore the totals are excluded from the table.

Table 5.5 shows the frequency of three other infections, non-tuberculous mycobacteria (NTM), *Stenotrophomonas maltophilia* and *Achromobacter species* in children.

Table 5.6 Prevalence of non-tuberculous mycobacteria, Stenotrophomonas maltophilia and Achromobacter species infection in adults seen in 2020 who have never had a transplant, by country and overall.

Country	Non-tuberculous mycobacteria (NTM) infection this year number (%)			*Stenotrophomonas maltophilia* infection this year number (%)			*Achromobacter species* infection this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	27 (7.56)	303 (84.87)	27 (7.56)	5 (1.40)	297 (83.19)	55 (15.41)	6 (1.68)	326 (91.32)	25 (7.00)
Belgium[1]	0 (0.00)	648 (96.86)	21 (3.14)	0 (0.00)	586 (87.59)	83 (12.41)	0 (0.00)	600 (89.69)	69 (10.31)
Bulgaria	79 (97.53)	1 (1.23)	1 (1.23)	0 (0)	81 (100)	0 (0)	0 (0.00)	80 (98.77)	1 (1.23)
Croatia	8 (18.18)	35 (79.55)	1 (2.27)	2 (4.55)	41 (93.18)	1 (2.27)	2 (4.55)	41 (93.18)	1 (2.27)
Cyprus	1 (8.33)	11 (91.67)	0 (0.00)	1 (8.33)	11 (91.67)	0 (0.00)	1 (8.33)	9 (75.00)	2 (16.67)
Czech Republic	44 (17.32)	198 (77.95)	12 (4.72)	8 (3.15)	230 (90.55)	16 (6.30)	8 (3.15)	234 (92.13)	12 (4.72)
Denmark	0 (0.00)	251 (94.72)	14 (5.28)	0 (0.00)	204 (76.98)	61 (23.02)	0 (0.00)	229 (86.42)	36 (13.58)
France	0 (0.00)	3135 (94.68)	176 (5.32)	0 (0.00)	2960 (89.40)	351 (10.60)	0 (0.00)	3015 (91.06)	296 (8.94)
Germany	2102 (60.45)	1233 (35.46)	142 (4.08)	179 (5.15)	2931 (84.30)	367 (10.56)	179 (5.15)	3078 (88.52)	220 (6.33)
Greece	0 (0.00)	269 (94.72)	15 (5.28)	16 (5.63)	248 (87.32)	20 (7.04)	16 (5.63)	244 (85.92)	24 (8.45)
Hungary	4 (2.16)	170 (91.89)	11 (5.95)	4 (2.16)	168 (90.81)	13 (7.03)	185 (100)	0 (0)	0 (0)
Iceland	0 (0)	6 (100)	0 (0)	0 (0.00)	5 (83.33)	1 (16.67)	0 (0.00)	4 (66.67)	2 (33.33)
Ireland	0 (0.00)	626 (98.58)	9 (1.42)	0 (0.00)	597 (94.02)	38 (5.98)	0 (0.00)	609 (95.91)	26 (4.09)
Israel	23 (6.82)	282 (83.68)	32 (9.50)	16 (4.75)	291 (86.35)	30 (8.90)	16 (4.75)	302 (89.61)	19 (5.64)
Italy	7 (0.22)	3175 (99.06)	23 (0.72)	6 (0.19)	2955 (92.20)	244 (7.61)	6 (0.19)	2923 (91.20)	276 (8.61)
Latvia	1 (7.69)	12 (92.31)	0 (0.00)	1 (7.69)	10 (76.92)	2 (15.38)	1 (7.69)	10 (76.92)	2 (15.38)
Lithuania	0 (0)	20 (100)	0 (0)	0 (0)	20 (100)	0 (0)	0 (0)	20 (100)	0 (0)

[1] Belgium: Achromobacter xylosoxidans (Alcaligenes) rather than Achromobacter species are collected.

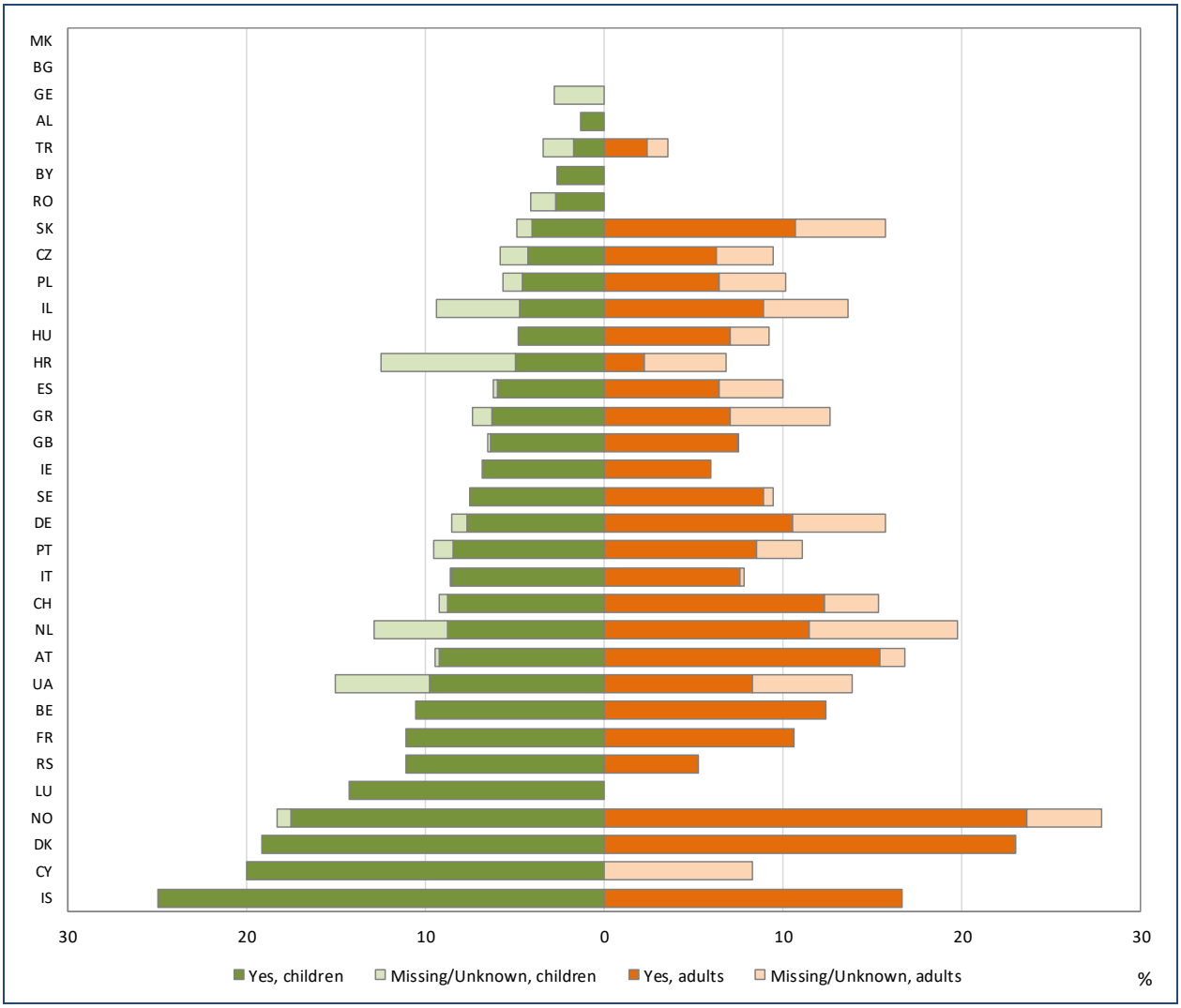
Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and are not shown in this table but are considered in the total.

[table 5.6 continued]

Country	Non-tuberculous mycobacteria (NTM) infection this year number (%)			*Stenotrophomonas maltophilia* infection this year number (%)			*Achromobacter species* infection this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	11 (100)	0 (0)	0 (0)	11 (100)	0 (0)	0 (0)	11 (100)	0 (0)	0 (0)
The Netherlands	179 (19.91)	684 (76.08)	36 (4.00)	75 (8.34)	721 (80.20)	103 (11.46)	79 (8.79)	775 (86.21)	45 (5.01)
North Macedonia	0 (0)	41 (100)	0 (0)	0 (0)	41 (100)	0 (0)	0 (0)	41 (100)	0 (0)
Norway	22 (13.02)	136 (80.47)	11 (6.51)	7 (4.14)	122 (72.19)	40 (23.67)	7 (4.14)	150 (88.76)	12 (7.10)
Poland	22 (6.75)	301 (92.33)	3 (0.92)	12 (3.68)	293 (89.88)	21 (6.44)	10 (3.07)	287 (88.04)	29 (8.90)
Portugal	5 (3.27)	146 (95.42)	2 (1.31)	4 (2.61)	136 (88.89)	13 (8.50)	5 (3.27)	133 (86.939	15 (9.80)
Romania	0 (0.00)	7 (87.50)	1 (12.50)	0 (0)	8 (100)	0 (0)	0 (0)	8 (100)	0 (0)
Russian Federation	478 (73.31)	169 (25.92)	5 (0.77)	460 (70.55)	179 (27.45)	13 (1.99)	460 (70.55)	167 (25.61)	25 (3.83)
Serbia	0 (0)	57 (100)	0 (0)	0 (0.00)	54 (94.74)	3 (5.26)	0 (0.00)	53 (92.98)	4 (7.02)
Slovak Republic	5 (3.57)	131 (93.57)	4 (2.86)	7 (5.00)	118 (84.29)	15 (10.71)	5 (3.57)	126 (90.00)	9 (6.43)
Slovenia	5 (12.20)	34 (82.93)	2 (4.88)	5 (12.20)	28 (68.29)	8 (19.51)	5 (12.20)	35 (85.37)	1 (2.44)
Spain	42 (3.91)	980 (91.33)	51 (4.75)	38 (3.54)	966 (90.03)	69 (6.43)	38 (3.54)	935 (87.14)	100 (9.32)
Sweden	0 (0.00)	333 (95.42)	16 (4.58)	2 (0.57)	316 (90.54)	31 (8.88)	1 (0.29)	337 (96.56)	11 (3.15)
Switzerland	26 (5.18)	440 (87.65)	36 (7.17)	15 (2.99)	425 (84.66)	62 (12.35)	16 (3.19)	457 (91.04)	29 (5.78)
Turkey	178 (70.92)	68 (27.09)	5 (1.99)	3 (1.20)	242 (96.41)	6 (2.39)	0 (0.00)	237 (94.42)	14 (5.58)
Ukraine	31 (86.11)	4 (11.11)	1 (2.78)	2 (5.56)	31 (86.11)	3 (8.33)	2 (5.56)	32 (88.89)	2 (5.56)
United Kingdom	185 (3.45)	4720 (88.01)	458 (8.54)	3 (0.06)	4962 (92.52)	398 (7.42)	3 (0.06)	5100 (95.10)	260 (4.85)
Total	3491 (15.03)	18628 (80.18)	1115 (4.80)	883 (3.80)	20284 (87.30)	2067 (8.90)	1063 (4.58)	20604 (88.68)	1567 (6.74)

Table 5.6 shows the frequency of three other infections, non-tuberculous mycobacteria (NTM), *Stenotrophomonas maltophilia* and *Achromobacter species* in adults.

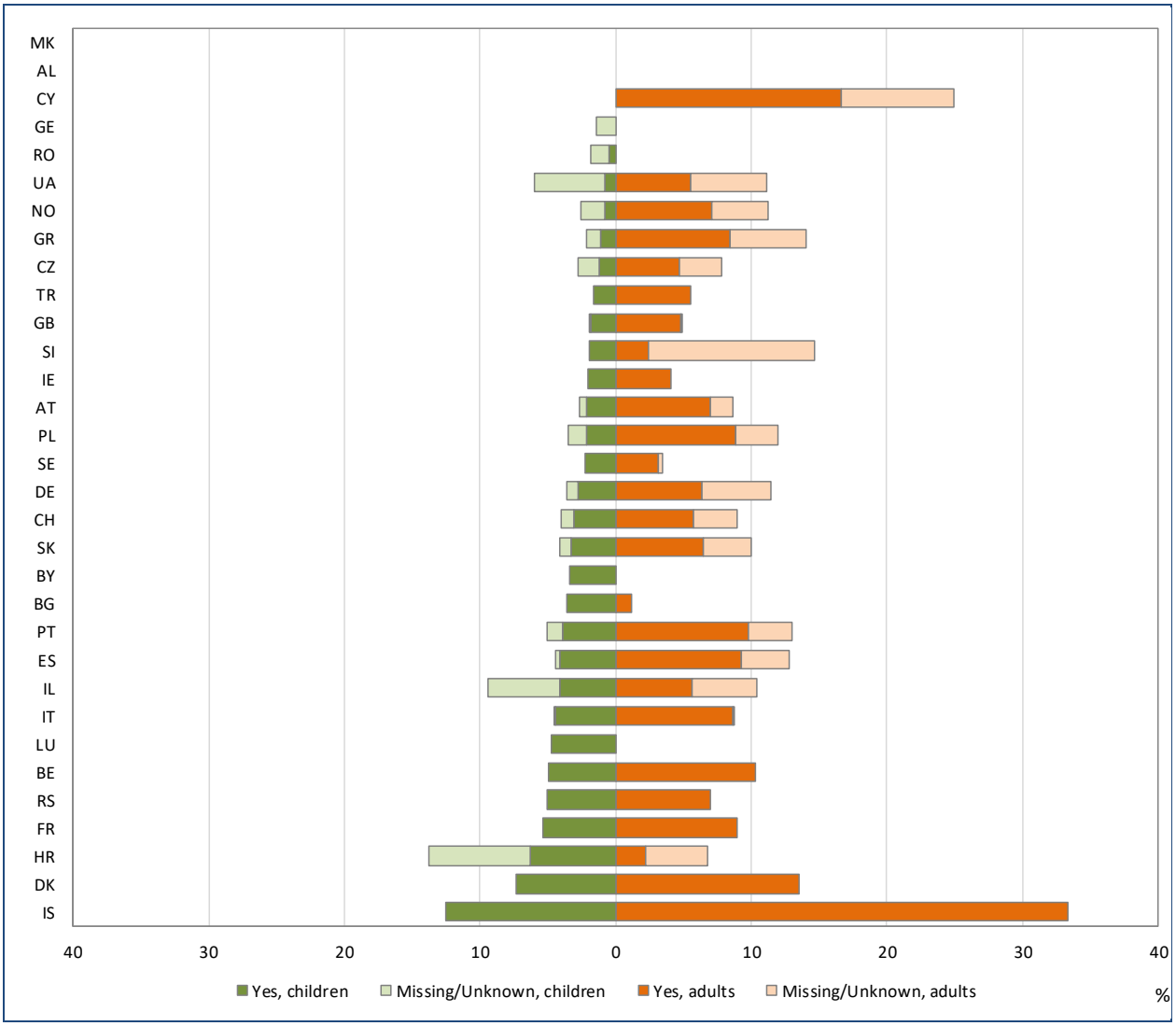
Figure 5.6 Prevalence of Stenotrophomonas maltophilia infection in children and adults seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on *Stenotrophomonas maltophilia* is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

This graph represents the percentage of people with *Stenotrophomonas maltophilia* infection (in dark colours) and the percentage of people where information on *Stenotrophomonas maltophilia* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults. The frequency varies considerably between countries.

Figure 5.7 Prevalence of Achromobacter species in children and adults seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on *Achromobacter species* is missing for more than 10% of the children and/or adults.
Belarus and Georgia have 0% coverage for adults and the adults bars are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and the adults bars are excluded from the graph.

Note: Belgium: Achromobacter xylosoxidans (Alcaligenes) rather than Achromobacter species are collected.

This graph represents the percentage of people with *Achromobacter species* infection (in dark colours) and the percentage of people where information on *Achromobacter species* infection is missing/unknown (in light colours). The horizontal bars on the left of the graph refer to children, while the horizontal bars on the right refer to adults.

6. Nutrition

Pancreatic insufficiency is usually defined as absence of pancreatic enzymes in two stool samples or elevated levels of fat in stools (faecal fat). Since information on faecal fat is rarely collected by the national registries, we therefore applied the information on the use of pancreatic enzymes as an indicator of pancreatic insufficiency.

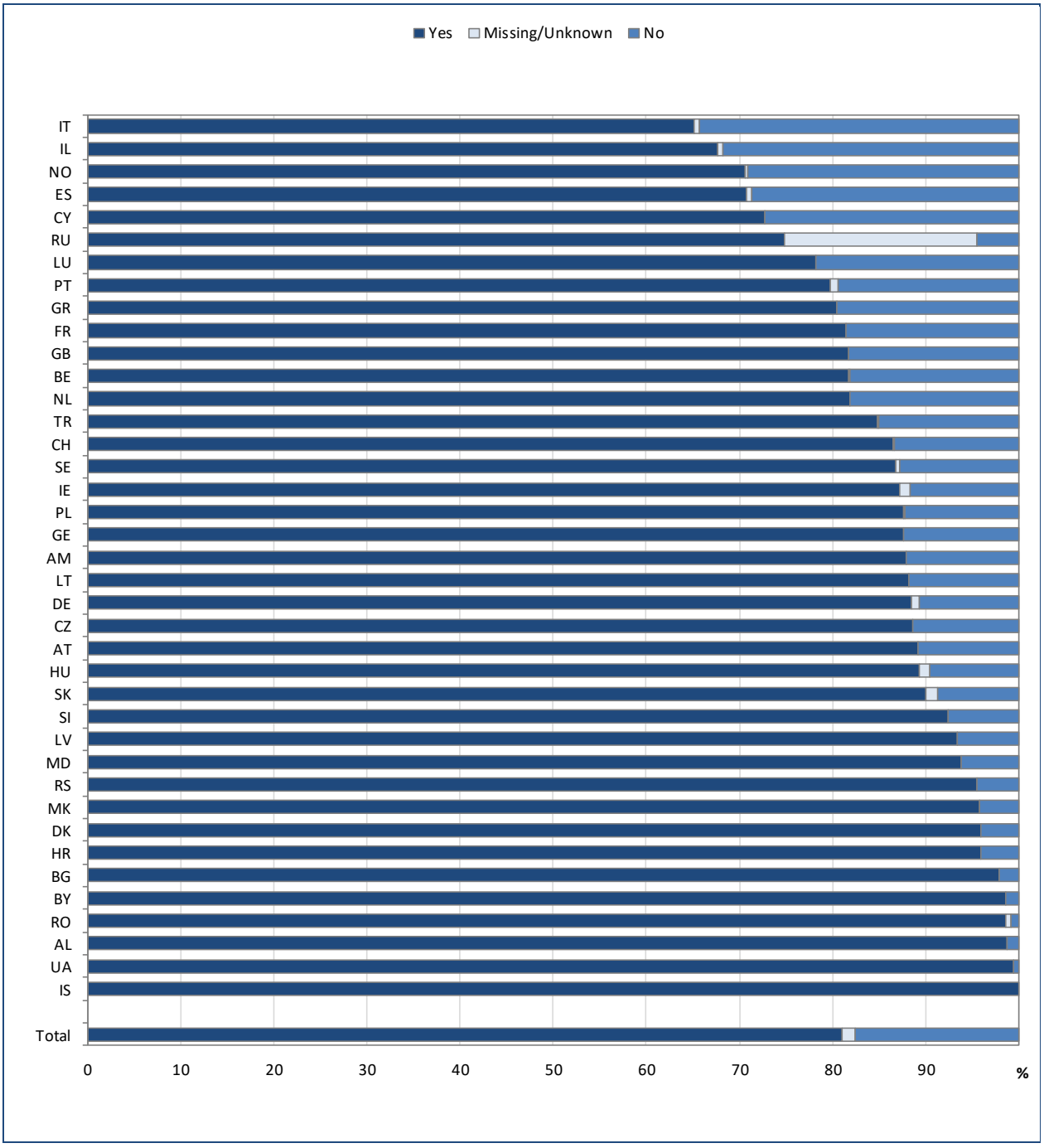
We collected weight and height measured on the date the best FEV1 value (of the highest FEV1% predicted of the year) was recorded. For patients that did not perform spirometry, the last weight and height measurements of the year were considered. From these raw values we calculated body mass index (BMI). A patient with a low weight is not necessarily underweight if the height is also low, therefore BMI may better illustrate the nutritional status because it describes the weight/height relationship. The ECFS Standards of Care guidelines recommend: for adults, a BMI of above 20 kg/m^2; for older children and adolescents, the 50^{th} percentile for BMI; for infants and children up to 2 years of age, weight and height percentiles similar to those for the non-CF population.[1]

Weight, height and BMI were then expressed in terms of z-scores by using a reference population of healthy individuals (in this case the US population with reference values issued by the Centre for Disease Control, USA, see Appendix 3, page 152, for details).

A z-score of 0 means that the height/weight/BMI is equal to the mean height/weight/BMI of people of the same age and sex of the reference population. A z-score of -2 means that the height/weight/BMI value is 2 standard deviations below the mean height/weight/BMI of people of the same age and sex of the reference population; a z-score of +2 means that the value is 2 standard deviations above that mean. In the reference population, 95% of all individuals have a z-score for weight between -2 and +2 (the same for height) and it is expected that the same happens for approximately 95% of individuals of a population without conditions that affect weight (or height). The average z-score for a largely healthy population should be very close to zero.

[1] A.R. Smyth et al, JCF 2014;13, S23–S42.

Figure 6.1 Use of pancreatic enzymes in 2020 for all patients who have never had a transplant, by country and overall.



This graph shows the use of pancreatic enzymes by country. This can be seen as an estimate of pancreatic insufficiency.

Table 6.1 Z-scores for BMI: descriptive statistics by country. All patients seen in 2020 aged 2-17 years who never had a transplant.

Country	N	N Miss	Mean	Min	25th pctl (25% of the patients are below this z-score for BMI)	Median (50% of the patients are below this z-score for BMI)	75th pctl (75% of the patients are below this z-score for BMI)	Max
Albania	63	4	-0.2	-3.4	-0.7	-0.1	0.4	2.6
Armenia	23	0	-0.4	-5.0	-1.0	-0.4	0.7	3.1
Austria	351	0	-0.1	-3.7	-0.7	0.0	0.5	2.5
Belarus	86	1	-0.8	-6.0	-1.7	-0.5	0.3	2.0
Belgium	434	0	-0.2	-3.2	-0.8	-0.2	0.4	2.6
Bulgaria	97	0	-0.7	-5.4	-1.4	-0.4	0.3	2.7
Croatia	75	0	-0.6	-3.8	-1.3	-0.4	0.3	3.4
Cyprus	10	0	-0.8	-3.1	-1.0	-0.6	-0.4	0.3
Czech Republic	286	0	-0.3	-4.9	-0.9	-0.2	0.4	2.1
Denmark	181	0	-0.1	-3.3	-0.6	-0.1	0.4	3.4
France	2496	15	-0.3	-5.0	-1.0	-0.3	0.3	4.7
Georgia	53	9	0.5	-2.8	-0.4	0.3	1.8	3.4
Germany	2434	3	-0.2	-6.5	-0.9	-0.2	0.4	2.8
Greece	90	0	0.3	-3.1	-0.4	0.2	1.2	2.4
Hungary	230	0	-0.6	-4.1	-1.3	-0.6	0.1	2.5
Iceland	7	0	0.1	-1.1	-0.7	0.2	0.6	1.1
Ireland	477	5	0.3	-2.5	-0.3	0.3	0.9	4.1
Israel	174	1	-0.2	-4.1	-1.0	-0.1	0.6	2.5
Italy	2000	4	-0.1	-13.2	-0.7	0.0	0.7	4.3
Latvia	28	0	-0.7	-2.6	-1.2	-0.8	0.1	0.8
Lithuania	10	1	-1.0	-2.4	-1.9	-1.0	0.1	0.5
Luxembourg	15	0	-0.7	-2.1	-1.7	-0.5	-0.1	1.2
Rep of Moldova	39	0	-1.2	-5.5	-2.3	-1.0	0.2	3.0
The Netherlands	503	2	-0.2	-3.4	-0.7	-0.1	0.4	1.8
North Macedonia	67	0	-0.4	-5.2	-1.1	-0.3	0.6	2.1
Norway	105	0	-0.1	-2.3	-0.8	-0.1	0.5	2.3
Poland	733	7	-0.3	-5.0	-0.9	-0.2	0.4	6.2
Portugal	167	0	-0.3	-4.0	-1.0	-0.3	0.5	2.0
Romania	175	11	-1.0	-10.7	-1.8	-0.7	0.2	2.7
Russian Federation	1555	0	-0.7	-10.9	-1.4	-0.6	0.2	3.9
Serbia	93	0	-0.5	-4.8	-1.1	-0.3	0.3	2.2
Slovak Republic	105	8	-0.6	-4.6	-1.2	-0.6	0.1	2.5
Slovenia	51	0	-0.4	-3.1	-0.9	-0.2	0.2	2.0
Spain	983	2	-0.1	-5.7	-0.7	-0.1	0.6	2.6
Sweden	255	1	0.0	-2.9	-0.7	-0.1	0.6	2.6
Switzerland	393	3	-0.2	-2.9	-0.7	-0.1	0.4	2.5
Turkey	1583	0	-0.5	-9.9	-1.3	-0.4	0.5	4.2
Ukraine	123	0	-0.9	-7.1	-1.6	-0.8	-0.2	2.3
United Kingdom[1]	3720	111	0.1	-10.4	-0.5	0.1	0.8	3.4
Total	20270	188	-0.2	-13.2	-0.9	-0.2	0.5	6.2

[1] United Kingdom: height and weight at date of annual data is used instead of the date of best FEV_1. If no lung function measurement is reported, the date of the last visit is used.

This table reports the median z-score for BMI, the mean z-score for BMI and other descriptive statistics for children aged 2 to 17 years, by country.

Table 6.2 BMI: descriptive statistics by country. All patients seen in 2020 aged 18 years or older who never had a transplant.

Country	N	N Miss	Mean	Min	25th pctl (25% of the patients are below this BMI)	Median (50% of the patients are below this BMI)	75th pctl (75% of the patients are below this BMI)	Max
Austria	346	0	22.1	15.0	19.8	21.5	23.7	38.3
Belgium	655	0	22.7	15.4	20.3	22.2	24.4	36.3
Bulgaria	78	0	20.6	12.4	18.4	19.9	21.8	39.8
Croatia	37	0	21.4	13.4	19.6	21.6	23.3	29.0
Cyprus	10	1	24.5	18.5	21.1	23.3	25.4	40.8
Czech Republic	246	2	22.2	14.1	19.6	21.9	24.5	36.1
Denmark	261	0	23.1	16.4	20.1	22.7	24.6	41.1
France	3143	46	21.9	13.1	19.7	21.3	23.4	48.3
Germany	3383	10	22.1	14.0	19.8	21.5	23.7	46.1
Greece	241	2	22.6	14.8	20.3	22.1	24.3	38.1
Hungary	156	7	20.4	13.2	18.6	20.3	22.3	30.8
Iceland	6	0	23.2	17.1	21.2	23.7	26.7	26.8
Ireland	579	42	23.3	15.6	20.9	22.9	25.3	47.4
Israel	316	1	23.2	15.3	20.6	22.8	25.3	38.2
Italy	2757	20	22.6	14.2	20.2	22.1	24.5	56.2
Latvia	13	0	19.3	15.8	17.3	18.8	21.2	26.0
Lithuania	14	0	21.0	18.2	19.3	19.7	21.6	26.3
Rep of Moldova	10	0	18.6	15.2	17.0	18.4	19.5	22.8
The Netherlands	832	4	22.6	15.6	20.4	22.3	24.2	45.5
North Macedonia	37	0	22.2	15.6	20.4	22.4	24.3	27.4
Norway	158	1	22.9	15.3	20.2	22.1	24.7	37.4
Poland	275	0	21.3	13.7	18.9	20.7	23.0	38.6
Portugal	134	2	22.2	15.4	19.6	21.4	24.2	40.2
Romania	5	0	18.5	15.6	17.0	17.6	18.6	23.9
Russian Federation	613	2	19.6	12.5	17.5	19.0	21.2	34.3
Serbia	50	0	19.9	14.9	17.8	20.2	21.9	25.2
Slovak Republic	123	1	21.4	15.0	18.9	21.0	23.3	33.7
Slovenia	39	0	21.1	12.1	20.0	21.3	22.7	28.1
Spain	972	0	22.9	14.8	20.4	22.6	24.7	45.2
Sweden	334	10	22.9	15.2	20.5	22.3	24.3	41.7
Switzerland	492	0	21.8	14.5	19.7	21.5	23.4	36.6
Turkey	227	1	20.7	12.3	17.9	19.9	23.2	31.9
Ukraine	29	0	20.0	16.5	17.9	20.2	21.5	26.8
United Kingdom[1]	5045	169	23.5	13.4	20.7	22.8	25.3	57.5
Total	21622	321	22.5	12.1	20.0	21.9	24.3	57.5

[1] United Kingdom: height and weight at date of annual data is used instead of the date of best FEV_1. If no lung function measurement is reported, the date of the last visit is used.

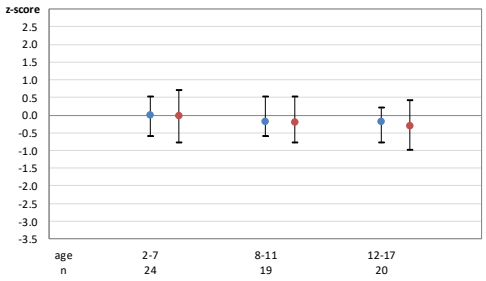
Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia, Luxembourg have <5 patients aged 18 years or more at BMI measurement and are excluded from the table.

This table reports the median BMI (expressed as absolute values, not as z-scores), the mean BMI and other descriptive statistics for all patients aged 18 years or older, by country.

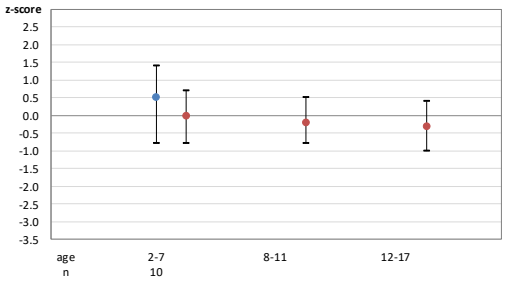
Figure 6.2 Quartiles of z-scores for BMI by age group and country. Patients aged 2-17 years in 2020 who never had a transplant.

The figures below show the z-scores for BMI by country. The dot is the median, and the whiskers show the 25th and 75th percentiles. In blue are the quartiles for the country, in red are the pooled quartiles computed on all other countries (i.e. excluding that country). We did not compute quartiles where the number of patients in the age group is <10. Therefore, there are no blue dots for those age groups (the number of patients in each age group is shown underneath the horizontal axis). We therefore excluded Cyprus, Iceland, Lithuania and Luxembourg from the graphs because none of the age groups in these countries had more than 10 patients.

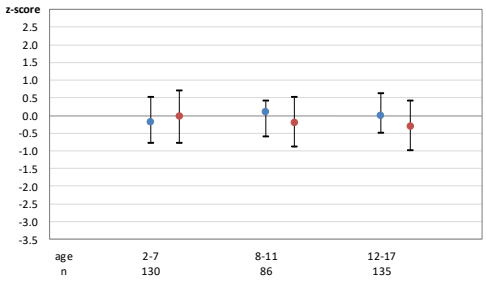
Quartiles of z-scores for BMI: Albania



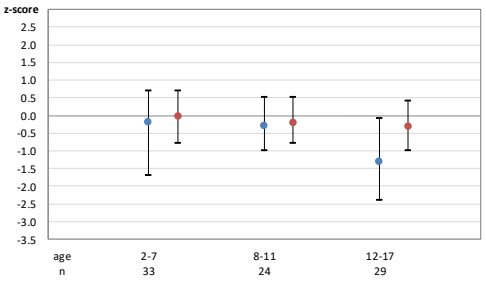
Quartiles of z-scores for BMI: Armenia



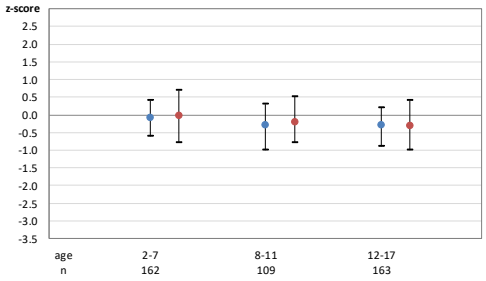
Quartiles of z-scores for BMI: Austria



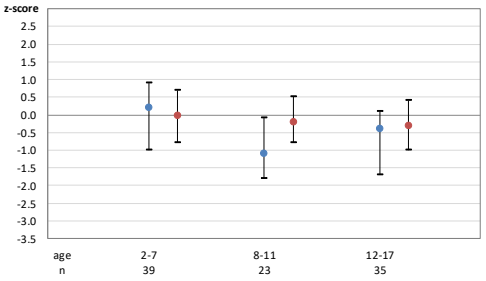
Quartiles of z-scores for BMI: Belarus



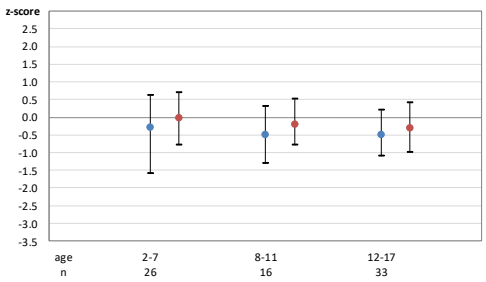
Quartiles of z-scores for BMI: Belgium



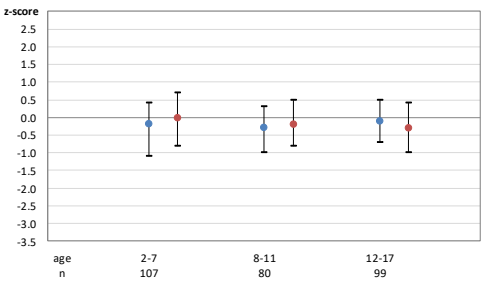
Quartiles of z-scores for BMI: Bulgaria



Quartiles of z-scores for BMI: Croatia

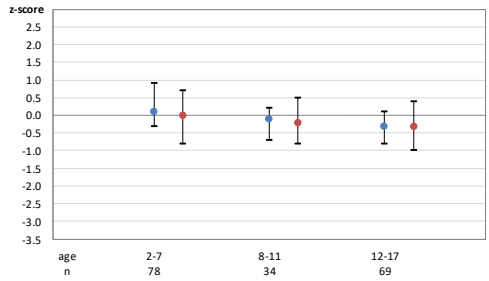


Quartiles of z-scores for BMI: Czech Republic

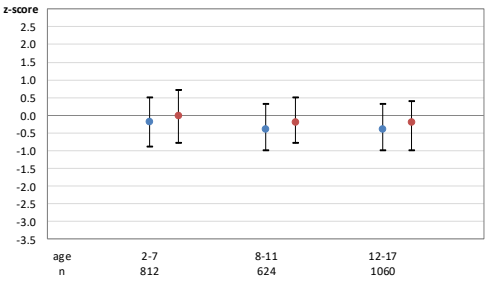


[figure 6.2 continued]

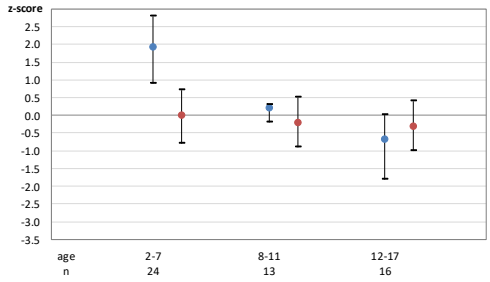
Quartiles of z-scores for BMI: Denmark



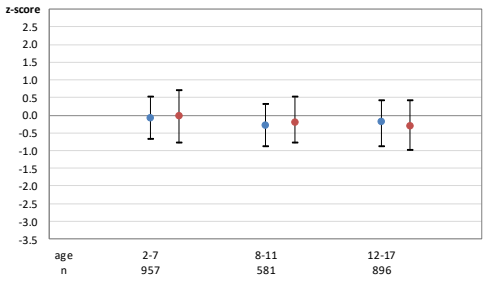
Quartiles of z-scores for BMI: France



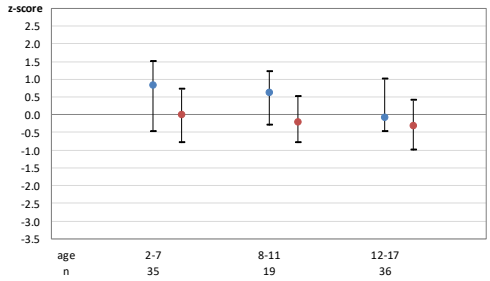
Quartiles of z-scores for BMI: Georgia



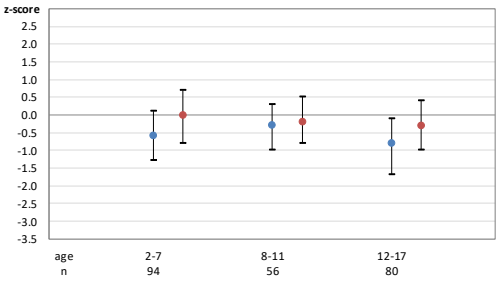
Quartiles of z-scores for BMI: Germany



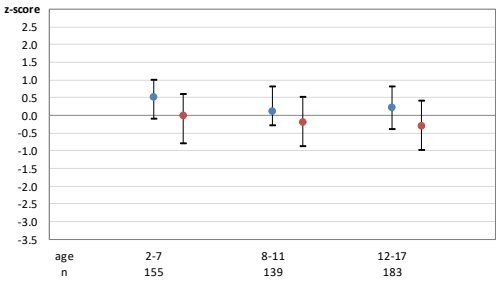
Quartiles of z-scores for BMI: Greece



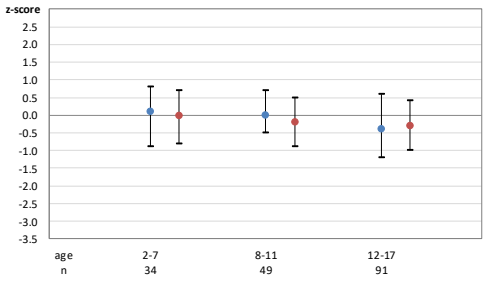
Quartiles of z-scores for BMI: Hungary



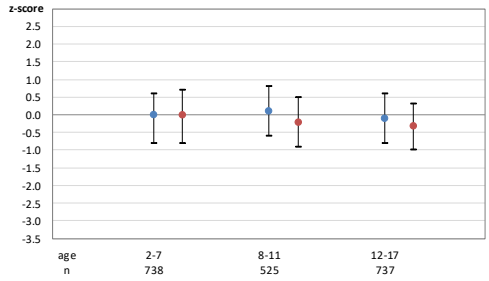
Quartiles of z-scores for BMI: Ireland



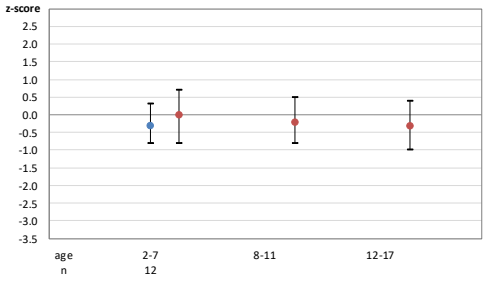
Quartiles of z-scores for BMI: Israel



Quartiles of z-scores for BMI: Italy

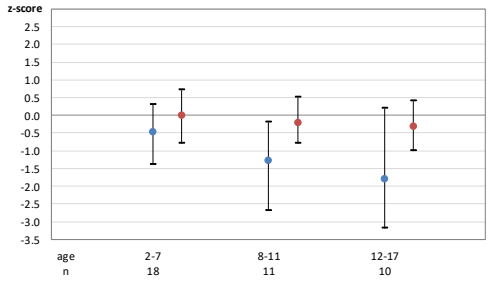


Quartiles of z-scores for BMI: Latvia

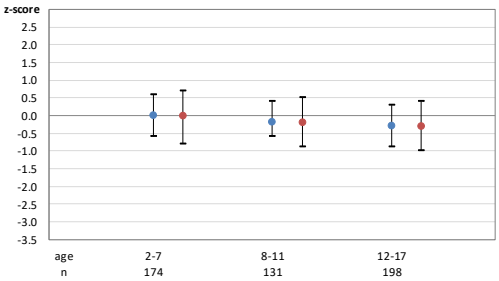


[figure 6.2 continued]

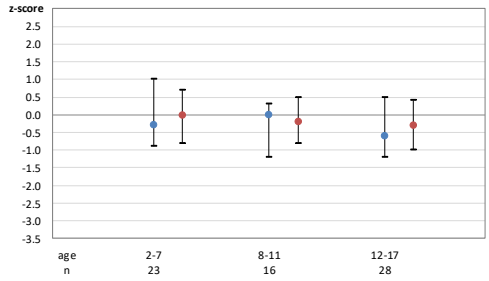
Quartiles of z-scores for BMI: Rep. of Moldova



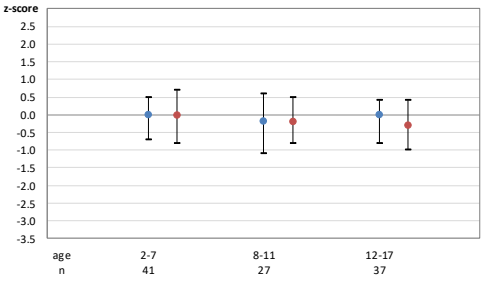
Quartiles of z-scores for BMI: The Netherlands



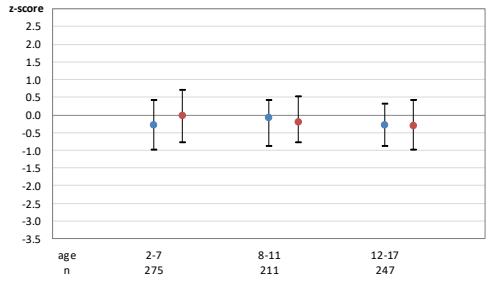
Quartiles of z-scores for BMI: North Macedonia



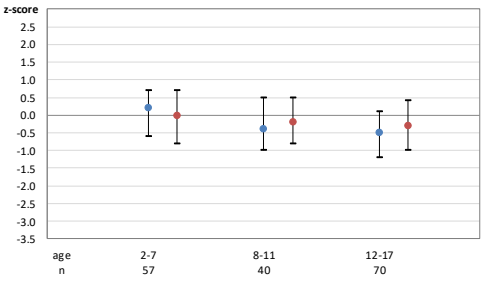
Quartiles of z-scores for BMI: Norway



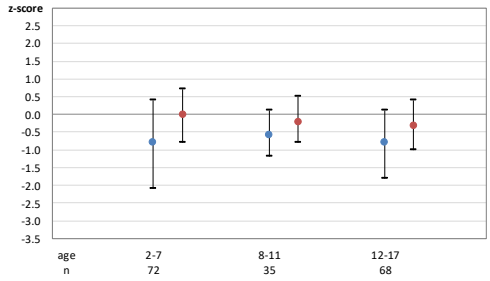
Quartiles of z-scores for BMI: Poland



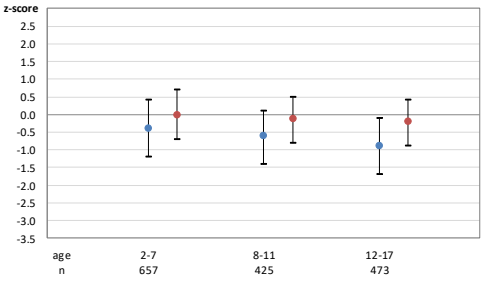
Quartiles of z-scores for BMI: Portugal



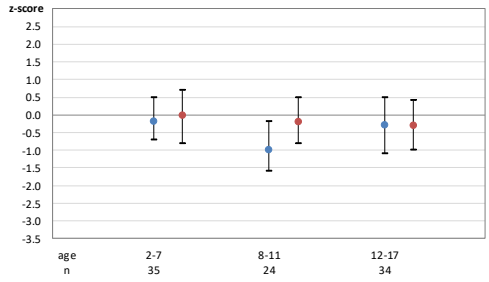
Quartiles of z-scores for BMI: Romania



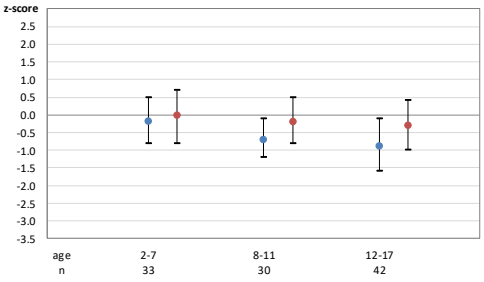
Quartiles of z-scores for BMI: Russian Federation



Quartiles of z-scores for BMI: Serbia

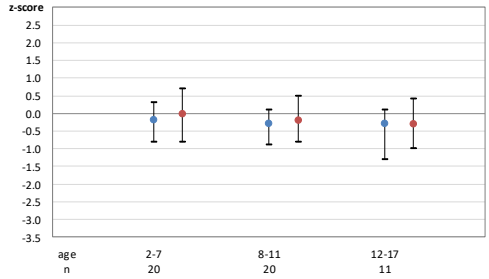


Quartiles of z-scores for BMI: Slovak Republic

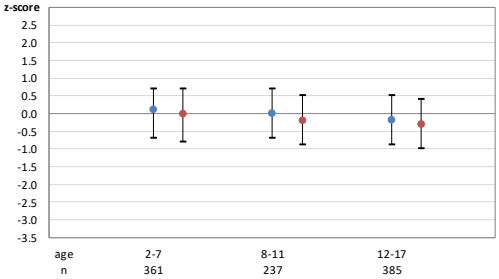


[figure 6.2 continued]

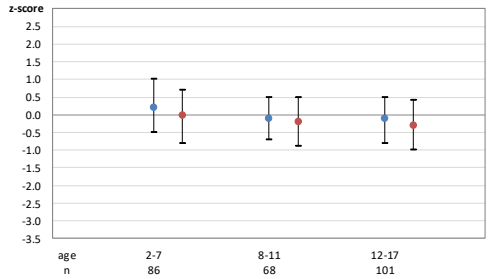
Quartiles of z-scores for BMI: Slovenia



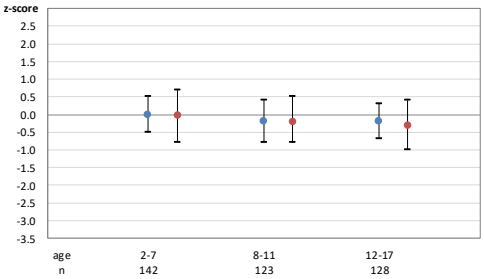
Quartiles of z-scores for BMI: Spain



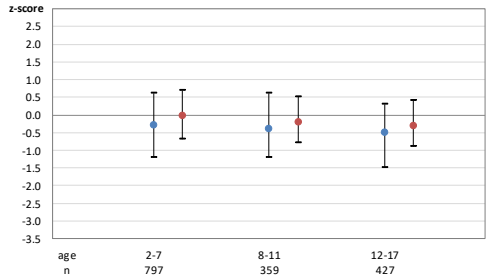
Quartiles of z-scores for BMI: Sweden



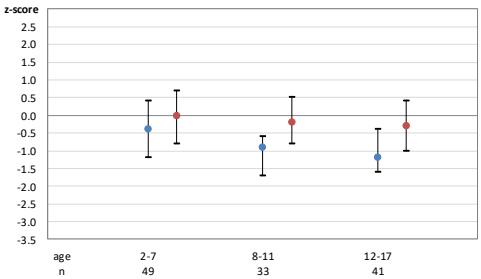
Quartiles of z-scores for BMI: Switzerland



Quartiles of z-scores for BMI: Turkey



Quartiles of z-scores for BMI: Ukraine



Quartiles of z-scores for BMI: United Kingdom

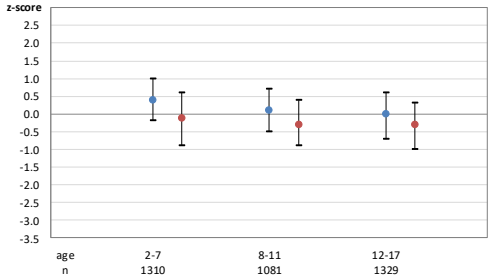
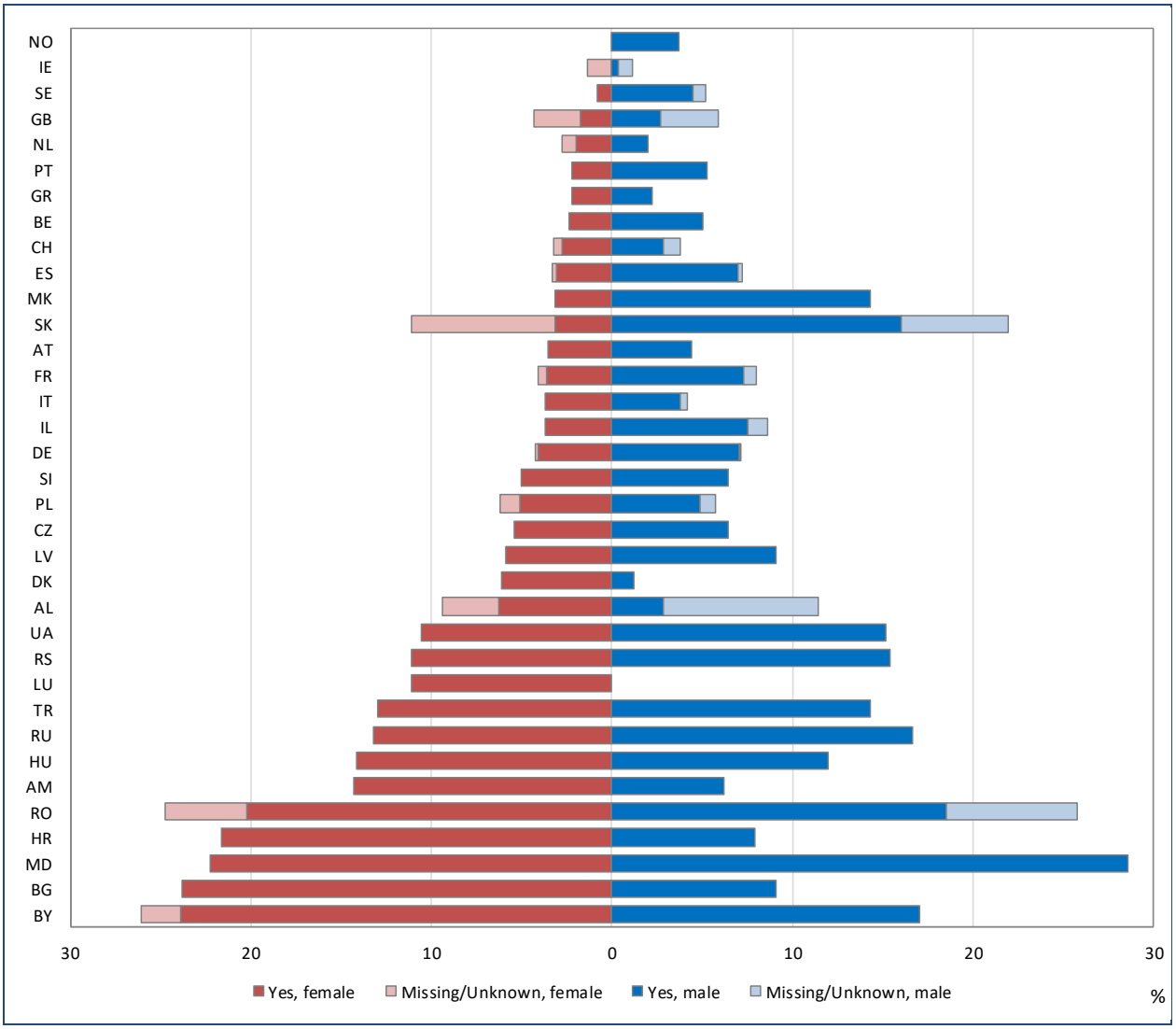


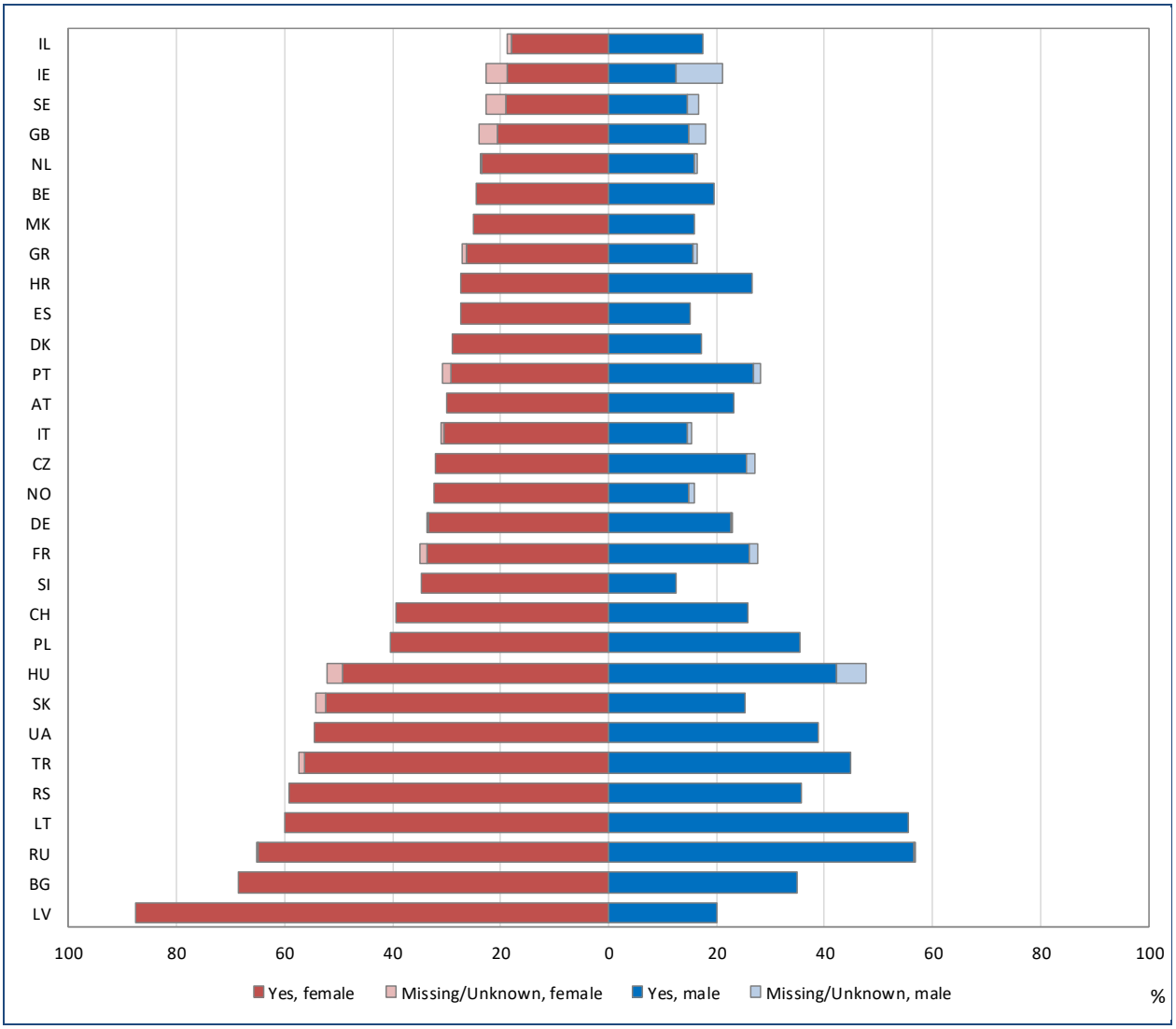
Figure 6.3 Proportion of children underweight (z-score of BMI<-2) by sex and by country. Patients aged 2-17 years in 2020 who never had a transplant.



Note: We excluded from the graph the countries for which the information on underweight children is missing for more than 10% of the patients.
Cyprus and Iceland have been excluded from this graph because the number of children in one of the sex groups is less than 5.

The coloured bars (red for females, blue for males) represent the percentage of underweight children in each country. The light-coloured bars (light red for females, light blue for males) represent the percentage of missing values on BMI for children in each country.

Figure 6.4 Proportion of adults with BMI<20 by sex and by country. Patients aged 18 years or older in 2020 who never had a transplant.



Note: We excluded from the graph the countries for which the information on underweight adults is missing for more than 10% of the patients.
Albania, Armenia, Cyprus, Iceland, Luxembourg, Republic of Moldova and Romania have been excluded from this graph because the number of adults in one of the sex groups is less than 5.

The coloured bars (red for females, blue for males) represent the percentage of underweight adults in each country. The light-coloured bars (light red for females, light blue for males) represent the percentage of missing values on BMI for adults in each country.

7. Respiratory complications and therapies

The information in this section should not be considered complete, for several reasons: national CF registries may use a different definition or different parameters for a complication; data about one or more of the complications is not collected; or the status of the complication is truly unknown. In the tables, therefore, we show the number of missing values for the various complications, but in the graphs we have included only countries where less than 10% of the data is missing. For a full list of complications and definitions please see Appendix 3, page 152.

In this section we also present data on selected therapies. We collected information on therapies using the generic name of the drug, not the brand name. For example, instead of naming individual antibiotics, we ask whether the patient has been taking “inhaled antibiotics for more than three months this year”.

Table 7.1 Prevalence of children with at least 1 day on IV antibiotics (for CF-related reasons) at home and in hospital[1], or in hospital only when at least for 1 day in hospital for any reason (routine check-up days not included). Patients seen in 2020, who have never had a transplant, by country and overall.

Country	At least 1 day on intravenous antibiotics (for CF-related reasons), at home + in hospital number (%)			At least 1 day on intravenous antibiotics (for CF-related reasons), in hospital only number (%)			At least 1 day in hospital, for any reason (routine check-up days not included) number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	0 (0.00)	47 (61.04)	30 (38.96)	0 (0.00)	47 (61.04)	30 (38.96)	0 (0.00)	46 (59.74)	31 (40.26)
Armenia	15 (62.50)	1 (4.17)	8 (33.33)	18 (75.00)	1 (4.17)	5 (20.83)	17 (70.83)	1 (4.17)	6 (25.00)
Austria	0 (0.00)	305 (80.47)	74 (19.539	3 (0.79)	303 (79.95)	73 (19.26)	0 (0.00)	256 (67.55)	123 (32.45)
Belarus	6 (4.00)	78 (52.00)	66 (44.00)	6 (4.00)	78 (52.00)	66 (44.00)	6 (4.00)	77 (51.33)	67 (44.67)
Belgium	0 (0.00)	360 (77.42)	105 (22.58)	0 (0.00)	361 (77.63)	104 (22.37)	0 (0.00)	302 (64.95)	163 (35.05)
Bulgaria	6 (5.36)	74 (66.07)	32 (28.57)	6 (5.36)	74 (66.07)	32 (28.57)	6 (5.36)	59 (52.68)	47 (41.96)
Croatia	1 (1.25)	63 (78.75)	16 (20.00)	1 (1.25)	63 (78.75)	16 (20.00)	1 (1.25)	55 (68.75)	24 (30.00)
Cyprus	0 (0.00)	9 (90.00)	1 (10.00)	0 (0.00)	9 (90.00)	1 (10.00)	0 (0.00)	9 (90.00)	1 (10.00)
Czech Republic	1 (0.30)	290 (88.15)	38 (11.55)	1 (0.30)	291 (88.45)	37 (11.25)	1 (0.30)	254 (77.20)	74 (22.49)
Denmark	2 (0.98)	160 (78.43)	42 (20.59)	150 (73.53)	49 (24.02)	5 (2.45)	55 (26.96)	112 (54.90)	37 (18.14)
France	7 (0.26)	2292 (84.05)	428 (15.69)	0 (0.00)	2393 (87.75)	334 (12.25)	420 (15.40)	1761 (64.58)	546 (20.02)
Georgia	10 (13.89)	54 (75.00)	8 (11.11)	10 (13.89)	55 (76.39)	7 (9.72)	10 (13.89)	55 (76.39)	7 (9.72)
Germany	2 (0.08)	2300 (86.43)	359 (13.49)	7 (0.26)	2334 (87.71)	320 (12.03)	191 (7.18)	1724 (64.79)	746 (28.03)
Greece	1 (1.05)	79 (83.16)	15 (15.79)	0 (0.00)	80 (84.21)	15 (15.79)	0 (0.00)	74 (77.89)	21 (22.11)
Hungary	248 (100)	0 (0)	0 (0)	248 (100)	0 (0)	0 (0)	248 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	2 (25.00)	6 (75.00)	0 (0.00)	3 (37.50)	5 (62.50)	0 (0.00)	3 (37.50)	5 (62.50)
Ireland	0 (0.00)	409 (82.46)	87 (17.54)	422 (85.08)	68 (13.71)	6 (1.21)	0 (0.00)	403 (81.25)	93 (18.75)
Israel	1 (0.59)	143 (84.12)	26 (15.29)	1 (0.59)	151 (88.82)	18 (10.59)	1 (0.59)	147 (86.47)	22 (12.94)
Italy	182 (8.00)	1738 (76.43)	354 (15.57)	178 (7.83)	1757 (77.26)	339 (14.91)	0 (0.00)	1764 (77.57)	510 (22.43)
Latvia	0 (0.00)	25 (75.76)	8 (24.24)	0 (0.00)	25 (75.76)	8 (24.24)	0 (0.00)	21 (63.64)	12 (36.36)
Lithuania	0 (0.00)	7 (50.00)	7 (50.00)	0 (0.00)	7 (50.00)	7 (50.00)	0 (0.00)	7 (50.00)	7 (50.00)
Luxembourg	0 (0.00)	15 (71.43)	6 (28.57)	0 (0.00)	15 (71.43)	6 (28.57)	0 (0.00)	14 (66.67)	7 (33.33)

[table 7.1 continued]

Country	At least 1 day on intravenous antibiotics (for CF-related reasons), at home + in hospital number (%)			At least 1 day on intravenous antibiotics (for CF-related reasons), in hospital only number (%)			At least 1 day in hospital, for any reason (routine check-up days not included) number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	1 (2.63)	26 (68.42)	11 (28.95)	1 (2.63)	26 (68.42)	11 (28.95)	1 (2.63)	26 (68.42)	11 (28.95)
The Netherlands	0 (0.00)	449 (83.93)	86 (16.07)	0 (0.00)	460 (85.98)	75 (14.02)	0 (0.00)	430 (80.37)	105 (19.63)
North Macedonia	0 (0.00)	46 (58.23)	33 (41.77)	0 (0.00)	46 (58.23)	33 (41.77)	0 (0.00)	45 (56.96)	34 (43.04)
Norway	0 (0.00)	106 (88.33)	14 (11.67)	0 (0.00)	109 (90.83)	11 (9.17)	0 (0.00)	94 (78.33)	26 (21.67)
Poland	24 (2.90)	591 (71.38)	213 (25.72)	2 (0.24)	603 (72.83)	223 (26.93)	3 (0.36)	399 (48.19)	426 (51.45)
Portugal	0 (0.00)	153 (85.96)	25 (14.04)	0 (0.00)	153 (85.96)	25 (14.04)	0 (0.00)	145 (81.46)	33 (18.54)
Romania	18 (8.22)	124 (56.62)	77 (35.16)	17 (7.76)	128 (58.45)	74 (33.79)	17 (7.76)	57 (26.03)	145 (66.21)
Russian Federation	8 (0.47)	876 (51.44)	819 (48.09)	68 (3.99)	862 (50.62)	773 (45.39)	144 (8.46)	698 (40.99)	861 (50.56)
Serbia	0 (0.00)	67 (67.68)	32 (32.32)	0 (0.00)	67 (67.68)	32 (32.32)	0 (0.00)	66 (66.67)	33 (33.33)
Slovak Republic	3 (2.44)	100 (81.30)	20 (16.26)	3 (2.44)	100 (81.30)	20 (16.26)	3 (2.44)	94 (76.42)	26 (21.14)
Slovenia	0 (0.00)	39 (75.00)	13 (25.00)	0 (0.00)	39 (75.00)	13 (25.00)	1 (1.92)	36 (69.23)	15 (28.85)
Spain	16 (1.49)	941 (87.53)	118 (10.98)	16 (1.49)	956 (88.93)	103 (9.58)	16 (1.49)	927 (86.23)	132 (12.28)
Sweden	0 (0.00)	187 (70.57)	78 (29.43)	265 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)	223 (84.15)	42 (15.85)
Switzerland	3 (0.71)	363 (85.61)	58 (13.68)	4 (0.94)	367 (86.56)	53 (12.50)	4 (0.94)	354 (83.49)	66 (15.57)
Turkey	1 (0.06)	1444 (79.91)	362 (20.03)	1 (0.06)	1453 (80.41)	353 (19.54)	1 (0.069	1323 (73.22)	483 (26.73)
Ukraine	3 (2.26)	34 (25.56)	96 (72.18)	3 (2.26)	35 (26.32)	95 (71.43)	2 (1.50)	35 (26.32)	96 (72.18)
United Kingdom	0 (0.00)	3067 (72.59)	1158 (27.41)	0 (0.00)	3163 (74.86)	1062 (25.14)	6 (0.14)	2796 (66.18)	1423 (33.68)
Total	559 (2.48)	17064 (75.67)	4929 (21.86)	1388 (6.15)	16772 (74.37)	4392 (19.47)	1154 (5.12)	14892 (66.03)	6506 (28.85)

Note: At home + in hospital means that the IV antibiotics were administered at home and/or in hospital.

Table 7.2 Prevalence of adults with at least 1 day on IV antibiotics (for CF-related reasons) at home and in hospital[1], or in hospital only with at least 1 day in hospital, for any reason (routine check-up days not included). Patients seen in 2020, who have never had a transplant, by country and overall.

Country	At least 1 day on intravenous antibiotics (for CF-related reasons), at home + in hospital number (%)			At least 1 day on intravenous antibiotics (for CF-related reasons), in hospital only number (%)			At least 1 day in hospital, for any reason (routine check-up days not included) number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	1 (0.28)	237 (66.39)	119 (33.33)	13 (3.64)	235 (65.83)	109 (30.53)	10 (2.80)	222 (62.18)	125 (35.01)
Belgium	0 (0.00)	410 (61.29)	259 (38.71)	0 (0.00)	450 (67.26)	219 (32.74)	1 (0.15)	411 (61.43)	257 (38.42)
Bulgaria	1 (1.23)	64 (79.01)	16 (19.75)	1 (1.23)	69 (85.19)	11 (13.58)	0 (0.00)	64 (79.01)	17 (20.99)
Croatia	19 (43.18)	12 (27.27)	13 (29.55)	20 (45.45)	12 (27.27)	12 (27.27)	19 (43.18)	11 (25.00)	14 (31.82)
Cyprus	0 (0.00)	10 (83.33)	2 (16.67)	0 (0.00)	10 (83.33)	2 (16.67)	0 (0.00)	10 (83.33)	2 (16.67)
Czech Republic	0 (0.00)	191 (75.20)	63 (24.80)	0 (0.00)	192 (75.59)	62 (24.41)	0 (0.00)	185 (72.83)	69 (27.17)
Denmark	0 (0.00)	211 (79.62)	54 (20.38)	265 (100)	0 (0)	0 (0)	172 (64.91)	78 (29.43)	15 (5.66)
France	45 (1.36)	2031 (61.34)	1235 (37.30)	0 (0.00)	2755 (83.21)	556 (16.79)	831 (25.10)	1660 (50.14)	820 (24.77)
Germany	52 (1.50)	2503 (71.99)	922 (26.52)	21 (0.60)	2760 (79.38)	696 (20.02)	147 (4.23)	2312 (66.49)	1018 (29.28)
Greece	0 (0.00)	163 (57.39)	121 (42.61)	0 (0.00)	173 (60.92)	111 (39.08)	1 (0.35)	163 (57.39)	120 (42.25)
Hungary	185 (100)	0 (0)	0 (0)	185 (100)	0 (0)	0 (0)	185 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	5 (83.33)	1 (16.67)	0 (0.00)	5 (83.33)	1 (16.67)	0 (0.00)	5 (83.33)	1 (16.67)
Ireland	0 (0.00)	401 (63.15)	234 (36.85)	635 (100)	0 (0)	0 (0)	0 (0.00)	410 (64.57)	225 (35.43)
Israel	2 (0.59)	242 (71.81)	93 (27.60)	2 (0.59)	292 (86.65)	43 (12.76)	3 (0.89)	272 (80.71)	62 (18.40)
Italy	463 (14.45)	2134 (66.58)	608 (18.97)	463 (14.45)	2202 (68.71)	540 (16.85)	2 (0.06)	2358 (73.57)	845 (26.37)
Latvia	0 (0.00)	5 (38.46)	8 (61.54)	0 (0.00)	5 (38.46)	8 (61.54)	0 (0.00)	5 (38.46)	8 (61.54)
Lithuania	0 (0.00)	11 (55.00)	9 (45.00)	0 (0.00)	11 (55.00)	9 (45.00)	0 (0.00)	9 (45.00)	11 (55.00)

[table 7.2 continued]

Country	At least 1 day on intravenous antibiotics (for CF-related reasons), at home + in hospital number (%)			At least 1 day on intravenous antibiotics (for CF-related reasons), in hospital only number (%)			At least 1 day in hospital, for any reason (routine check-up days not included) number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	3 (27.27)	8 (72.73)	0 (0.00)	9 (81.82)	2 (18.18)	0 (0.00)	9 (81.82)	2 (18.18)
the Netherlands	1 (0.11)	663 (73.75)	235 (26.14)	1 (0.11)	684 (76.08)	214 (23.80)	1 (0.11)	647 (71.97)	251 (27.92)
North Macedonia	0 (0.00)	11 (26.83)	30 (73.17)	0 (0.00)	11 (26.83)	30 (73.17)	0 (0.00)	11 (26.83)	30 (73.17)
Norway	3 (1.78)	109 (64.50)	57 (33.73)	1 (0.59)	137 (81.07)	31 (18.34)	5 (2.96)	121 (71.60)	43 (25.44)
Poland	22 (6.75)	131 (40.18)	173 (53.07)	10 (3.07)	135 (41.41)	181 (55.52)	10 (3.07)	122 (37.42)	194 (59.51)
Portugal	30 (19.61)	96 (62.75)	27 (17.65)	30 (19.61)	96 (62.75)	27 (17.65)	30 (19.61)	95 (62.09)	28 (18.30)
Romania	4 (50.00)	3 (37.50)	1 (12.50)	2 (25.00)	3 (37.50)	3 (37.50)	3 (37.50)	1 (12.50)	4 (50.00)
Russian Federation	455 (69.79)	65 (9.97)	132 (20.25)	459 (70.40)	71 (10.89)	122 (18.71)	465 (71.32)	69 (10.58)	118 (18.10)
Serbia	0 (0.00)	40 (70.18)	17 (29.82)	0 (0.00)	40 (70.18)	17 (29.82)	0 (0.00)	38 (66.67)	19 (33.33)
Slovak Republic	15 (10.71)	89 (63.57)	36 (25.71)	15 (10.71)	95 (67.86)	30 (21.43)	15 (10.71)	95 (67.86)	30 (21.43)
Slovenia	1 (2.44)	30 (73.17)	10 (24.39)	1 (2.44)	30 (73.17)	10 (24.39)	1 (2.44)	24 (58.54)	16 (39.02)
Spain	5 (0.47)	854 (79.59)	214 (19.94)	5 (0.47)	929 (86.58)	139 (12.95)	5 (0.47)	912 (85.00)	156 (14.54)
Sweden	0 (0.00)	150 (42.98)	199 (57.02)	349 (100)	0 (0)	0 (0)	0 (0.00)	279 (79.94)	70 (20.06)
Switzerland	1 (0.20)	357 (71.12)	144 (28.69)	1 (0.20)	414 (82.47)	87 (17.33)	3 (0.60)	393 (78.29)	106 (21.12)
Turkey	0 (0.00)	168 (66.93)	83 (33.07)	0 (0.00)	170 (67.73)	81 (32.27)	0 (0.00)	165 (65.74)	86 (34.26)
Ukraine	1 (2.78)	8 (22.22)	27 (75.00)	1 (2.78)	16 (44.44)	19 (52.78)	1 (2.78)	14 (38.89)	21 (58.33)
United Kingdom	0 (0.00)	2727 (50.85)	2636 (49.15)	0 (0.00)	3326 (62.02)	2037 (37.98)	1 (0.02)	3091 (57.64)	2271 (42.35)
Total	1307 (5.63)	14137 (60.85)	7790 (33.53)				1913 (8.23)	14264 (61.39)	7057 (30.37)

Note: At home + in hospital means that the IV antibiotics were administered at home and/or in hospital.
Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more at 31/12/2020 and are not shown in this table but considered in the total.
Note: For the number of days on intravenous antibiotics (for CF-related reasons) in hospital only, the total percentage of missing information is higher than 10% and, therefore, the totals are excluded from the table.

Table 7.3 Prevalence of allergic bronchopulmonary aspergillosis (ABPA), pneumothorax and haemoptysis major in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	ABPA this year number (%)			Pneumothorax this year number (%)			Haemoptysis major ≥ 250 ml this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	5 (6.17)	75 (92.59)	1 (1.23)	7 (8.64)	74 (91.36)	0 (0.00)	4 (4.94)	73 (90.12)	4 (4.94)
Armenia[1]	0 (0)	25 (100)	0 (0)	0 (0.00)	23 (92.00)	2 (8.00)	2 (8.00)	23 (92.00)	0 (0.00)
Austria	2 (0.27)	712 (96.74)	22 (2.99)	2 (0.27)	731 (99.32)	3 (0.41)	7 (0.95)	715 (97.15)	14 (1.90)
Belarus	0 (0)	150 (100)	0 (0)	0 (0)	150 (100)	0 (0)	0 (0.00)	149 (99.33)	1 (0.67)
Belgium	2 (0.18)	1031 (90.92)	101 (8.91)	2 (0.18)	1131 (99.74)	1 (0.09)	4 (0.35)	1110 (97.88)	20 (1.76)
Bulgaria	0 (0.00)	189 (97.93)	4 (2.07)	0 (0.00)	192 (99.48)	1 (0.52)	0 (0.00)	177 (91.71)	16 (8.29)
Croatia	1 (0.81)	122 (98.39)	1 (0.81)	1 (0.81)	122 (98.39)	1 (0.81)	1 (0.81)	118 (95.16)	5 (4.03)
Cyprus	0 (0)	22 (100)	0 (0)	0 (0)	22 (100)	0 (0)	0 (0)	22 (100)	0 (0)
Czech Republic	1 (0.17)	569 (97.60)	13 (2.23)	9 (1.54)	573 (98.28)	1 (0.17)	4 (0.69)	575 (98.63)	4 (0.69)
Denmark	0 (0.00)	457 (97.44)	12 (2.56)	0 (0)	469 (100)	0 (0)	0 (0.00)	467 (99.57)	2 (0.43)
France	0 (0.00)	5597 (92.70)	441 (7.30)	0 (0.00)	6021 (99.72)	17 (0.28)	0 (0.00)	5991 (99.22)	47 (0.78)
Georgia	3 (4.11)	70 (95.89)	0 (0.00)	2 (2.74)	71 (97.26)	0 (0.00)	0 (0.00)	71 (97.26)	2 (2.74)
Germany[1]	81 (1.32)	5811 (94.67)	246 (4.01)	80 (1.30)	6027 (98.19)	31 (0.51)	190 (3.10)	5938 (96.74)	10 (0.16)
Greece	19 (5.01)	349 (92.08)	11 (2.90)	13 (3.43)	365 (96.31)	1 (0.26)	12 (3.17)	361 (95.25)	6 (1.58)
Hungary	5 (1.15)	414 (95.61)	14 (3.23)	5 (1.15)	425 (98.15)	3 (0.69)	11 (2.54)	411 (94.92)	11 (2.54)
Iceland	0 (0.00)	13 (92.86)	1 (7.14)	0 (0)	14 (100)	0 (0)	0 (0.00)	12 (85.71)	2 (14.29)
Ireland[2]	38 (3.36)	1016 (89.83)	77 (6.81)	0 (0.0)	1130 (99.91)	<5 (0.09)	0 (0.00)	1118 (98.85)	13 (1.15)
Israel	17 (3.35)	464 (91.52)	26 (5.13)	23 (4.54)	484 (95.46)	0 (0.00)	20 (3.94)	485 (95.66)	2 (0.39)
Italy	125 (2.28)	5234 (95.53)	120 (2.19)	145 (2.65)	5324 (97.17)	10 (0.18)	129 (2.35)	5098 (93.05)	252 (4.60)
Latvia	1 (2.17)	45 (97.83)	0 (0.00)	0 (0.00)	45 (97.83)	1 (2.17)	0 (0.00)	39 (84.78)	7 (15.22)
Lithuania	0 (0.00)	33 (97.06)	1 (2.949	2 (5.88)	32 (94.12)	0 (0.00)	0 (0.00)	31 (91.18)	3 (8.82)
Luxembourg	1 (4.35)	21 (91.30)	1 (4.35)	0 (0)	23 (100)	0 (0)	0 (0)	23 (100)	0 (0)

[1] Germany: defines haemoptysis major > 240 ml.
[2] Ireland: haemoptysis major is defined as haemoptysis massive > 240ml/day or > 100ml/day for several days.

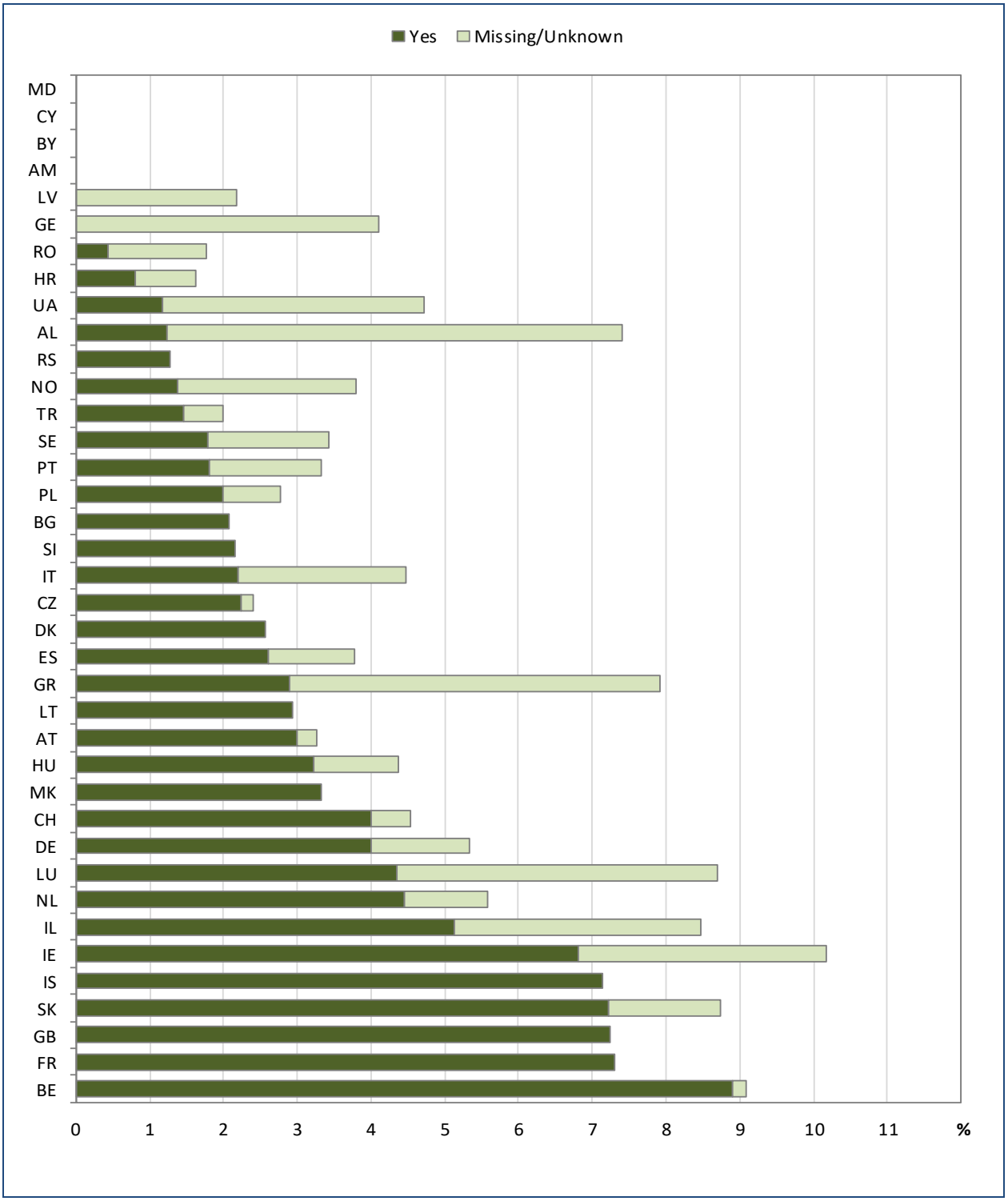
[table 7.3 continued]

Country	ABPA this year number (%)			Pneumothorax this year number (%)			Haemoptysis major over 250 ml this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0)	49 (100)	0 (0)	0 (0)	49 (100)	0 (0)	0 (0)	49 (100)	0 (0)
The Netherlands	16 (1.12)	1354 (94.42)	64 (4.46)	78 (5.44)	1350 (94.14)	6 (0.42)	82 (5.72)	1299 (90.59)	53 (3.70)
North Macedonia	0 (0.00)	116 (96.67)	4 (3.33)	0 (0)	120 (100)	0 (0)	0 (0.00)	118 (98.33)	2 (1.67)
Norway	7 (2.42)	278 (96.19)	4 (1.38)	0 (0.00)	288 (99.65)	1 (0.35)	289 (100)	0 (0)	0 (0)
Poland	9 (0.78)	1122 (97.23)	23 (1.99)	13 (1.13)	1139 (98.69)	2 (0.18)	12 (1.04)	1094 (94.80)	48 (4.16)
Portugal	5 (1.51)	320 (96.68)	6 (1.81)	12 (3.63)	317 (95.77)	2 (0.60)	7 (2.11)	291 (87.92)	33 (9.97)
Romania	3 (1.32)	223 (98.24)	1 (0.44)	5 (2.20)	222 (97.80)	0 (0.00)	7 (3.08)	214 (94.27)	6 (2.64)
Russian Federation	493 (20.93)	1826 (77.54)	36 (1.53)	480 (20.38)	1861 (79.02)	14 (0.60)	504 (21.40)	1835 (77.92)	16 (0.68)
Serbia	0 (0.00)	154 (98.72)	2 (1.28)	0 (0.00)	154 (98.72)	2 (1.28)	0 (0.00)	152 (97.44)	4 (2.56)
Slovak Republic	4 (1.52)	240 (91.25)	19 (7.22)	4 (1.52)	258 (98.10)	1 (0.38)	5 (1.90)	239 (90.87)	19 (7.22)
Slovenia	0 (0.00)	91 (97.85)	2 (2.15)	0 (0)	93 (100)	0 (0)	0 (0.00)	88 (94.62)	5 (5.38)
Spain	25 (1.16)	2067 (96.23)	56 (2.61)	32 (1.49)	2112 (98.32)	4 (0.19)	39 (1.82)	2051 (95.48)	58 (2.70)
Sweden	10 (1.63)	593 (96.58)	11 (1.79)	9 (1.47)	605 (98.53)	0 (0.00)	9 (1.47)	600 (97.72)	5 (0.81)
Switzerland	5 (0.54)	884 (95.46)	37 (4.00)	4 (0.43)	921 (99.46)	1 (0.11)	6 (0.65)	904 (97.62)	16 (1.73)
Turkey	11 (0.53)	2017 (98.01)	30 (1.46)	8 (0.39)	2047 (99.47)	3 (0.15)	8 (0.39)	2041 (99.17)	9 (0.44)
Ukraine	6 (3.55)	161 (95.27)	2 (1.18)	3 (1.78)	166 (98.22)	0 (0.00)	0 (0.00)	165 (97.63)	4 (2.37)
United Kingdom[3]	0 (0.00)	8894 (92.76)	694 (7.24)	1 (0.01)	9569 (99.80)	18 (0.19)	0 (0.00)	9572 (99.83)	16 (0.17)
Total	895 (1.95)	42808 (93.50)	2083 (4.55)	940 (2.05)	44719 (97.67)	137 (0.28)	1352 (2.95)	43719 (95.49)	715 (1.56)

[3] United Kingdom: for ABPA clinician reported aspergillus. United Kingdom defines haemoptysis major > 240 ml.

Table 7.3 shows the frequency of allergic bronchopulmonary aspergillosis by country (see Appendix 3, page 152, for ABPA definition) and shows the frequency of two extremely rare complications: Pneumothorax (collapsed lung), and haemoptysis (coughing up of blood) major of 250 ml or more.

Figure 7.1 Prevalence of allergic bronchopulmonary aspergillosis in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on allergic bronchopulmonary aspergillosis (ABPA) is missing for more than 10% of the patients.

Note: United Kingdom: for ABPA clinician reported aspergillus.

This graph shows the frequency of allergic bronchopulmonary aspergillosis (ABPA) by country. For the definition of ABPA see Appendix 3 (page 152) the dark green part of the bar shows the percentage of patients with ABPA, the light green part shows the percentage of patients for which this information is missing.

Table 7.4 Use of hypertonic saline, rhDNase and inhaled mannitol in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Hypertonic saline (NaCl) inhaled > 3 months this year number (%)			rhDNase inhaled > 3 months this year number (%)			Mannitol inhaled > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	1 (1.23)	1 (1.23)	79 (97.53)	2 (2.47)	76 (93.83)	3 (3.70)	2 (2.47)	79 (97.53)	0 (0.00)
Armenia	0 (0)	0 (0)	25 (100)	0 (0.00)	17 (68.00)	8 (32.00)	2 (8.00)	21 (84.00)	2 (8.00)
Austria	1 (0.14)	123 (16.71)	612 (83.15)	2 (0.27)	329 (44.70)	405 (55.03)	3 (0.41)	724 (98.37)	9 (1.22)
Belarus	0 (0.00)	54 (36.00)	96 (64.00)	0 (0.00)	145 (96.67)	5 (3.33)	0 (0)	150 (100)	0 (0)
Belgium	1 (0.09)	341 (30.07)	792 (69.84)	1 (0.09)	160 (14.11)	973 (85.80)	1134 (100)	0 (0)	0 (0)
Bulgaria	0 (0.00)	88 (45.60)	105 (54.40)	0 (0.00)	37 (19.17)	156 (80.83)	0 (0)	193 (100)	0 (0)
Croatia	0 (0.00)	20 (16.13)	104 (83.87)	0 (0.00)	37 (29.84)	87 (70.16)	0 (0)	124 (100)	0 (0)
Cyprus	0 (0.00)	18 (81.82)	4 (18.18)	0 (0.00)	4 (18.18)	18 (81.82)	0 (0)	22 (100)	0 (0)
Czech Republic	0 (0.00)	112 (19.21)	471 (80.79)	0 (0.00)	199 (34.13)	384 (65.87)	0 (0.00)	576 (98.80)	7 (1.20)
Denmark	3 (0.64)	326 (69.51)	140 (29.85)	0 (0.00)	50 (10.66)	419 (89.34)	197 (42.00)	257 (54.80)	15 (3.20)
France	0 (0.00)	5127 (84.91)	911 (15.09)	0 (0.00)	2882 (47.73)	3156 (52.27)	0 (0)	6038 (100)	0 (0)
Georgia	1 (1.37)	35 (47.95)	37 (50.68)	2 (2.74)	67 (91.78)	4 (5.48)	2 (2.74)	70 (95.89)	1 (1.37)
Germany	59 (0.96)	1129 (18.39)	4950 (80.65)	70 (1.14)	2938 (47.87)	3130 (50.99)	72 (1.17)	5869 (95.62)	197 (3.21)
Greece	1 (0.26)	265 (69.92)	113 (29.82)	2 (0.53)	98 (25.86)	279 (73.61)	2 (0.53)	371 (97.89)	6 (1.58)
Hungary	8 (1.85)	70 (16.17)	355 (81.99)	9 (2.08)	136 (31.41)	288 (66.51)	433 (100)	0 (0)	0 (0)
Iceland	0 (0)	0 (0)	14 (100)	0 (0.00)	1 (7.14)	13 (92.86)	0 (0)	14 (100)	0 (0)
Ireland	0 (0.00)	431 (38.11)	700 (61.89)	0 (0.00)	477 (42.18)	654 (57.82)	1131 (100)	0 (0)	0 (0)
Israel	9 (1.78)	102 (20.12)	396 (78.11)	3 (0.59)	126 (24.85)	378 (74.56)	2 (0.39)	504 (99.41)	1 (0.20)
Italy	34 (0.62)	2904 (53.00)	2541 (46.38)	34 (0.62)	3038 (55.45)	2407 (43.93)	37 (0.68)	5345 (97.55)	97 (1.77)
Latvia	3 (6.52)	4 (8.70)	39 (84.78)	2 (4.35)	26 (56.52)	18 (39.13)	0 (0.00)	45 (97.83)	1 (2.17)
Lithuania	0 (0.00)	29 (85.29)	5 (14.71)	0 (0.00)	8 (23.53)	26 (76.47)	0 (0)	34 (100)	0 (0)
Luxembourg	0 (0.00)	2 (8.70)	21 (91.30)	0 (0.00)	7 (30.43)	16 (69.57)	0 (0)	23 (100)	0 (0)

[table 7.4 continued]

Country	Hypertonic saline (NaCl) inhaled > 3 months this year number (%)			rhDNase inhaled > 3 months this year number (%)			Mannitol inhaled > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	4 (8.16)	45 (91.84)	0 (0.00)	48 (97.96)	1 (2.04)	0 (0)	49 (100)	0 (0)
The Netherlands	4 (0.28)	960 (66.95)	470 (32.78)	0 (0.00)	492 (34.31)	942 (65.69)	0 (0)	1434 (100)	0 (0)
North Macedonia	0 (0.00)	30 (25.00)	90 (75.00)	0 (0.00)	33 (27.50)	87 (72.50)	1 (0.83)	119 (99.17)	0 (0.00)
Norway	2 (0.69)	69 (23.88)	218 (75.43)	1 (0.35)	98 (33.91)	190 (65.74)	0 (0)	289 (100)	0 (0)
Poland	6 (0.52)	137 (11.87)	1011 (87.61)	4 (0.35)	163 (14.12)	987 (85.53)	6 (0.52)	1148 (99.48)	0 (0.00)
Portugal	5 (1.51)	189 (57.10)	137 (41.39)	4 (1.21)	53 (16.01)	274 (82.78)	2 (0.60)	329 (99.40)	0 (0.00)
Romania	1 (0.44)	40 (17.62)	186 (81.94)	1 (0.44)	46 (20.26)	180 (79.30)	5 (2.20)	222 (97.80)	0 (0.00)
Russian Federation	510 (21.66)	499 (21.19)	1346 (57.15)	485 (20.59)	56 (2.38)	1814 (77.03)	489 (20.769	1790 (76.01)	76 (3.23)
Serbia	0 (0.00)	3 (1.92)	153 (98.08)	0 (0.00)	41 (26.28)	115 (73.72)	0 (0)	156 (100)	0 (0)
Slovak Republic	2 (0.76)	149 (56.65)	112 (42.59)	3 (1.14)	83 (31.56)	177 (67.30)	3 (1.14)	260 (98.86)	0 (0.00)
Slovenia	0 (0.00)	1 (1.08)	92 (98.92)	0 (0.00)	66 (70.97)	27 (29.03)	1 (1.08)	92 (98.92)	0 (0.00)
Spain	14 (0.65)	756 (35.20)	1378 (64.15)	11 (0.51)	1329 (61.87)	808 (37.62)	9 (0.42)	2135 (99.39)	4 (0.19)
Sweden	7 (1.14)	88 (14.33)	519 (84.53)	8 (1.30)	420 (68.40)	186 (30.29)	9 (1.47)	597 (97.23)	8 (1.30)
Switzerland	2 (0.22)	201 (21.71)	723 (78.08)	2 (0.22)	476 (51.40)	448 (48.38)	2 (0.22)	922 (99.57)	2 (0.22)
Turkey	1 (0.05)	1645 (79.93)	412 (20.02)	5 (0.24)	185 (8.99)	1868 (90.77)	1 (0.05)	1984 (96.40)	73 (3.55)
Ukraine	0 (0.00)	4 (2.37)	165 (97.63)	0 (0.00)	25 (14.79)	144 (85.21)	0 (0)	169 (100)	0 (0)
United Kingdom[1]	0 (0.00)	5873 (61.25)	3715 (38.75)	0 (0.00)	2776 (28.95)	6812 (71.05)	0 (0.00)	9251 (96.49)	337 (3.51)
Total	675 (1.47)	21829 (47.68)	23282 (50.85)	651 (1.42)	17248 (37.67)	27887 (60.91)	3545 (7.74)	41405 (90.43)	836 (1.83)

[1] United Kingdom: the duration of use of inhaled hypertonic saline and inhaled Mannitol is not specified.

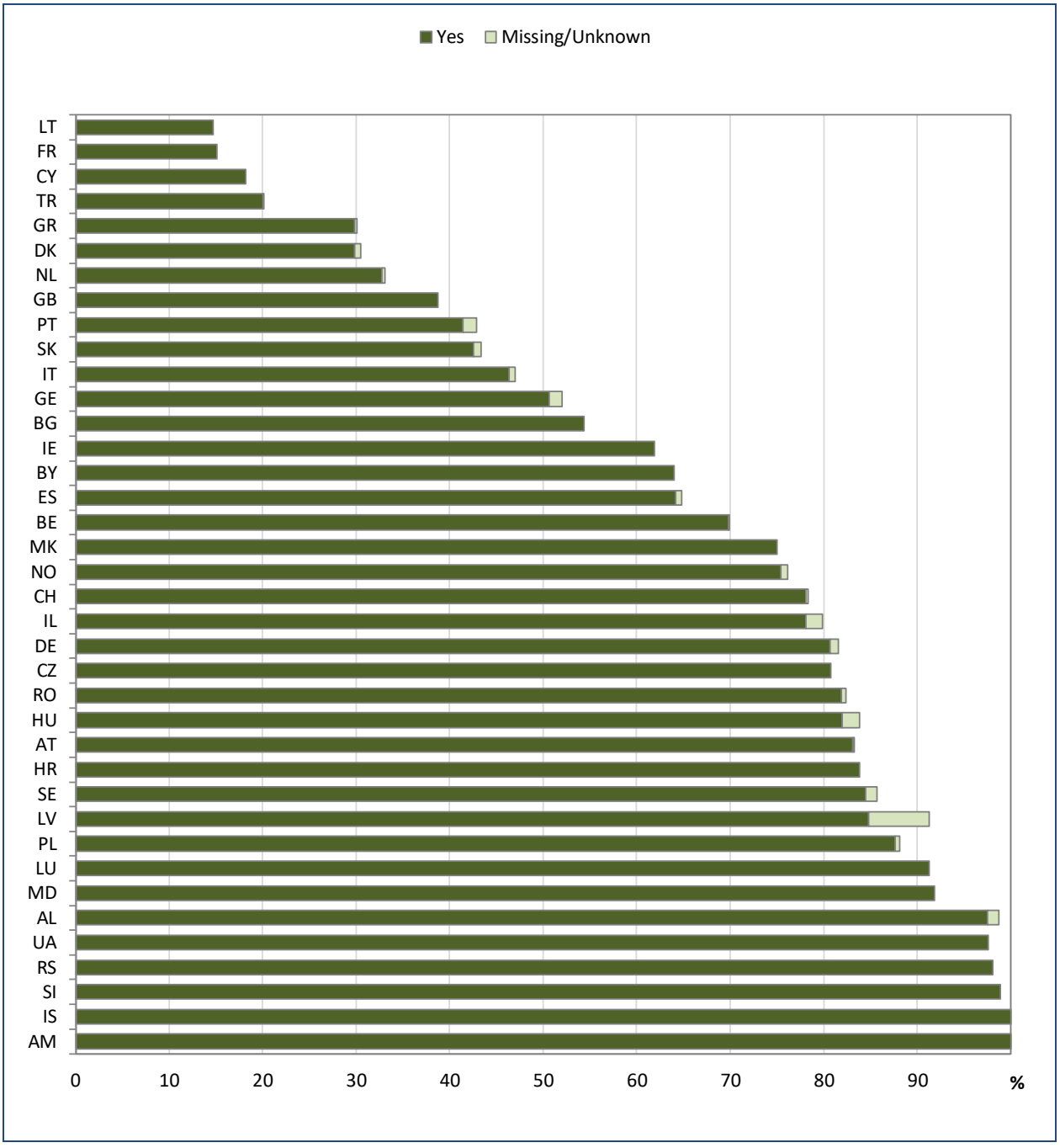
Note: Inhaled hypertonic saline is reimbursed in most countries except in Albania, Armenia, Bulgaria, Lithuania, Republic of Moldova, Poland, Romania, Russian Federation, Serbia. In Ukraine it is reimbursed for children, and in Turkey for children ≥ 6 years.

Note: Inhaled rhDNase is reimbursed in most countries except in Albania, Armenia and Republic of Moldova. In Bulgaria, Georgia, Germany, Israel, Luxembourg, North Macedonia, Norway, Romania, Spain, Ukraine, United Kingdom it is reimbursed for patients ≥ 5 years; in Latvia it is reimbursed for patients ≥ 6 years.

Note: Inhaled Mannitol is reimbursed in Austria, Czech Republic, Denmark, Germany (≥ 18 years), Greece (≥ 18 years), Italy (≥ 18 years), Russian Federation (depending on the region of residence), Slovenia, Turkey (≥ 6 years), United Kingdom (≥ 18 years), but not in the other countries.

Table 7.4 shows the use of three different inhaled medications: hypertonic saline, rhDNase (Pulmozyme®) and mannitol (see page 155 for an explanation of terms). Hypertonic saline can be any saline of a concentration > 0.9% NaCl, but most commonly between 3% and 11%.

Figure 7.2 Use of inhaled hypertonic saline in all patients seen in 2020 who have never had a transplant, by country.



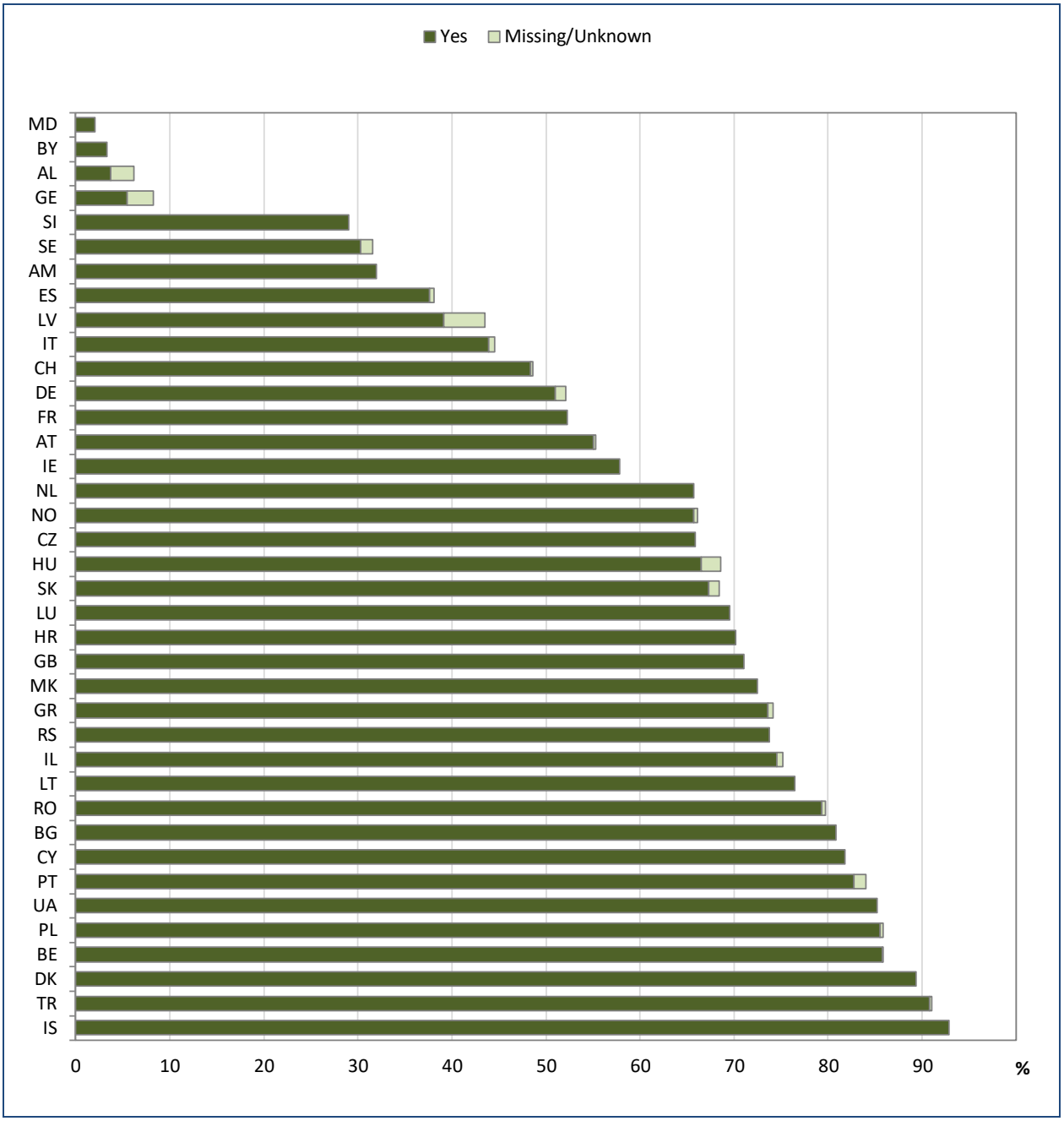
Note: We excluded from the graph the countries for which the information on inhaled hypertonic saline is missing for more than 10% of the patients.

Note: United Kingdom: the duration of use of inhaled hypertonic saline is not specified.

Note: Inhaled hypertonic saline is reimbursed in most countries except in Albania, Armenia, Bulgaria, Lithuania, Republic of Moldova, Poland, Romania, Russian Federation, Serbia. In Ukraine it is reimbursed for children, and in Turkey for children ≥ 6 years.

This graph shows the use of inhaled hypertonic saline for more than three months during the survey year. The dark green part of the bar indicates the percentage of patients taking the medication, the light green part shows the percentage of patients for whom this information is missing.

Figure 7.3 Use of rhDNase in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on inhaled rhDNase is missing for more than 10% of the patients.

Note: United Kingdom: the duration of use of inhaled rhDNase is not specified.

Note: Inhaled rhDNase is reimbursed in most countries except in Albania, Armenia and Republic of Moldova. In Bulgaria, Georgia, Germany, Israel, Luxembourg, Macedonia, Norway, Romania, Spain, Ukraine, United Kingdom it is reimbursed for patients ≥ 5 years; in Latvia it is reimbursed for patients ≥ 6 years.

This graph shows the use of rhDNase as inhalations for more than 3 months during the survey year. The dark green part of the bar indicates the percentage of patients taking this drug, the light green part shows the percentage of patients for whom this information is missing.

Table 7.5 Use of inhaled antibiotics, bronchodilators and macrolides in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Antibiotics inhaled > 3 months this year number (%)			Bronchodilators inhaled > 3 months this year number (%)			Macrolides > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	1 (1.23)	60 (74.07)	20 (24.69)	1 (1.23)	18 (22.22)	62 (76.54)	1 (1.23)	68 (83.95)	12 (14.81)
Armenia	0 (0.00)	15 (60.00)	10 (40.00)	0 (0.00)	2 (8.00)	23 (92.00)	0 (0.00)	15 (60.00)	10 (40.00)
Austria	2 (0.27)	471 (63.99)	263 (35.73)	4 (0.54)	26 (3.53)	706 (95.92)	2 (0.27)	699 (94.97)	35 (4.76)
Belarus	0 (0.00)	107 (71.33)	43 (28.67)	0 (0.00)	103 (68.67)	47 (31.33)	0 (0.00)	114 (76.00)	36 (24.00)
Belgium	1 (0.09)	537 (47.35)	596 (52.56)	1 (0.09)	279 (24.60)	854 (75.31)	2 (0.18)	533 (47.00)	599 (52.82)
Bulgaria	0 (0.00)	100 (51.81)	93 (48.19)	0 (0.00)	160 (82.90)	33 (17.10)	0 (0.00)	182 (94.30)	11 (5.70)
Croatia	0 (0.00)	74 (59.68)	50 (40.32)	0 (0.00)	102 (82.26)	22 (17.74)	0 (0.00)	80 (64.52)	44 (35.48)
Cyprus	0 (0.00)	13 (59.09)	9 (40.91)	0 (0.00)	11 (50.00)	11 (50.00)	0 (0.00)	9 (40.91)	13 (59.09)
Czech Republic	0 (0.00)	465 (79.76)	118 (20.24)	0 (0.00)	273 (46.83)	310 (53.17)	0 (0.00)	553 (94.85)	30 (5.15)
Denmark	0 (0.00)	299 (63.75)	170 (36.25)	469 (100)	0 (0)	0 (0)	0 (0.00)	354 (75.48)	115 (24.52)
France	0 (0.00)	3623 (60.00)	2415 (40.00)	0 (0.00)	2135 (35.36)	3903 (64.64)	0 (0.00)	3887 (64.38)	2151 (35.62)
Georgia	0 (0.00)	70 (95.89)	3 (4.11)	0 (0.00)	67 (91.78)	6 (8.22)	0 (0.00)	48 (65.75)	25 (34.25)
Germany	82 (1.34)	3558 (57.97)	2498 (40.70)	64 (1.04)	1165 (18.98)	4909 (79.98)	80 (1.30)	5180 (84.39)	878 (14.30)
Greece	0 (0.00)	122 (32.19)	257 (67.81)	0 (0.00)	127 (33.51)	252 (66.49)	2 (0.53)	266 (70.18)	111 (29.29)
Hungary	5 (1.15)	200 (46.19)	228 (52.66)	8 (1.85)	181 (41.80)	244 (56.35)	12 (2.77)	301 (69.52)	120 (27.71)
Iceland	0 (0.00)	10 (71.43)	4 (28.57)	0 (0.00)	1 (7.14)	13 (92.86)	0 (0.00)	4 (28.57)	10 (71.43)
Ireland	0 (0.00)	627 (55.44)	504 (44.56)	0 (0.00)	264 (23.34)	867 (76.66)	0 (0.00)	606 (53.58)	525 (46.42)
Israel	1 (0.20)	249 (49.11)	257 (50.69)	2 (0.39)	209 (41.22)	296 (58.38)	3 (0.59)	276 (54.44)	228 (44.97)
Italy	36 (0.66)	3364 (61.40)	2079 (37.94)	33 (0.60)	1938 (35.37)	3508 (64.03)	34 (0.62)	3976 (72.57)	1469 (26.81)
Latvia	1 (2.17)	30 (65.22)	15 (32.61)	1 (2.17)	3 (6.52)	42 (91.30)	0 (0.00)	45 (97.83)	1 (2.17)
Lithuania	0 (0.00)	27 (79.41)	7 (20.59)	1 (2.94)	14 (41.18)	19 (55.88)	0 (0)	34 (100)	0 (0)
Luxembourg	0 (0.00)	17 (73.91)	6 (26.09)	0 (0.00)	3 (13.04)	20 (86.96)	1 (4.35)	16 (69.57)	6 (26.09)

[table 7.5 continued]

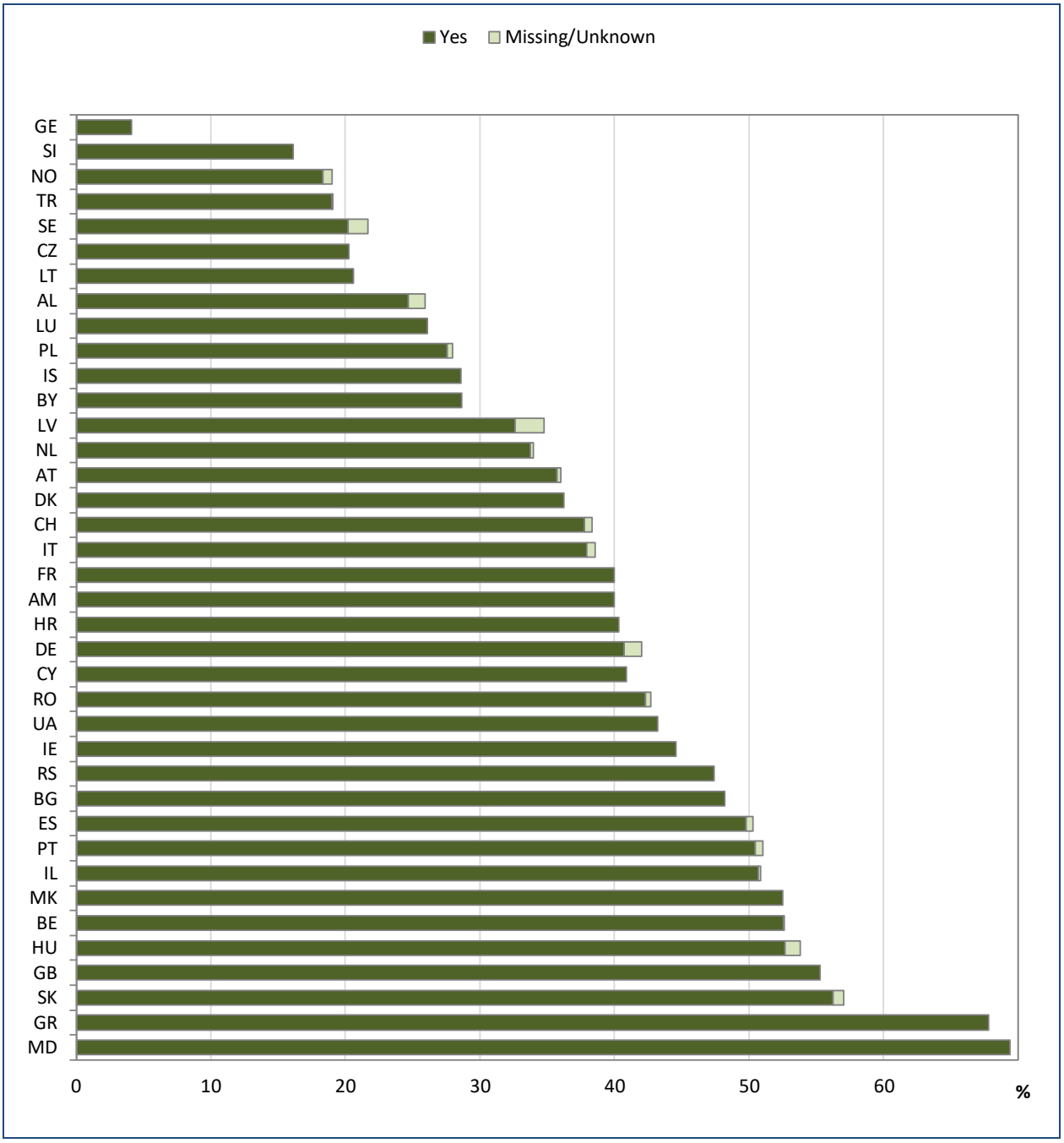
Country	Antibiotics inhaled > 3 months this year number (%)			Bronchodilators inhaled > 3 months this year number (%)			Macrolides > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	15 (30.61)	34 (69.39)	0 (0.00)	32 (65.31)	17 (34.69)	0 (0.00)	40 (81.63)	9 (18.37)
The Netherlands	3 (0.21)	947 (66.04)	484 (33.75)	3 (0.21)	617 (43.03)	814 (56.76)	3 (0.21)	945 (65.90)	486 (33.89)
North Macedonia	0 (0.00)	57 (47.50)	63 (52.50)	0 (0.00)	6 (5.00)	114 (95.00)	0 (0.00)	89 (74.17)	31 (25.83)
Norway	2 (0.69)	234 (80.97)	53 (18.34)	4 (1.38)	65 (22.49)	220 (76.12)	8 (2.77)	237 (82.01)	44 (15.22)
Poland	5 (0.43)	831 (72.01)	318 (27.56)	2 (0.17)	232 (20.10)	920 (79.72)	7 (0.61)	934 (80.94)	213 (18.46)
Portugal	2 (0.60)	162 (48.94)	167 (50.45)	2 (0.60)	131 (39.58)	198 (59.82)	3 (0.91)	208 (62.84)	120 (36.25)
Romania	1 (0.44)	130 (57.27)	96 (42.29)	2 (0.88)	143 (63.00)	82 (36.12)	1 (0.44)	198 (87.22)	28 (12.33)
Russian Federation	508 (21.57)	1008 (42.80)	839 (35.63)	502 (21.32)	1068 (45.35)	785 (33.33)	532 (22.59)	1365 (57.96)	458 (19.45)
Serbia	0 (0.00)	82 (52.56)	74 (47.44)	0 (0.00)	2 (1.28)	154 (98.72)	0 (0.00)	133 (85.26)	23 (14.74)
Slovak Republic	2 (0.76)	113 (42.97)	148 (56.27)	2 (0.76)	97 (36.88)	164 (62.36)	3 (1.14)	146 (55.51)	114 (43.35)
Slovenia	0 (0.00)	78 (83.87)	15 (16.13)	0 (0.00)	80 (86.02)	13 (13.98)	0 (0.00)	80 (86.02)	13 (13.98)
Spain	11 (0.51)	1067 (49.67)	1070 (49.81)	11 (0.51)	633 (29.47)	1504 (70.02)	11 (0.51)	1336 (62.20)	801 (37.29)
Sweden	9 (1.47)	481 (78.34)	124 (20.20)	8 (1.30)	32 (5.21)	574 (93.49)	7 (1.14)	476 (77.52)	131 (21.34)
Switzerland	5 (0.54)	571 (61.66)	350 (37.80)	1 (0.11)	207 (22.35)	718 (77.54)	4 (0.43)	712 (76.89)	210 (22.68)
Turkey	1 (0.05)	1666 (80.95)	391 (19.00)	2 (0.10)	1299 (63.12)	757 (36.78)	2 (0.10)	1901 (92.37)	155 (7.53)
Ukraine	0 (0.00)	96 (56.80)	73 (43.20)	1 (0.59)	43 (25.44)	125 (73.96)	1 (0.59)	32 (18.93)	136 (80.47)
United Kingdom[1]	0 (0.00)	4289 (44.73)	5299 (55.27)	0 (0.00)	3731 (38.91)	5857 (61.09)	0 (0.00)	6216 (64.83)	3372 (35.17)
Total	678 (1.48)	25865 (56.49)	19243 (42.03)	1124 (2.45)	15499 (33.85)	29163 (63.69)	719 (1.57)	32294 (70.53)	12773 (27.90)

[1] United Kingdom: the duration of use of inhaled antibiotics and bronchodilators is not specified.

Note: Inhaled antibiotics are reimbursed in all countries with the exception of Armenia.
Note: Inhaled bronchodilators are reimbursed in most countries except in Bulgaria and Serbia. In Ukraine they are reimbursed for children.
Note: Oral macrolides are reimbursed in most countries except in Bulgaria and Serbia. In the Republic of Moldova, they are reimbursed for children.

This table shows the use of inhaled antibiotics for more than 3 months during the survey year (any kind), inhaled bronchodilators for more than 3 months during the survey year (any kind), and macrolides (e.g. azithromycin) for more than three months.

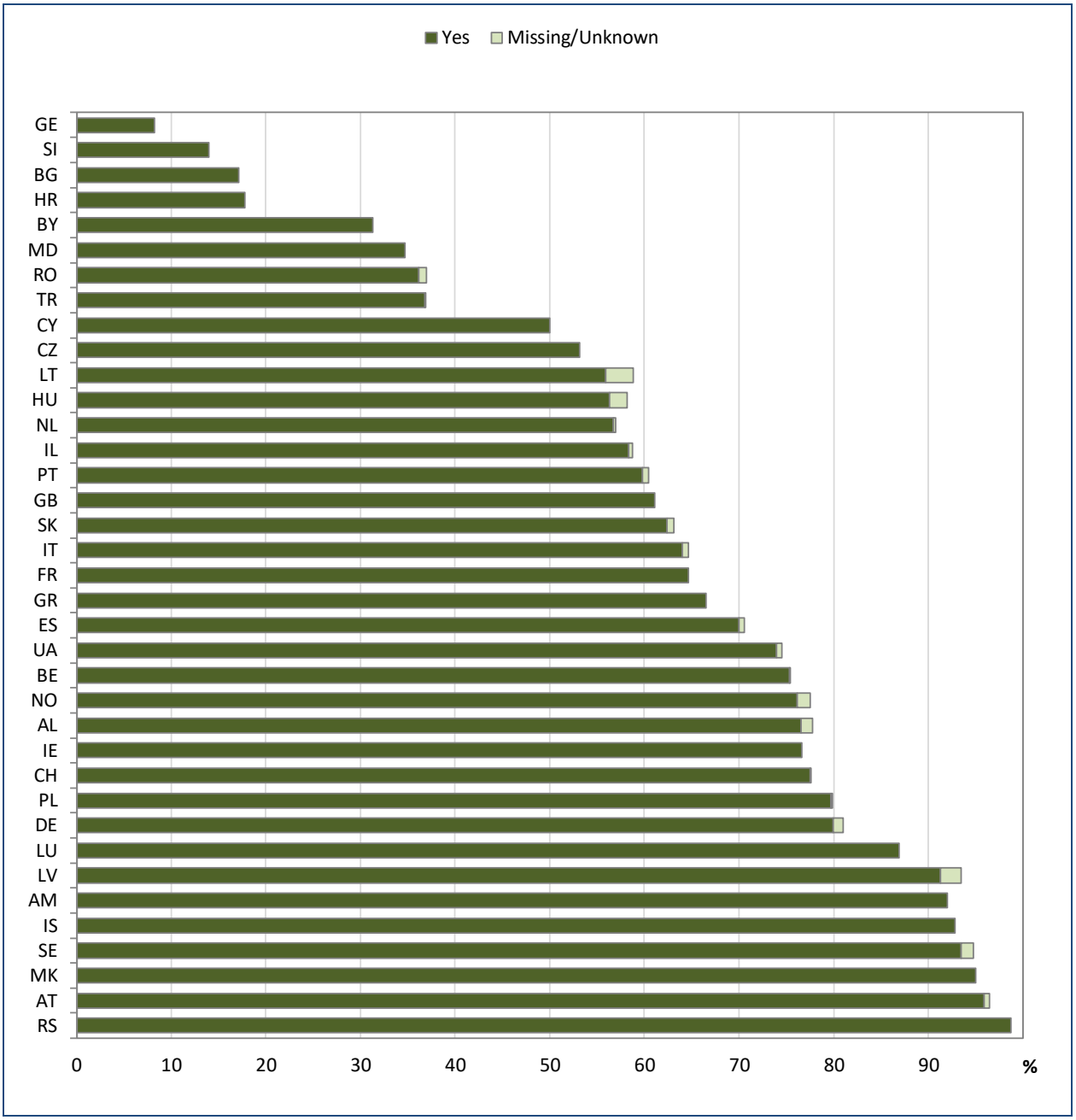
Figure 7.4 Use of inhaled antibiotics in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on inhaled antibiotics is missing for more than 10% of the patients.
Note: United Kingdom: the duration of use of inhaled antibiotics is not specified.
Note: Inhaled antibiotics are reimbursed in all countries with the exception of Armenia.

This graph shows the use of inhaled antibiotics (of any kind) for more than three months during the survey year. The frequency varies considerably, from 4.11 to 69.39 The dark green part of the bar shows the percentage of patients taking this drug, the light green part shows the percentage of patients for whom this information is missing.

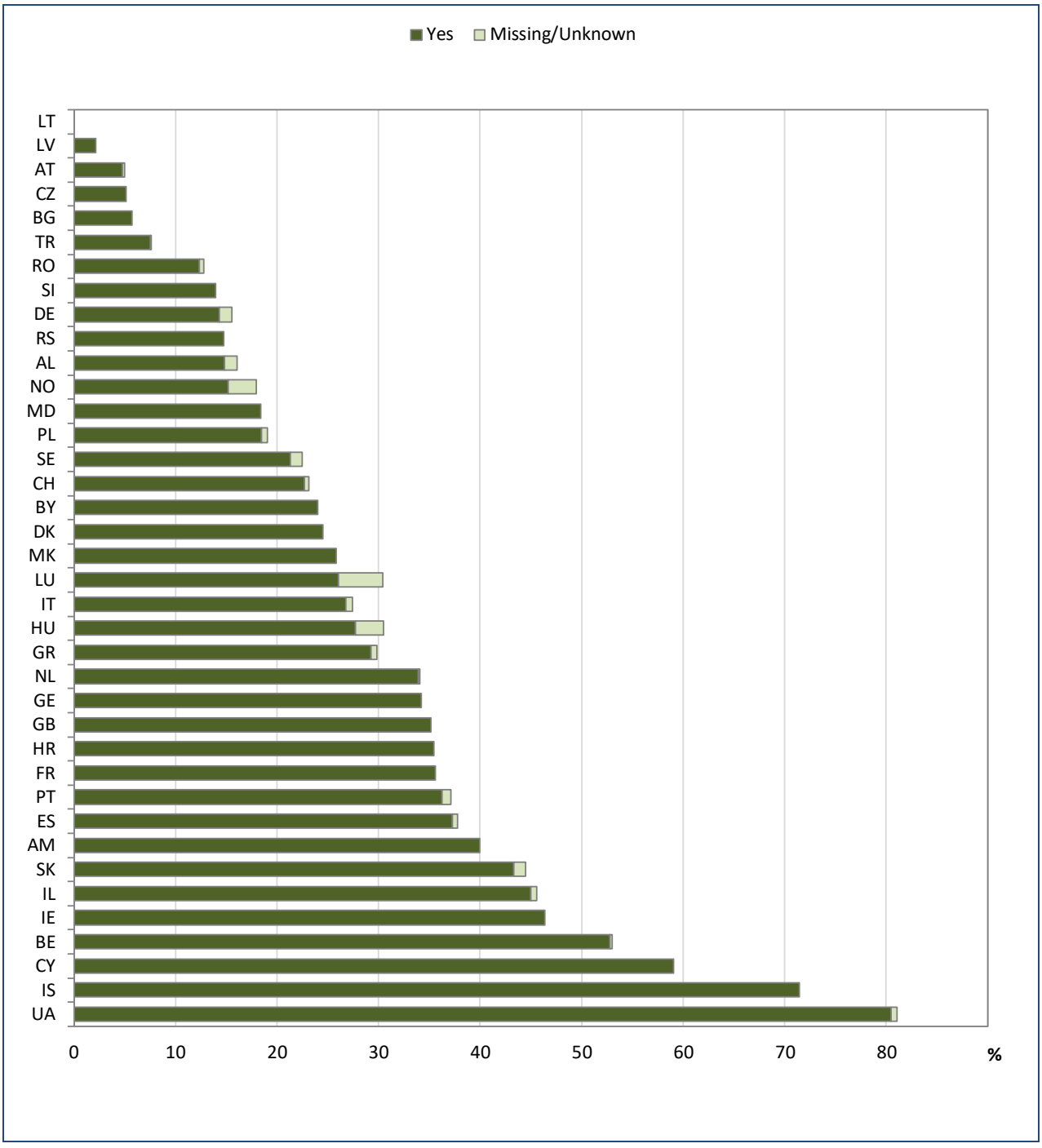
Figure 7.5 Use of bronchodilators in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on the use of bronchodilators is missing for more than 10% of the patients.
Note: United Kingdom: the duration of use of bronchodilators is not specified.
Note: Inhaled bronchodilators are reimbursed in most countries except in Bulgaria and Serbia. In Ukraine they are reimbursed for children.

This graph shows the use of bronchodilators for more than three months during the survey year. This is the most widely used inhaled medication, but still there are significant differences in frequency of use between countries. The dark green part of the bar indicates the percentage of patients taking this drug, the light green part shows the percentage of patients for whom this information is missing.

Figure 7.6 Use of macrolides in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on the use of macrolides is missing for more than 10% of the patients.

Note: United Kingdom: the duration of use of macrolides is not specified.

Note: Oral macrolides are reimbursed in most countries except in Bulgaria and Serbia. In the Republic of Moldova, they are reimbursed for children.

This graph shows the use of macrolides (e.g. azithromycin) for more than 3 months during 2020. Macrolides are antibiotics but taken continuously they can also modulate the immune system, probably by their anti-inflammatory properties. Clinical studies have shown that patients with chronic Pseudomonas aeruginosa infection benefit from continuous azithromycin treatment with regard to lung function and pulmonary exacerbation rates.

The dark green part of the bar indicates the percentage of patients taking this drug, the light green part shows the percentage of patients for whom this information is missing.

Table 7.6 Use of oxygen and non-invasive positive pressure ventilation (NIPPV) in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Oxygen therapy this year number (%)			NIPPV > 3 months this year number (%)			
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes, BiPAP (Bilevel Positive Airways Pressure)	Yes, CPAP (Continuous Positive Airways Pressure)
Albania	3 (3.70)	75 (92.59)	3 (3.70)	1 (1.23)	80 (98.77)	0 (0.00)	0 (0.00)
Armenia	0 (0.00)	23 (92.00)	2 (8.00)	0 (0)	25 (100)	0 (0)	0 (0)
Austria	2 (0.27)	703 (95.52)	31 (4.21)	2 (0.27)	731) (99.32)	1 (0.14)	2 (0.27)
Belarus	0 (0.00)	145 (96.67)	5 (3.33)	0 (0.00)	148 (98.67)	0 (0.00)	2 (1.33)
Belgium	29 (2.56)	1072 (94.53)	33 (2.91)	1 (0.09)	1121 (98.85)	10 (0.88)	2 (0.18)
Bulgaria	0 (0.00)	188 (97.41)	5 (2.59)	0 (0.00)	192 (99.48)	1 (0.52)	0 (0.00)
Croatia	1 (0.81)	116 (93.55)	7 (5.65)	0 (0.00)	123 (99.19)	0 (0.00)	1 (0.81)
Cyprus	0 (0)	22 (100)	0 (0)	0 (0)	22 (100)	0 (0)	0 (0)
Czech Republic	0 (0.00)	572 (98.11)	11 (1.89)	0 (0.00)	580 (99.49)	2 (0.34)	1 (0.17)
Denmark	0 (0.00)	468 (99.79)	1 (0.21)	0 (0)	469 (100)	0 (0)	0 (0)
France	0 (0.00)	5813 (96.27)	225 (3.73)	6038 (100)	0 (0)	0 (0)	0 (0)
Georgia	0 (0.00)	72 (98.63)	1 (1.37)	1 (1.37)	72 (98.63)	0 (0.00)	0 (0.00)
Germany[1]	69 (1.12)	5668 (92.34)	401 (6.53)	68 (1.11)	6002 (97.78)	0 (0.00)	68 (1.11)
Greece	3 (0.79)	365 (96.31)	11 (2.90)	7 (1.85)	371 (97.89)	1 (0.26)	0 (0.00)
Hungary	11 (2.54)	378 (87.30)	44 (10.16)	433 (100)	0 (0)	0 (0)	0 (0)
Iceland	0 (0)	14 (100)	0 (0)	0 (0)	14 (100)	0 (0)	0 (0)
Ireland	73 (6.45)	1007 (89.04)	51 (4.51)	71 (6.28)	996 (88.06)	59 (5.22)	5 (0.44)
Israel	4 (0.79)	491 (96.84)	12 (2.37)	7 (1.38)	487 (96.06)	12 (2.37)	1 (0.20)
Italy	34 (0.62)	5222 (95.31)	223 (4.07)	5217 (95.22)	232 (4.23)	0 (0.00)	30 (0.55)
Latvia	0 (0.00)	44 (95.65)	2 (4.35)	0 (0.00)	45 (97.83)	0 (0.00)	1 (2.17)
Lithuania	2 (5.88)	30 (88.24)	2 (5.88)	2 (5.88)	32 (94.12)	0 (0.00)	0 (0.00)
Luxembourg	0 (0.00)	20 (86.96)	3 (13.04)	0 (0.00)	22 (95.65)	1 (4.35)	0 (0.00)

[1] Germany reported all patients with NIPPV as Continuous Positive Airways Pressure (CPAP); they don't use the categories BiPAP or CPAP.

[table 7.6 continued]

Country	Oxygen therapy this year number (%)			NIPPV > 3 months this year number (%)			
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes, BiPAP (Bilevel Positive Airways Pressure)	Yes, CPAP (Continuous Positive Airways Pressure)
Rep of Moldova	0 (0.00)	47 (95.92)	2 (4.08)	0 (0)	49 (100)	0 (0)	0 (0)
The Netherlands[2]	2 (0.14)	1401 (97.70)	31 (2.16)	5 (0.35)	1422 (99.16)	0 (0.00)	7 (0.49)
North Macedonia	0 (0.00)	115 (95.83)	5 (4.17)	1 (0.83)	119 (99.17)	0 (0.00)	0 (0.00)
Norway	1 (0.35)	282 (97.58)	6 (2.08)	2 (0.69)	286 (98.96)	0 (0.00)	1 (0.35)
Poland	10 (0.87)	1093 (94.71)	51 (4.42)	8 (0.69)	1142 (98.96)	4 (0.35)	0 (0.00)
Portugal	4 (1.21)	305 (92.15)	22 (6.65)	5 (1.51)	313 (94.56)	12 (3.63)	1 (0.30)
Romania	3 (1.32)	220 (96.92)	4 (1.76)	3 (1.32)	223 (98.24)	1 (0.44)	0 (0.00)
Russian Federation	484 (20.55)	1809 (76.82)	62 (2.63)	486 (20.64)	1852 (78.64)	0 (0.00)	17 (0.72)
Serbia	0 (0.00)	150 (96.15)	6 (3.85)	0 (0.00)	152 (97.44)	4 (2.56)	0 (0.00)
Slovak Republic	3 (1.14)	242 (92.02)	18 (6.84)	2 (0.76)	259 (98.48)	1 (0.38)	1 (0.38)
Slovenia	0 (0.00)	93 (100)	0 (0.00)	0 (0.00)	92 (98.92)	1 (1.08)	0 (0.00)
Spain	14 (0.65)	2072 (96.46)	62 (2.89)	15 (0.70)	2126 (98.98)	5 (0.23)	2 (0.09)
Sweden	8 (1.30)	594 (96.74)	12 (1.95)	9 (1.47)	596 (97.07)	8 (1.30)	1 (0.16)
Switzerland	4 (0.43)	894 (96.54)	28 (3.02)	4 (0.43)	917 (99.03)	2 (0.22)	3 (0.32)
Turkey	1 (0.05)	1984 (96.40)	73 (3.55)	1 (0.05)	2003 (97.33)	53 (2.58)	1 (0.05)
Ukraine	1 (0.59)	132 (78.11)	36 (21.30)	1 (0.59)	168 (99.41)	0 (0.00)	0 (0.00)
United Kingdom	0 (0.00)	9083 (94.73)	505 (5.27)	0 (0.00)	9425 (98.30)	0 (0.00)	163 (1.70)
Total	766 (1.67)	43024 (93.97)	1996 (4.36)				

[2] The Netherlands reported all patients with NIPPV as Continuous Positive Airways Pressure (CPAP); the categories BiPAP or CPAP are not used.

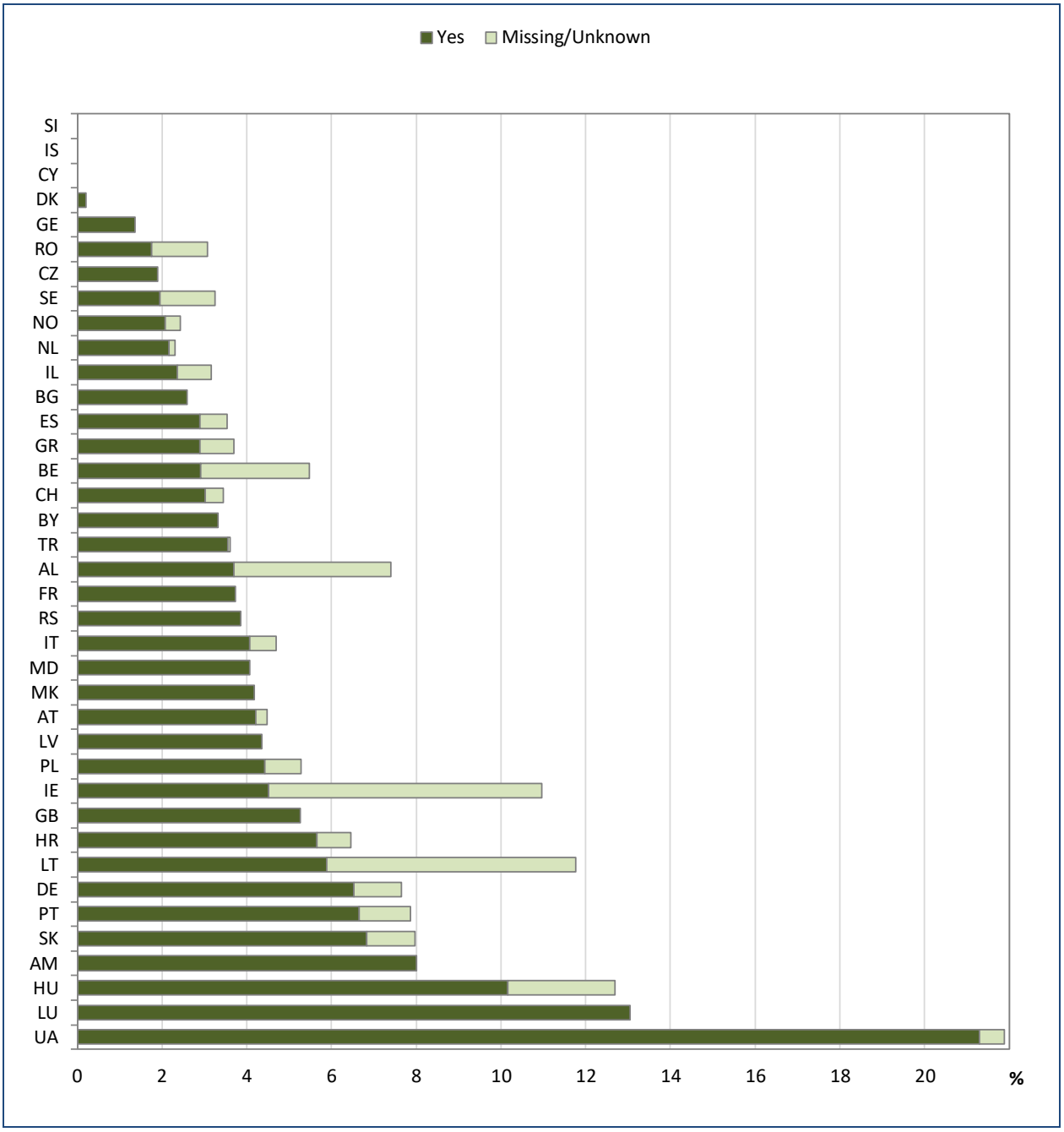
Note: For non-invasive positive pressure ventilation (NIPPV) the total percentage of missing information is higher than 10%, therefore the totals are excluded from the table.

Note: Oxygen therapy is reimbursed in most countries except in Armenia, Bulgaria, Republic of Moldova, Russian Federation, Serbia and Ukraine.

Note: Noninvasive positive pressure ventilation (NIPPV) is reimbursed in most countries except in Albania, Belarus, Bulgaria, Hungary, North Macedonia, Republic of Moldova, Russian Federation, Serbia and Ukraine.

This table shows the use of oxygen and non-invasive positive pressure ventilation (NIPPV) for more than three months.

Figure 7.7 Use of oxygen in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on the use of oxygen is missing for more than 10% of the patients.

Note: Oxygen therapy is reimbursed in most countries except in Armenia, Bulgaria, Republic of Moldova, Russian Federation, Serbia and Ukraine.

This graph shows the use of oxygen during 2020. Oxygen is used for severe lung disease. The dark green part of the bar indicates the percentage of patients using oxygen supplementation, the light green part shows the percentage of patients for whom this information is missing.

Table 7.7 Use of inhaled steroids and oral steroids in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Inhaled steroids > 3 months this year number (%)			Oral steroids > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	1 (1.23)	69 (85.19)	11 (13.58)	0 (0.00)	80 (98.77)	1 (1.23)
Armenia	0 (0.00)	19 (76.00)	6 (24.00)	1 (4.00)	24 (96.00)	0 (0.00)
Austria	3 (0.41)	635 (86.28)	98 (13.32)	2 (0.27)	721 (97.96)	13 (1.77)
Belarus	0 (0.00)	113 (75.33)	37 (24.67)	0 (0.00)	145 (96.67)	5 (3.33)
Belgium	1 (0.09)	530 (46.74)	603 (53.17)	4 (0.35)	1098 (96.83)	32 (2.82)
Bulgaria	0 (0.00)	177 (91.71)	16 (8.29)	0 (0.00)	192 (99.48)	1 (0.52)
Croatia	2 (1.61)	100 (80.65)	22 (17.74)	2 (1.61)	122 (98.39)	0 (0.00)
Cyprus	0 (0.00)	12 (54.55)	10 (45.45)	0 (0)	22 (100)	0 (0)
Czech Republic	0 (0.00)	391 (67.07)	192 (32.93)	0 (0.00)	572 (98.11)	11 (1.89)
Denmark	0 (0.00)	310 (66.10)	159 (33.90)	0 (0.00)	444 (94.67)	25 (5.33)
France	0 (0.00)	2602 (43.09)	3436 (56.91)	0 (0.00)	5802 (96.09)	236 (3.91)
Georgia	0 (0)	73 (100)	0 (0)	1 (1.37)	72 (98.63)	0 (0.00)
Germany	82 (1.34)	3999 (65.15)	2057 (33.51)	84 (1.37)	5782 (94.20)	272 (4.43)
Greece	1 (0.26)	239 (63.06)	139 (36.68)	3 (0.79)	363 (95.78)	13 (3.43)
Hungary	433 (100)	0 (0)	0 (0)	433 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	8 (57.14)	6 (42.86)	0 (0)	14 (100)	0 (0)
Ireland	0 (0.00)	780 (68.97)	351 (31.03)	0 (0.00)	1093 (96.64)	38 (3.36)
Israel	4 (0.79)	265 (52.27)	238 (46.94)	3 (0.59)	482 (95.07)	22 (4.34)
Italy	36 (0.66)	3905 (71.27)	1538 (28.07)	31 (0.57)	4447 (81.16)	1001 (18.27)
Latvia	0 (0.00)	41 (89.13)	5 (10.87)	0 (0)	46 (100)	0 (0)
Lithuania	0 (0.00)	32 (94.12)	2 (5.88)	0 (0.00)	33 (97.06)	1 (2.94)
Luxembourg	0 (0.00)	13 (56.52)	10 (43.48)	0 (0)	23 (100)	0 (0)

[table 7.7 continued]

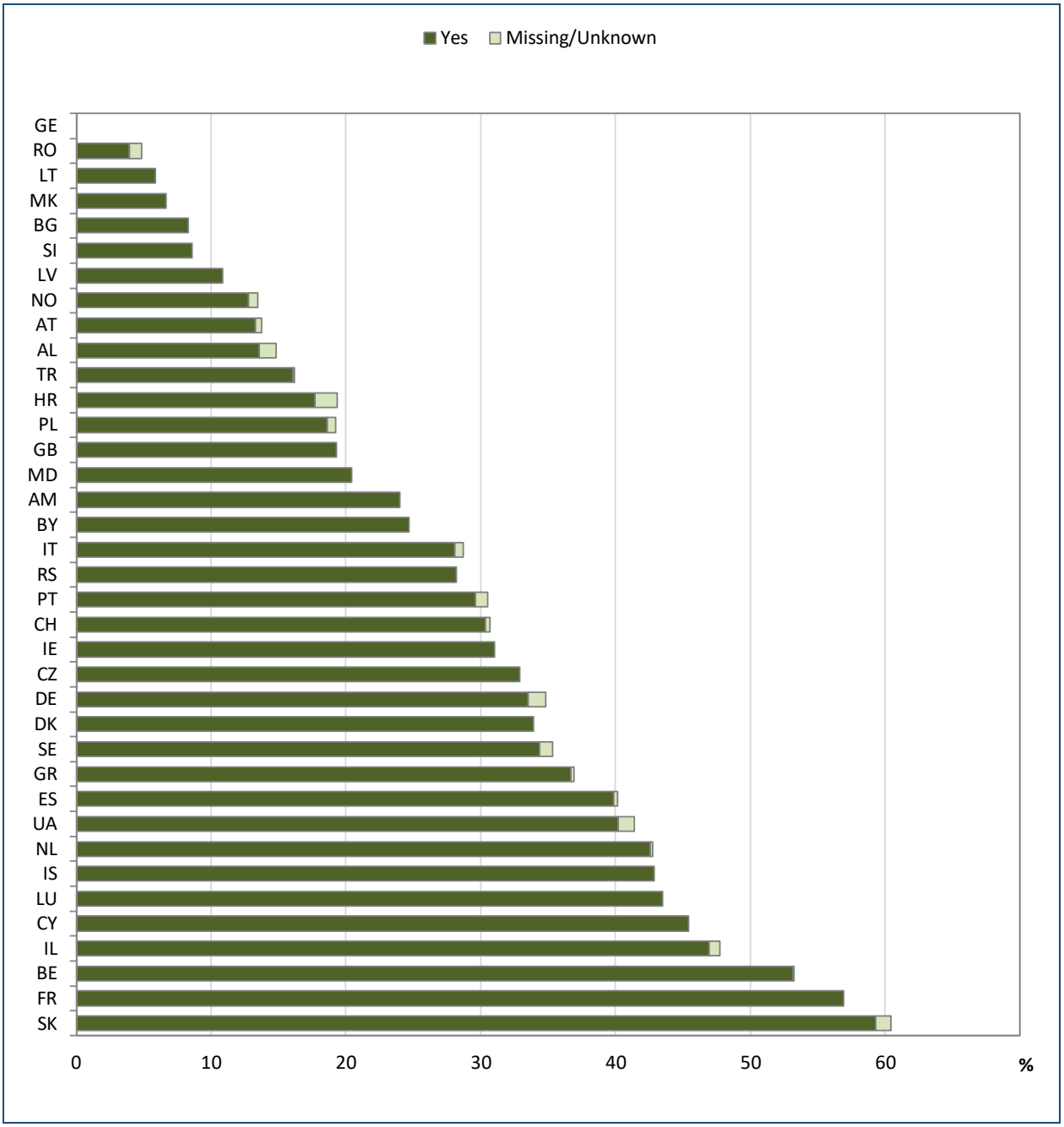
Country	Inhaled steroids > 3 months this year number (%)			Oral steroids > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	39 (79.59)	10 (20.41)	0 (0.00)	45 (91.84)	4 (8.16)
The Netherlands	2 (0.14)	821 (57.25)	611 (42.61)	2 (0.14)	1274 (88.84)	158 (11.02)
North Macedonia	0 (0.00)	112 (93.33)	8 (6.67)	0 (0)	120 (100)	0 (0)
Norway	2 (0.69)	250 (86.51)	37 (12.80)	1 (0.35)	283 (97.92)	5 (1.73)
Poland	7 (0.61)	932 (80.76)	215 (18.63)	10 (0.87)	1120 (97.05)	24 (2.08)
Portugal	3 (0.91)	230 (69.49)	98 (29.61)	3 (0.91)	317 (95.77)	11 (3.32)
Romania	2 (0.88)	216 (95.15)	9 (3.96)	1 (0.44)	225 (99.12)	1 (0.44)
Russian Federation	497 (21.10)	1674 (71.08)	184 (7.81)	499 (21.19)	1801 (76.48)	55 (2.34)
Serbia	0 (0.00)	112 (71.79)	44 (28.21)	0 (0.00)	154 (98.72)	2 (1.28)
Slovak Republic	3 (1.14)	104 (39.54)	156 (59.32)	2 (0.76)	237 (90.11)	24 (9.13)
Slovenia	0 (0.00)	85 (91.40)	8 (8.60)	0 (0.00)	92 (98.92)	1 (1.08)
Spain	6 (0.28)	1285 (59.82)	857 (39.90)	11 (0.51)	2066 (96.18)	71 (3.31)
Sweden	6 (0.98)	397 (64.66)	211 (34.36)	9 (1.47)	583 (94.95)	22 (3.58)
Switzerland	3 (0.32)	642 (69.33)	281 (30.35)	3 (0.32)	885 (95.57)	38 (4.10)
Turkey	2 (0.10)	1725 (83.82)	331 (16.08)	2 (0.10)	2041 (99.17)	15 (0.73)
Ukraine	2 (1.18)	99 (58.58)	68 (40.24)	1 (0.59)	164 (97.04)	4 (2.37)
United Kingdom	0 (0.00)	7739 (80.72)	1849 (19.28)	0 (0.00)	8912 (92.95)	676 (7.05)
Total	1098 (2.40)	30775 (67.21)	13913 (30.39)	1108 (2.42)	41896 (91.50)	2782 (6.08)

Note: Inhaled steroids are reimbursed in most countries except in Georgia, Lithuania and Serbia. In Republic of Moldova they are reimbursed for children. In Bulgaria they are reimbursed if patients also have Asthma or chronic obstructive pulmonary disease (COPD) diagnosis.

Note: Oral steroids are reimbursed in most countries except in Bulgaria, Lithuania, Republic of Moldova, Poland and Ukraine. In Latvia they are reimbursed for children.

This table shows the use of inhaled and oral steroids for more than 3 months during the survey year.

Figure 7.8 Use of inhaled steroids in all patients seen in 2020 who have never had a transplant, by country.

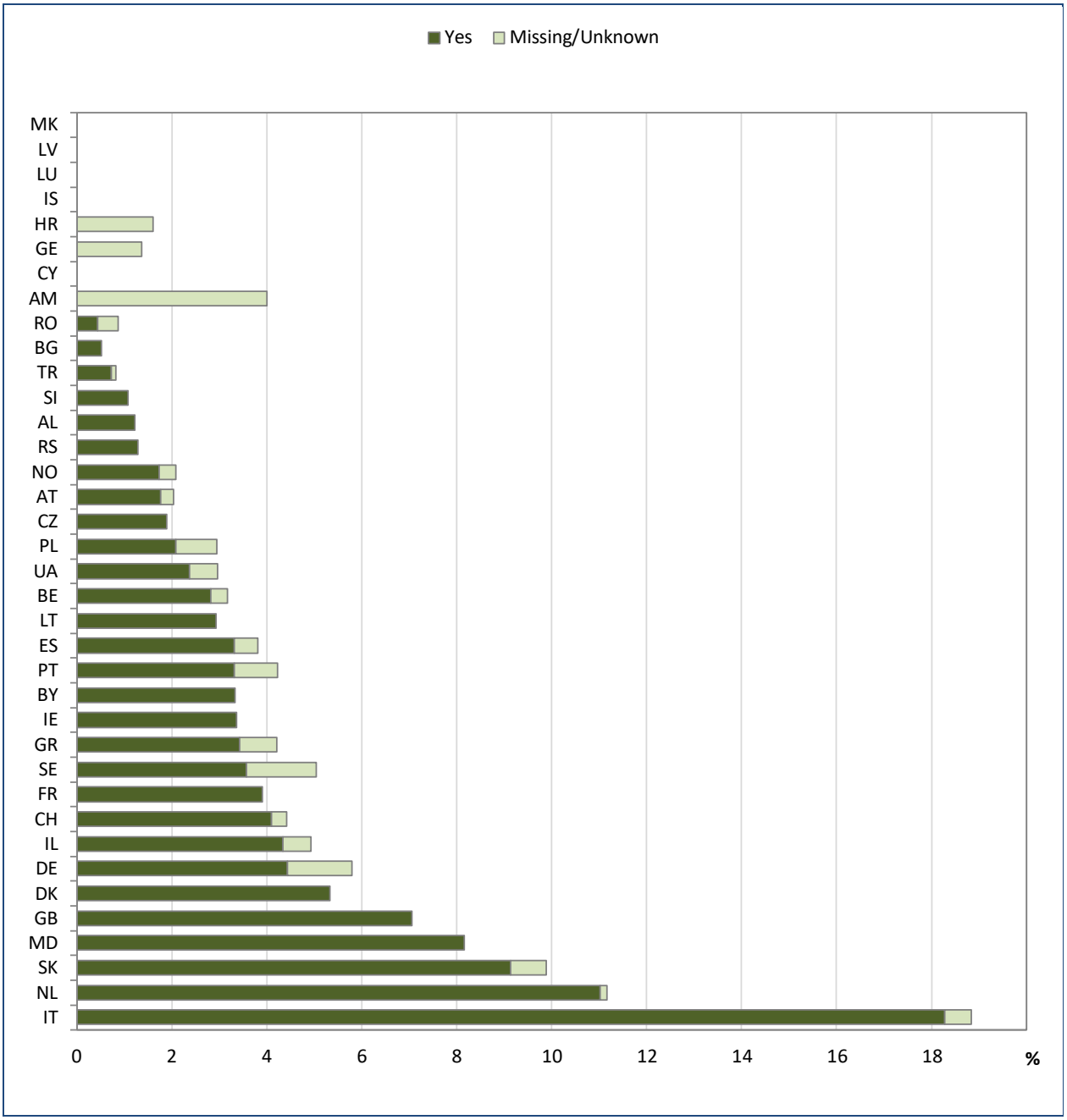


Note: We excluded from the graph the countries for which the information on use of inhaled steroids is missing for more than 10% of the patients.

Note: Inhaled steroids are reimbursed in most countries except in Georgia, Lithuania and Serbia. In Republic of Moldova, they are reimbursed for children. In Bulgaria it is reimbursed if patients also have an Asthma or chronic obstructive pulmonary disease (COPD) diagnosis.

This graph shows the use of inhaled steroids for more than 3 months during the survey year. The dark green part of the bar indicates the percentage of patients taking these drugs, the light green part shows the percentage of patients for whom this information is missing.

Figure 7.9 Use of oral steroids in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on use of oral steroids is missing for more than 10% of the patients.

Note: Oral steroids are reimbursed in most countries except in Bulgaria, Lithuania, Republic of Moldova, Poland and Ukraine. In Latvia they are reimbursed for children.

This graph shows the use of oral steroids for more than 3 months during the survey year. The dark green part of the bar indicates the percentage of patients taking these drugs, the light green part shows the percentage of patients for whom this information is missing.

8. Gastro-intestinal complications and therapies

The information in this section should not be considered complete, for several reasons: national registries may use a different definition or different parameters for a complication; data about one or more of the complications is not collected; the status of the complication is truly unknown (e.g. liver disease, where the definition requires ultrasound examination and this is not always done for a patient). In the tables, therefore, we show the number of missing values for the various complications, but in the graphs we have included only countries where less than 10% of the data is missing. For a full list of complications and definitions please see Appendix 3 on page 152.

Table 8.1 Prevalence of CF-related diabetes (CFRD) in 2020 in adult patients seen in 2020 who never had a transplant, by country and overall.

Country	CFRD this year number (%)					
	Missing/ unknown	No	Yes, treated with daily insulin	Yes, treated with oral hypo-glycaemic agents	Yes, dietary advice only	Yes, therapy unknown
Austria	3 (0.84)	260 (72.83)	76 (21.29)	1 (0.28)	16 (4.48)	1 (0.28)
Belgium	79 (11.81)	399 (59.64)	136 (20.33)	18 (2.69)	37 (5.53)	0 (0.00)
Bulgaria	0 (0.00)	73 (90.12)	8 (9.88)	0 (0.00)	0 (0.00)	0 (0.00)
Croatia	1 (2.27)	33 (75.00)	10 (22.73)	0 (0.00)	0 (0.00)	0 (0.00)
Cyprus	0 (0.00)	11 (91.67)	0 (0.00)	0 (0.00)	1 (8.33)	0 (0.00)
Czech Republic	0 (0.00)	161 (63.39)	79 (31.10)	0 (0.00)	9 (3.54)	5 (1.97)
Denmark	0 (0.00)	197 (74.34)	68 (25.66)	0 (0.00)	0 (0.00)	0 (0.00)
France	0 (0.00)	2687 (81.15)	624 (18.85)	0 (0.00)	0 (0.00)	0 (0.00)
Germany	84 (2.42)	2348 (67.53)	768 (22.09)	52 (1.50)	34 (0.98)	191 (5.49)
Greece	0 (0.00)	213 (75.00)	64 (22.54)	0 (0.00)	6 (2.11)	1 (0.35)
Hungary	5 (2.70)	145 (78.38)	35 (18.92)	0 (0.00)	0 (0.00)	0 (0.00)
Iceland	0 (0.00)	1 (16.67)	5 (83.33)	0 (0.00)	0 (0.00)	0 (0.00)
Ireland	0 (0.00)	467 (73.54)	128 (20.16)	0 (0.00)	40 (6.30)	0 (0.009
Israel	3 (0.89)	228 (67.66)	93 (27.60)	4 (1.19)	8 (2.37)	1 (0.30)
Italy	70 (2.18)	2491 (77.72)	627 (19.56)	4 (0.12)	13 (0.41)	0 (0.00)
Latvia	0 (0.00)	11 (84.62)	2 (15.38)	0 (0.00)	0 (0.00)	0 (0.00)
Lithuania	0 (0.00)	19 (95.00)	1 (5.00)	0 (0.00)	0 (0.00)	0 (0.00)

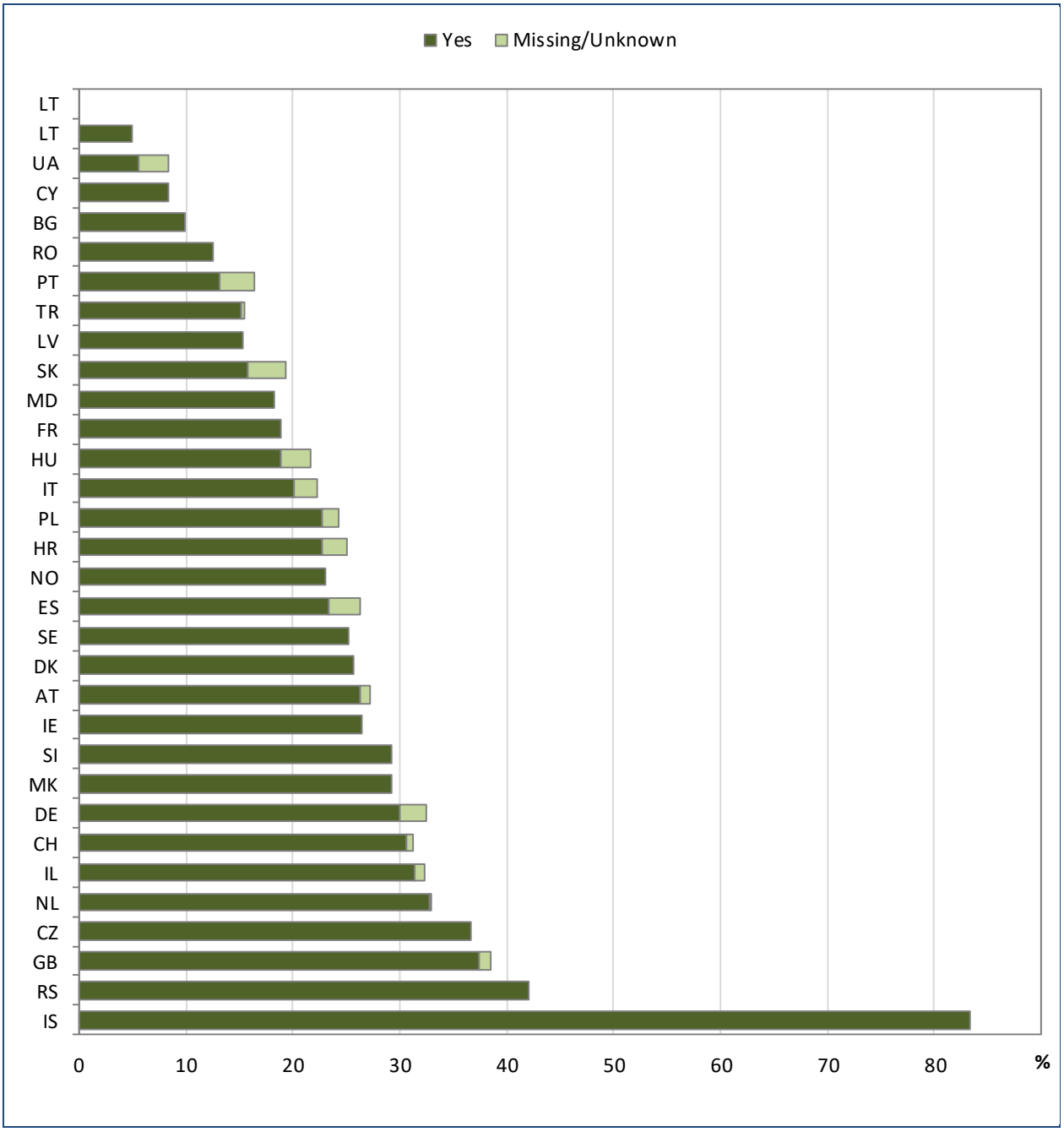
[table 8.1 continued]

Country	CFRD this year number (%)					
	Missing/ unknown	No	Yes, treated with daily insulin	Yes, treated with oral hypo-glycaemic agents	Yes, dietary advice only	Yes, therapy unknown
Rep of Moldova	0 (0.00)	9 (81.82)	2 (18.18)	0 (0.00)	0 (0.00)	0 (0.00)
The Netherlands	1 (0.11)	603 (67.07)	247 (27.47)	13 (1.45)	35 (3.89)	0 (0.00)
North Macedonia	0 (0.00)	29 (70.73)	12 (29.27)	0 (0.00)	0 (0.00)	0 (0.00)
Norway	0 (0.00)	130 (76.92)	27 (15.98)	1 (0.59)	4 (2.37)	7 (4.14)
Poland	5 (1.53)	247 (75.77)	51 (15.64)	3 (0.92)	20 (6.13)	0 (0.00)
Portugal	5 (3.27)	128 (83.66)	18 (11.76)	0 (0.00)	2 (1.31)	0 (0.00)
Romania	0 (0.00)	7 (87.50)	1 (12.50)	0 (0.00)	0 (0.00)	0 (0.00)
Russian Federation	455 (69.79)	164 (25.15)	23 (3.53)	0 (0.00)	7 (1.07)	3 (0.46)
Serbia	0 (0.00)	33 (57.89)	24 (42.11)	0 (0.00)	0 (0.00)	0 (0.00)
Slovak Republic	5 (3.57)	113 (80.71)	18 (12.86)	0 (0.00)	4 (2.86)	0 (0.00)
Slovenia	0 (0.00)	29 (70.73)	10 (24.39)	0 (0.00)	2 (4.88)	0 (0.00)
Spain	32 (2.98)	791 (73.72)	191 (17.80)	16 (1.49)	43 (4.01)	0 (0.00)
Sweden	0 (0.00)	261 (74.79)	62 (17.77)	7 (2.01)	0 (0.00)	19 (5.44)
Switzerland	3 (0.60)	345 (68.73)	125 (24.90)	3 (0.60)	24 (4.78)	2 (0.40)
Turkey	1 (0.40)	212 (84.46)	36 (14.34)	0 (0.00)	1 (0.40)	1 (0.40)
Ukraine	1 (2.78)	33 (91.67)	2 (5.56)	0 (0.00)	0 (0.00)	0 (0.00)
United Kingdom	61 (1.14)	3297 (61.48)	1531 (28.55)	140 (2.61)	107 (2.00)	227 (4.23)
Total	814 (3.50)	16180 (69.64)	5106 (21.98)	262 (1.13)	414 (1.78)	458 (1.97)

Note: Belarus and Georgia have 0% coverage for adults and are excluded from the table.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more on 31/12/2020 and are not shown in the table, but the patients are included in the total.

Table 8.1 shows the frequency of CF-related diabetes (CFRD) by country. Only patients 18 years and older are included.

Figure 8.1 Prevalence of CFRD, by country. All patients seen in 2020 aged 18 years or older who have never had a transplant.



Note: We excluded from the graph the countries for which the information on CFRD is missing for more than 10% of the adult patients.
Belarus and Georgia have 0% coverage for adults and are excluded from the graph.
Albania, Armenia and Luxembourg have <5 patients aged 18 years or more on 31/12/2020 and are excluded from the graph.

This graph shows the prevalence of CF-related diabetes (CFRD) by country. The dark green part of the bar shows the percentage of patients who have CFRD, the light green part shows the percentage of patients for whom this information is missing. Only patients aged 18 years or older were included in this graph.

Table 8.2 Prevalence of liver disease in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Liver disease this year number (%)						
	Missing/ unknown	No liver disease	Cirrhosis with portal hypertension/ hypersplenism	Cirrhosis no portal hypertension/ hypersplenism	Cirrhosis. Portal hypertension unknown	Liver disease without cirrhosis	Variceal bleeding
Albania	4 (4.94)	37 (45.68)	0 (0.00)	0 (0.00)	0 (0.00)	40 (49.38)	0 (0.00)
Armenia	0 (0.00)	13 (52.00)	1 (4.00)	1 (4.00)	0 (0.00)	10 (40.00)	0 (0.00)
Austria	3 (0.41)	384 (52.17)	9 (1.22)	29 (3.94)	2 (0.27)	309 (41.98)	0 (0.00)
Belarus	0 (0.00)	104 (69.33)	3 (2.00)	2 (1.33)	0 (0.00)	41 (27.33)	0 (0.00)
Belgium[1]	7 (0.62)	1069 (94.27)	58 (5.11)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Bulgaria	0 (0.00)	131 (67.88)	5 (2.59)	9 (4.66)	1 (0.52)	47 (24.35)	0 (0.00)
Croatia	1 (0.81)	106 (85.48)	3 (2.42)	3 (2.42)	0 (0.00)	11 (8.87)	0 (0.00)
Cyprus	0 (0.00)	21 (95.45)	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.55)	0 (0.00)
Czech Republic	0 (0.00)	474 (81.30)	12 (2.06)	5 (0.86)	2 (0.34)	90 (15.44)	0 (0.00)
Denmark	0 (0.00)	394 (84.01)	22 (4.69)	8 (1.71)	1 (0.21)	44 (9.38)	0 (0.00)
France	0 (0.00)	5017 (83.09)	111 (1.84)	175 (2.90)	0 (0.00)	735 (12.17)	0 (0.00)
Georgia	1 (1.37)	57 (78.08)	0 (0.00)	1 (1.37)	1 (1.37)	13 (17.81)	0 (0.00)
Germany[2]	315 (5.13)	4206 (68.52)	131 (2.13)	88 (1.43)	75 (1.22)	1323 (21.55)	0 (0.00)
Greece	58 (15.30)	236 (62.27)	9 (2.37)	5 (1.32)	0 (0.00)	71 (18.73)	0 (0.00)
Hungary	6 (1.39)	318 (73.44)	72 (16.63)	12 (2.77)	13 (3.00)	12 (2.77)	0 (0.00)
Iceland	0 (0.00)	13 (92.86)	0 (0.00)	0 (0.00)	1 (7.14)	0 (0.00)	0 (0.00)
Ireland	37 (3.27)	948 (83.82)	34 (3.01)	8 (0.71)	11 (0.97)	93 (8.22)	0 (0.00)
Israel	17 (3.35)	392 (77.32)	10 (1.97)	6 (1.18)	0 (0.00)	80 (15.78)	2 (0.39)
Italy	97 (1.77)	3574 (65.23)	67 (1.22)	31 (0.57)	1 (0.02)	1708 (31.17)	1 (0.02)
Latvia	0 (0.00)	32 (69.57)	2 (4.35)	0 (0.00)	0 (0.00)	12 (26.09)	0 (0.00)
Lithuania	0 (0)	34 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Luxembourg	1 (4.35)	17 (73.91)	0 (0.00)	0 (0.00)	0 (0.00)	5 (21.74)	0 (0.00)

[1] Belgium: collects only cirrhosis with portal hypertension "yes" or "no", therefore no liver disease means no cirrhosis with portal hypertension.

[2] Germany: variceal bleeding information is not reported.

[table 8.2 continued]

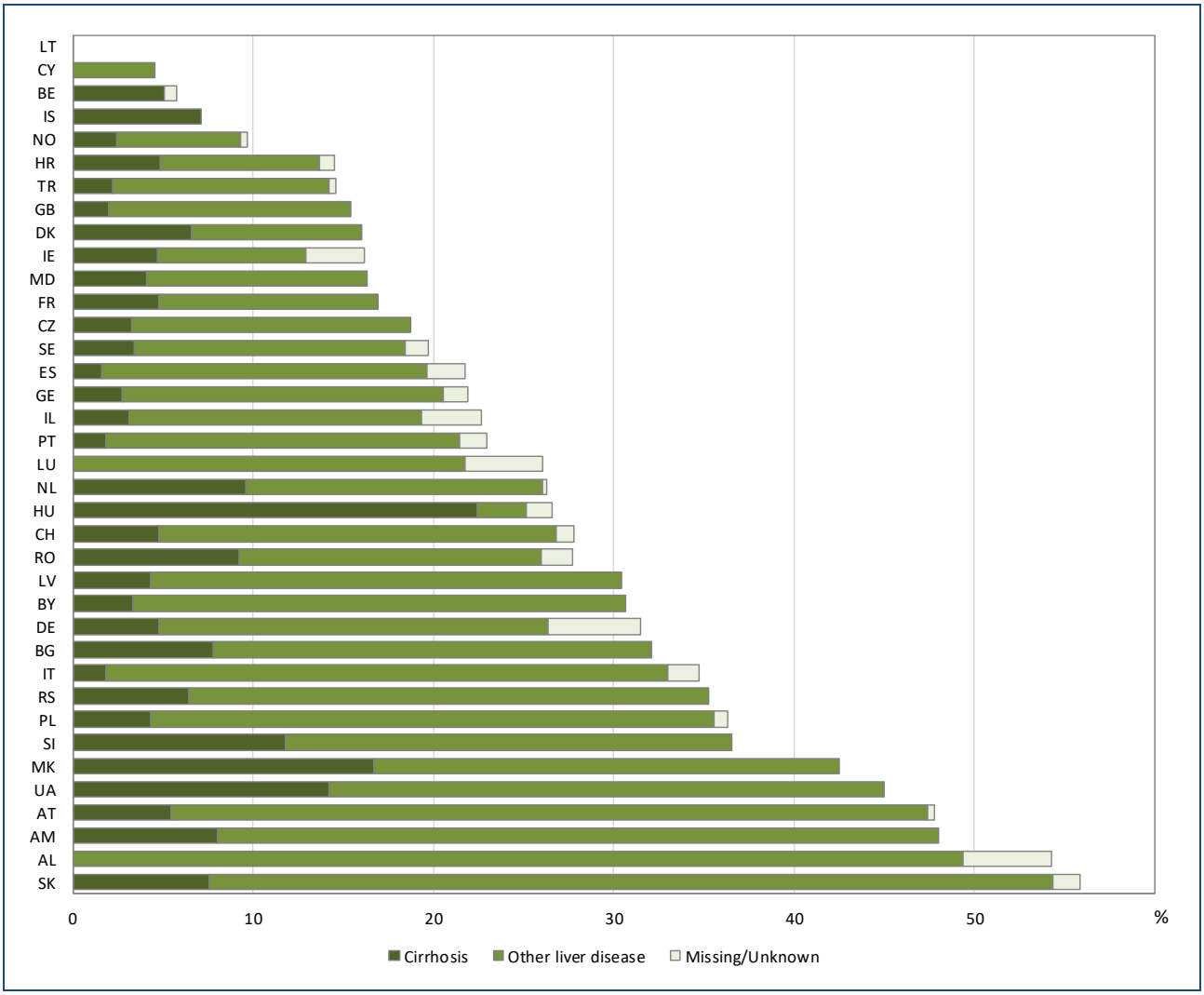
Country	Liver disease this year number (%)						
	Missing/ unknown	No liver disease	Cirrhosis			Liver disease without cirrhosis	Variceal bleeding
			Cirrhosis with portal hypertension/ hypersplenism	Cirrhosis no portal hypertension/ hypersplenism	Cirrhosis. Portal hypertension unknown		
Rep of Moldova	0 (0.00)	41 (83.67)	1 (2.04)	1 (2.04)	0 (0.00)	6 (12.24)	0 (0.00)
The Netherlands	4 (0.28)	1057 (73.71)	93 (6.49)	39 (2.72)	6 (0.42)	235 (16.39)	0 (0.00)
North Macedonia	0 (0.00)	69 (57.50)	5 (4.17)	15 (12.50)	0 (0.00)	31 (25.83)	0 (0.00)
Norway	1 (0.35)	261 (90.31)	4 (1.38)	1 (0.35)	2 (0.69)	20 (6.92)	0 (0.00)
Poland	9 (0.78)	735 (63.69)	40 (3.47)	6 (0.52)	4 (0.35)	358 (31.02)	2 (0.17)
Portugal	5 (1.51)	255 (77.04)	5 (1.51)	1 (0.30)	0 (0.00)	65 (19.64)	0 (0.00)
Romania	4 (1.76)	164 (72.25)	15 (6.61)	4 (1.76)	2 (0.88)	38 (16.74)	0 (0.00)
Russian Federation	484 (20.55)	1351 (57.37)	69 (2.93)	64 (2.72)	4 (0.17)	383 (16.26)	0 (0.00)
Serbia[3]	0 (0.00)	101 (64.74)	6 (3.85)	3 (1.92)	1 (0.64)	45 (28.85)	0 (0.00)
Slovak Republic	4 (1.52)	116 (44.11)	14 (5.32)	5 (1.90)	1 (0.38)	123 (46.77)	0 (0.00)
Slovenia	0 (0.00)	59 (63.44)	8 (8.60)	3 (3.23)	0 (0.00)	23 (24.73)	0 (0.00)
Spain	46 (2.14)	1681 (78.26)	21 (0.98)	12 (0.56)	1 (0.05)	387 (18.02)	0 (0.00)
Sweden	8 (1.30)	493 (80.29)	10 (1.63)	11 (1.79)	0 (0.00)	91 (14.82)	1 (0.16)
Switzerland	9 (0.97)	669 (72.25)	25 (2.70)	17 (1.84)	2 (0.22)	203 (21.92)	1 (0.11)
Turkey	7 (0.34)	1758 (85.42)	21 (1.02)	18 (0.87)	6 (0.29)	246 (11.95)	2 (0.10)
Ukraine[4]	0 (0.00)	93 (55.03)	9 (5.33)	14 (8.28)	1 (0.59)	52 (30.77)	0 (0.00)
United Kingdom	0 (0.00)	8106 (84.54)	126 (1.31)	67 (0.70)	0 (0.00)	1289 (13.44)	0 (0.00)
Total	1128 (2.46)	34586 (75.54)	1021 (2.23)	664 (1.45)	138 (0.30)	8240 (18.00)	9 (0.02)

[3] Serbia: cirrhosis without portal hypertension/hypersplenism means the presence of CF-related liver disease with normal liver function.

[4] Ukraine: Liver disease without cirrhosis also includes ultrasound signs of changes in the liver.

This table shows the frequency and severity of liver disease according to the ECFSPR definitions (see Appendix 3, page 152). The frequency and severity of liver disease differs greatly throughout the ECFSPR data.

Figure 8.2 Prevalence and severity of liver disease in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on liver disease is missing for more than 10% of the patients.

Note: Belgium: collects only cirrhosis with portal hypertension "yes" or "no", therefore no liver disease means no cirrhosis with portal hypertension.
Germany: variceal bleeding information is not reported.
Serbia: cirrhosis without portal hypertension/hypersplenism means the presence of CF-related disease with normal liver function.
Ukraine: Liver disease without cirrhosis also includes ultrasound signs of changes in the liver.

Figure 7.3 shows the frequency of liver disease by country. Liver disease is defined according to severity of portal hypertension (increased blood pressure in the liver veins, often resulting in blood shunting past the cirrhotic liver) divided into five categories, including no liver disease (see Appendix 3, page 152). This graph emphasises better than the table the vast differences in frequency and severity, which may be due to problems in definitions and diagnostic tools.

Table 8.3 Prevalence of the use of ursodeoxycholic acid and the use of proton pump inhibitors (PPI) in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Ursodeoxycholic acid this year number (%)			PPI > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	2 (2.47)	39 (48.15)	40 (49.38)	0 (0.00)	69 (85.19)	12 (14.81)
Armenia	0 (0.00)	13 (52.00)	12 (48.00)	0 (0.00)	6 (24.00)	19 (76.00)
Austria	4 (0.54)	382 (51.90)	350 (47.55)	6 (0.82)	673 (91.44)	57 (7.74)
Belarus	0 (0.00)	35 (23.33)	115 (76.67)	0 (0.00)	122 (81.33)	28 (18.67)
Belgium	2 (0.18)	912 (80.42)	220 (19.40)	3 (0.26)	577 (50.88)	554 (48.85)
Bulgaria	0 (0.00)	141 (73.06)	52 (26.94)	0 (0.00)	154 (79.79)	39 (20.21)
Croatia	1 (0.81)	84 (67.74)	39 (31.45)	0 (0.00)	94 (75.81)	30 (24.19)
Cyprus	0 (0.00)	20 (90.91)	2 (9.09)	0 (0.00)	19 (86.36)	3 (13.64)
Czech Republic	0 (0.00)	399 (68.44)	184 (31.56)	0 (0.00)	452 (77.53)	131 (22.47)
Denmark	0 (0.00)	321 (68.44)	148 (31.56)	0 (0.00)	274 (58.42)	195 (41.58)
France	0 (0.00)	4660 (77.18)	1378 (22.82)	0 (0.00)	3636 (60.22)	2402 (39.78)
Georgia	2 (2.74)	51 (69.86)	20 (27.40)	0 (0.00)	72 (98.63)	1 (1.37)
Germany	66 (1.08)	3139 (51.14)	2933 (47.78)	70 (1.14)	4881 (79.52)	1187 (19.34)
Greece	2 (0.53)	251 (66.23)	126 (33.25)	4 (1.06)	311 (82.06)	64 (16.89)
Hungary	8 (1.85)	251 (57.97)	174 (40.18)	433 (100)	0 (0)	0 (0)
Iceland	0 (0.00)	13 (92.86)	1 (7.14)	0 (0.00)	7 (50.00)	7 (50.00)
Ireland	30 (2.65)	1013 (89.57)	88 (7.78)	0 (0.00)	612 (54.11)	519 (45.89)
Israel	2 (0.39)	422 (83.23)	83 (16.37)	8 (1.58)	332 (65.48)	167 (32.94)
Italy	36 (0.66)	3630 (66.25)	1813 (33.09)	27 (0.49)	3937 (71.86)	1515 (27.65)
Latvia	1 (2.17)	31 (67.39)	14 (30.43)	0 (0.00)	28 (60.87)	18 (39.13)
Lithuania	1 (2.94)	28 (82.35)	5 (14.71)	0 (0.00)	30 (88.24)	4 (11.76)
Luxembourg	0 (0.00)	17 (73.91)	6 (26.09)	0 (0.00)	15 (65.22)	8 (34.78)

[table 8.3 continued]

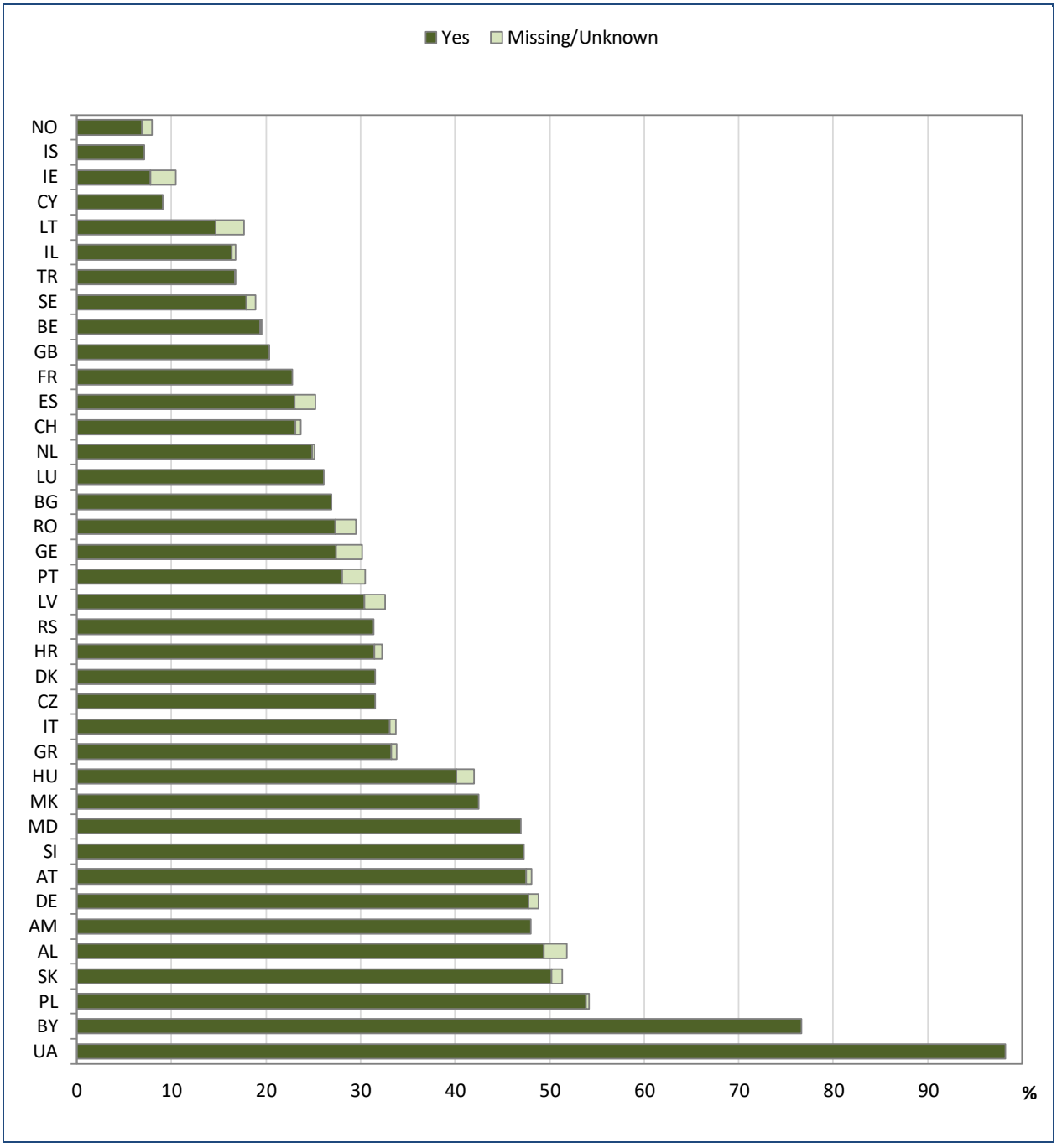
Country	Ursodeoxycholic acid this year number (%)			PPI > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0.00)	26 (53.06)	23 (46.94)	0 (0.00)	46 (93.88)	3 (6.12)
The Netherlands	4 (0.28)	1073 (74.83)	357 (24.90)	2 (0.14)	745 (51.95)	687 (47.91)
North Macedonia	0 (0.00)	69 (57.50)	51 (42.50)	0 (0.00)	63 (52.50)	57 (47.50)
Norway	3 (1.04)	266 (92.04)	20 (6.92)	0 (0.00)	238 (82.35)	51 (17.65)
Poland	4 (0.35)	529 (45.84)	621 (53.81)	7 (0.61)	967 (83.80)	180 (15.60)
Portugal	8 (2.42)	230 (69.49)	93 (28.10)	6 (1.81)	246 (74.32)	79 (23.87)
Romania	5 (2.20)	160 (70.48)	62 (27.31)	1 (0.44)	198 (87.22)	28 (12.33)
Russian Federation	487 (20.68)	184 (7.81)	1684 (71.51)	522 (22.17)	1440 (61.15)	393 (16.69)
Serbia	0 (0.00)	107 (68.59)	49 (31.41)	0 (0.00)	113 (72.44)	43 (27.56)
Slovak Republic	3 (1.14)	128 (48.67)	132 (50.19)	6 (2.28)	211 (80.23)	46 (17.49)
Slovenia	0 (0.00)	49 (52.69)	44 (47.31)	1 (1.08)	69 (74.19)	23 (24.73)
Spain	48 (2.23)	1606 (74.77)	494 (23.00)	38 (1.77)	1448 (67.41)	662 (30.82)
Sweden	6 (0.98)	498 (81.11)	110 (17.92)	15 (2.44)	468 (76.22)	131 (21.34)
Switzerland	5 (0.54)	707 (76.35)	214 (23.11)	3 (0.32)	746 (80.56)	177 (19.11)
Turkey	3 (0.15)	1712 (83.19)	343 (16.67)	3 (0.15)	1826 (88.73)	229 (11.13)
Ukraine	0 (0.00)	3 (1.78)	166 (98.22)	1 (0.59)	121 (71.60)	47 (27.81)
United Kingdom	0 (0.00)	7634 (79.62)	1954 (20.38)	0 (0.00)	5002 (52.17)	4586 (47.83)
Total	733 (1.60)	30833 (67.34)	14220 (31.06)	1156 (2.52)	30248 (66.06)	14382 (31.41)

Note: Oral ursodesoxycholic acid is reimbursed in most countries in Europe, except in Armenia, Bulgaria, Lithuania, Serbia and Ukraine. In Republic of Moldova, it is reimbursed for children and 70% for adults.

Note: Oral proton pump inhibitors are reimbursed in most countries except in Bulgaria, Lithuania, Republic of Moldova, Serbia and Ukraine.

This table shows the proton pump inhibitors (PPI) for more than 3 months during the survey year and the frequency of the use of ursodeoxycholic acid, a commonly used treatment for CF liver disease. The frequency and severity of liver disease differs greatly throughout the ECFSPR data and does not correspond to the number of patients on ursodeoxycholic acid.

Figure 8.3 Use of ursodeoxycholic acid in all patients seen in 2020 who have never had a transplant, by country.

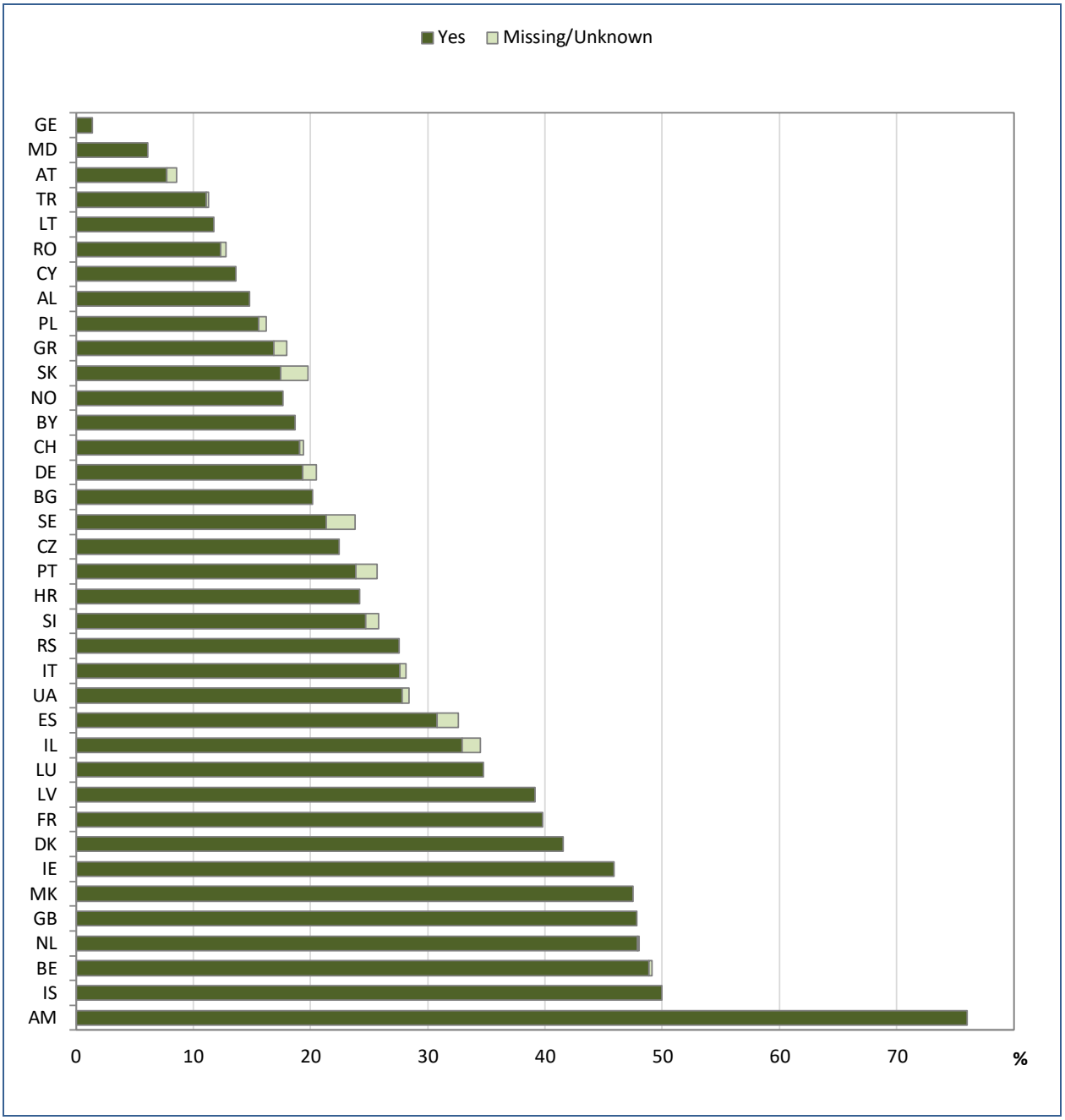


Note: We excluded from the graph the countries for which the information on oral ursodesoxycholic acid use is missing for more than 10% of the patients.

Note: Oral ursodesoxycholic acid is reimbursed in most countries in Europe, except in Armenia, Bulgaria, Lithuania, Serbia and Ukraine. In Republic of Moldova, it is reimbursed for children and 70% for adults.

This graph shows how many patients used ursodeoxycholic acid during 2020. Ursodeoxycholic acid is used as a treatment for CF liver disease. The dark green part of the bar indicates the percentage of patients taking this drug, the light green part shows the percentage of patients for whom this information is missing.

Figure 8.4 Use of proton pump inhibitors (PPI) in all patients seen in 2020 who have never had a transplant, by country.



Note: We excluded from the graph the countries for which the information on the use of PPI is missing for more than 10% of the patients.

Note: Oral proton pump inhibitors are reimbursed in most countries except in Bulgaria, Lithuania, Republic of Moldova, Serbia and Ukraine.

This graph shows the use of proton pump inhibitors (PPI) for more than 3 months during the survey year. The dark green part of the bar indicates the percentage of patients using PPI, the light green part shows the percentage of patients for whom this information is missing.

Table 8.4 Occurrence of malignancy this year and prevalence of distal intestinal obstruction syndrome (DIOS) in all patients seen in 2020 who have never had a transplant, by country and overall.

Country	Malignancy occurred this year number (%)			DIOS this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Albania	5 (6.17)	76 (93.83)	0 (0.00)	6 (7.41)	73 (90.12)	2 (2.47)
Armenia	0 (0)	25 (100)	0 (0)	0 (0.00)	23 (92.00)	2 (8.00)
Austria	0 (0.00)	734 (99.73)	2 (0.27)	1 (0.14)	716 (97.28)	19 (2.58)
Belarus	0 (0)	150 (100)	0 (0)	0 (0.00)	147 (98.00)	3 (2.00)
Belgium[1]	3 (0.26)	1125 (99.21)	6 (0.53)	4 (0.35)	1084 (95.59)	46 (4.06)
Bulgaria	0 (0.00)	192 (99.48)	1 (0.52)	0 (0)	193 (100)	0 (0)
Croatia	1 (0.81)	123 (99.19)	0 (0.00)	1 (0.81)	121 (97.58)	2 (1.61)
Cyprus	0 (0)	22 (100)	0 (0)	0 (0.00)	21 (95.45)	1 (4.55)
Czech Republic	24 (4.12)	557 (95.54)	2 (0.34)	3 (0.51)	580 (99.49)	0 (0.00)
Denmark[2]	0 (0)	469 (100)	0 (0)	0 (0.00)	458 (97.65)	11 (2.35)
France	4 (0.07)	6019 (99.69)	15 (0.25)	0 (0.00)	5865 (97.13)	173 (2.87)
Georgia	2 (2.74)	71 (97.26)	0 (0.00)	0 (0)	73 (100)	0 (0)
Germany	99 (1.61)	5998 (97.72)	41 (0.67)	117 (1.91)	5780 (94.17)	241 (3.93)
Greece	0 (0.00)	375 (98.94)	4 (1.06)	10 (2.64)	361 (95.25)	8 (2.11)
Hungary	5 (1.15)	426 (98.38)	2 (0.46)	433 (100)	0 (0)	0 (0)
Iceland	0 (0)	14 (100)	0 (0)	0 (0.00)	13 (92.86)	1 (7.14)
Ireland	41 (3.63)	1090 (96.37)	0 (0.00)	0 (0.00)	1089 (96.29)	42 (3.71)
Israel	20 (3.94)	486 (95.86)	1 (0.20)	17 (3.35)	484 (95.46)	6 (1.18)
Italy	145 (2.65)	5312 (96.95)	22 (0.40)	142 (2.59)	5228 (95.42)	109 (1.99)
Latvia	1 (2.17)	45 (97.83)	0 (0.00)	0 (0.00)	45 (97.83)	1 (2.17)
Lithuania	0 (0)	34 (100)	0 (0)	0 (0)	34 (100)	0 (0)
Luxembourg	0 (0)	23 (100)	0 (0)	0 (0.00)	22 (95.65)	1 (4.35)

[1] Belgium report prevalence of malignancy, not new occurrence of cancer this year, so some malignancies may have been diagnosed earlier.

[2] Denmark has only reported DIOS requiring hospitalisation.

[table 8.4 continued]

Country	Malignancy occurred this year number (%)			DIOS this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Rep of Moldova	0 (0)	49 (100)	0 (0)	0 (0)	49 (100)	0 (0)
The Netherlands	1 (0.07)	1429 (99.65)	4 (0.28)	9 (0.63)	1392 (97.07)	33 (2.30)
North Macedonia	0 (0)	120 (100)	0 (0)	0 (0.00)	118 (98.33)	2 (1.67)
Norway	6 (2.08)	281 (97.23)	2 (0.69)	2 (0.69)	277 (95.85)	10 (3.46)
Poland	12 (1.04)	1141 (98.87)	1 (0.09)	7 (0.61)	1136 (98.44)	11 (0.95)
Portugal	5 (1.51)	325 (98.19)	1 (0.30)	4 (1.21)	324 (97.89)	3 (0.91)
Romania	3 (1.32)	223 (98.24)	1 (0.44)	4 (1.76)	216 (95.15)	7 (3.08)
Russian Federation	485 (20.59)	1868 (79.32)	2 (0.08)	467 (19.83)	1845 (78.34)	43 (1.83)
Serbia	0 (0)	156 (100)	0 (0)	0 (0.00)	154 (98.72)	2 (1.28)
Slovak Republic	5 (1.90)	258 (98.10)	0 (0.00)	5 (1.90)	256 (97.34)	2 (0.76)
Slovenia	0 (0)	93 (100)	0 (0)	0 (0)	93 (100)	0 (0)
Spain	33 (1.54)	2108 (98.14)	7 (0.33)	19 (0.88)	2105 (98.00)	24 (1.12)
Sweden	9 (1.47)	604 (98.37)	1 (0.16)	10 (1.63)	586 (95.44)	18 (2.93)
Switzerland	4 (0.43)	918 (99.14)	4 (0.43)	3 (0.32)	898 (96.98)	25 (2.70)
Turkey	7 (0.34)	2049 (99.56)	2 (0.10)	9 (0.44)	2035 (98.88)	14 (0.68)
Ukraine	0 (0.00)	168 (99.41)	1 (0.59)	0 (0.00)	163 (96.45)	6 (3.55)
United Kingdom	189 (1.97)	9380 (97.83)	19 (0.20)	0 (0.00)	9132 (95.24)	456 (4.76)
Total	1109 (2.42)	44536 (97.27)	141 (0.31)	1273 (2.78)	43189 (94.33)	1324 (2.89)

Table 8.4 shows the frequency of two rare complications: occurrence of malignancy (cancer) and distal intestinal obstruction syndrome (DIOS).

9. CFTR modulator therapies

The introduction of the CFTR modulator therapies that have been developed so far have a great impact on health status and quality of life of people with CF as well as on CF care. These therapies target defects in the structure and function of the cystic fibrosis transmembrane conductance regulator protein. However, the CFTR modulator therapies are only effective in people with specific mutation classes since different mutations cause different defects in the protein.

In this chapter we present information about the use of the different CFTR modulator therapies for people with CF according to eligibility by product license in the country. Also, we provide maps with the availability of these therapies, depending on national reimbursement, in each country to support interpretation of the results and to understand the country-specific variations in therapy use.

Table 9.1 Use of Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.

Country	Age at follow-up (years)	Use of Ivacaftor this year, number (%)					
		Missing/unknown		No		Yes	
Albania	**0-17**	0	(0)	2	(100)	0	(0)
Austria	**0-17**	0	(0)	10	(50.00)	10	(50.00)
	≥18	0	(0)	6	(33.33)	12	(66.67)
Belgium	**0-17**	0	(0)	6	(27.27)	16	(72.73)
	≥18	0	(0)	21	(39.62)	32	(60.38)
Bulgaria	**0-17**	0	(0)	1	(20.00)	4	(80.00)
	≥18	0	(0)	1	(100)	0	(0)
Croatia	**0-17**	0	(0)	1	(100)	0	(0)
	≥18	0	(0)	1	(100)	0	(0)
Czech Republic	**0-17**	0	(0)	1	(10.00)	9	(90.00)
	≥18	0	(0)	4	(22.22)	14	(77.78)
Denmark	**0-17**	0	(0)	3	(100)	0	(0)
	≥18	0	(0)	10	(83.33)	2	(16.67)
France	**0-17**	0	(0)	38	(36.19)	67	(63.81)
	≥18	0	(0)	43	(31.85)	92	(68.15)
Germany	**0-17**	0	(0)	28	(28.00)	72	(72.00)
	≥18	1	(0.57)	36	(20.69)	137	(78.74)
Greece	**≥18**	0	(0)	0	(0)	1	(100)
Hungary	**0-17**	0	(0)	4	(100)	0	(0)
	≥18	0	(0)	1	(100)	0	(0)
Iceland	**0-17**	0	(0)	0	(0)	1	(100)
Ireland	**0-17**	0	(0)	13	(13.98)	80	(86.02)
	≥18	0	(0)	18	(11.46)	139	(88.54)
Israel	**0-17**	0	(0)	0	(0)	5	(100)
	≥18	0	(0)	0	(0)	9	(100)
Italy	**0-17**	0	(0)	46	(43.81)	59	(56.19)
	≥18	0	(0)	39	(30.00)	91	(70.00)
Rep of Moldova	**0-17**	0	(0)	1	(100)	0	(0)
The Netherlands	**0-17**	0	(0)	15	(60.00)	10	(40.00)
	≥18	0	(0)	21	(42.00)	29	(58.00)
North Macedonia	**0-17**	0	(0)	2	(100)	0	(0)
	≥18	0	(0)	2	(100)	0	(0)
Norway	**0-17**	0	(0)	1	(20.00)	4	(80.00)
	≥18	0	(0)	5	(35.71)	9	(64.29)
Poland	**0-17**	0	(0)	9	(100)	0	(0)
	≥18	0	(0)	2	(66.67)	1	(33.33)
Portugal	**≥18**	0	(0)	3	(75.00)	1	(25.00)
Romania	**0-17**	0	(0)	2	(100)	0	(0)
Russian Federation	**0-17**	0	(0)	3	(100)	0	(0)
	≥18	0	(0)	2	(100)	0	(0)
Slovak Republic	**0-17**	0	(0)	6	(100)	0	(0)
	≥18	0	(0)	5	(100)	0	(0)
Spain	**0-17**	0	(0)	8	(47.06)	9	(52.94)
	≥18	0	(0)	13	(43.33)	17	(56.67)
Sweden	**0-17**	0	(0)	0	(0)	7	(100)
	≥18	0	(0)	9	(75.00)	3	(25.00)
Switzerland	**0-17**	0	(0)	0	(0)	6	(100)
	≥18	0	(0)	5	(50.00)	5	(50.00)

Country	Age at follow-up (years)	Use of Ivacaftor this year, number (%)					
		Missing/unknown		No		Yes	
Turkey	**0-17**	0	(0)	25	(100)	0	(0)
	≥18	0	(0)	3	(100)	0	(0)
United Kingdom	**0-17**	0	(0)	268	(51.34)	254	(48.66)
	≥18	0	(0)	130	(20.41)	507	(79.59)
Total	**0-17**	4	(0.36)	489	(44.22)	613	(55.42)
	≥18	2	(0.13)	379	(25.58)	1101	(74.29)

Note: Countries that do not have patients who are eligible for Ivacaftor are not included in the table.

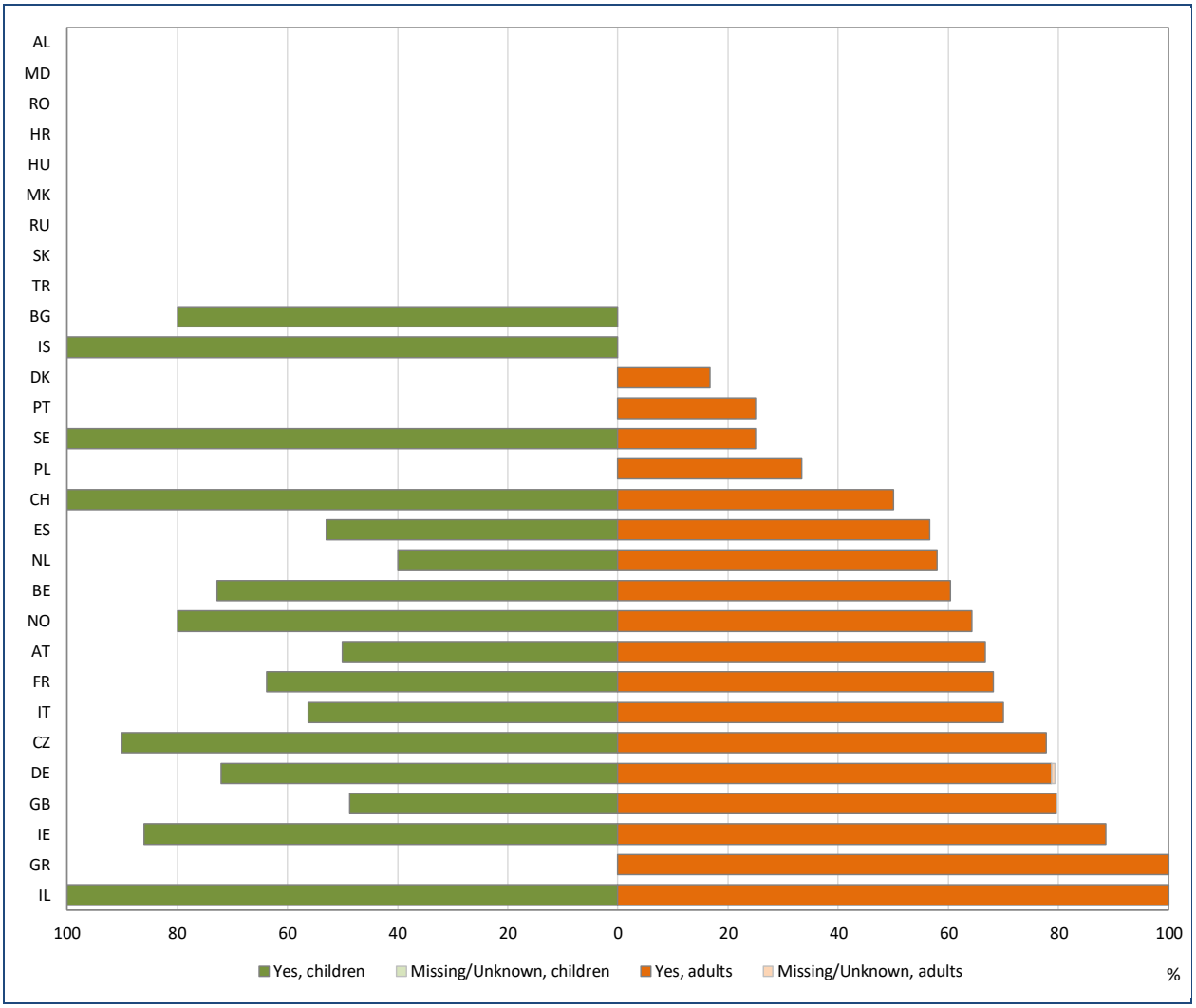
We adopted the eligibility criteria of the European Medicine Agency (EMA) for the countries in and outside Europe. Exceptions are Israel and Switzerland where specific eligibility criteria have been applied according to the national regulatory authorities.

The eligibility criteria for Ivacaftor in 2020 are:

- The patient is 6 months, and from 4 November 2020 4 months, (2 years in Israel) and older with at least one of the following mutations: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R;
- The patient is 18 years and older with at least one of the following mutations: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549R, S549N, R117H (Czech Republic, France and Israel have no approval for this mutation).

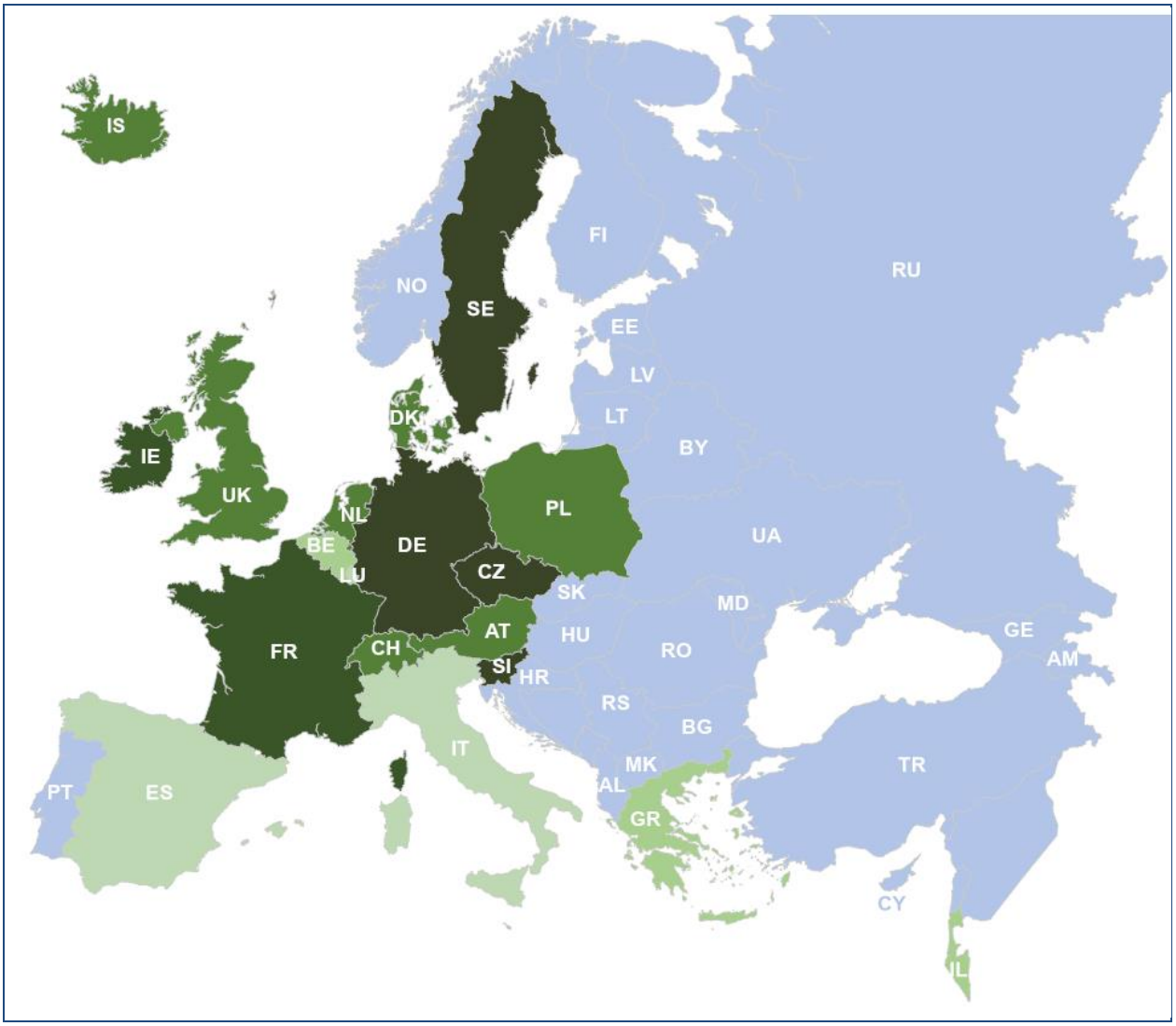
In countries where the therapy is licensed but not reimbursed, or not licensed nor reimbursed, eligible patients may sometimes have access to the therapy because of a clinical trial or a compassionate use programme.

Figure 9.1 Use of Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.



Note: We excluded from the graph the countries for which the information on Ivacaftor use is missing for more than 10% of the patients.

Figure 9.2 Countries where Ivacaftor is reimbursed in year 2020.



Note: Belgium: reimbursement only for patients with two CF-causing mutations or sweat chloride > 60mmol/L and with pulmonary or GI symptoms and/or growth deviation; excluded are patients with R117H mutation and patients with a lung transplantation.
Sweden: no official reimbursement; the therapy is available through the healthcare system for patients with the eligible CFTR mutations (excluding R117H).

In this graph we highlighted the countries where Ivacaftor was licensed and reimbursed in 2020.

Table 9.2 Use of Lumacaftor/Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.

Country	Age at follow-up (years)	Use of Lumacaftor/Ivacaftor this year number (%)					
		Missing/unknown		No		Yes	
Albania	**2-17**	3	(6.00)	47	(94.00)	0	(0)
	≥18	0	(0)	2	(100)	0	(0)
Armenia	**2-17**	0	(0)	1	(100)	0	(0)
Austria	**2-17**	0	(0)	97	(60.25)	64	(39.75)
	≥18	0	(0)	127	(70.17)	54	(29.83)
Belarus	**2-17**	0	(0)	41	(100)	0	(0)
Belgium	**2-17**	0	(0)	172	(90.53)	18	(9.47)
	≥18	0	(0)	240	(84.81)	43	(15.19)
Bulgaria	**2-17**	0	(0)	30	(76.92)	9	(23.08)
	≥18	0	(0)	24	(100)	0	(0)
Croatia	**2-17**	0	(0)	43	(100)	0	(0)
	≥18	0	(0)	34	(100)	0	(0)
Cyprus	**2-17**	0	(0)	0	(0)	2	(100)
	≥18	0	(0)	0	(0)	2	(100)
Czech Republic	**2-17**	0	(0)	58	(46.40)	67	(53.60)
	≥18	0	(0)	84	(80.77)	20	(19.23)
Denmark	**2-17**	0	(0)	38	(29.23)	92	(70.77)
	≥18	0	(0)	146	(82.49)	31	(17.51)
France	**2-17**	0	(0)	153	(13.95)	944	(86.05)
	≥18	0	(0)	451	(33.86)	881	(66.14)
Georgia	**2-17**	0	(0)	1	(100)	0	(0)
Germany	**2-17**	1	(0.09)	565	(53.06)	499	(46.85)
	≥18	21	(1.28)	1321	(80.30)	303	(18.42)
Greece	**2-17**	0	(0)	7	(19.44)	29	(80.56)
	≥18	3	(3.37)	23	(25.84)	63	(70.79)
Hungary	**2-17**	0	(0)	100	(100)	0	(0)
	≥18	0	(0)	62	(100)	0	(0)
Iceland	**2-17**	0	(0)	0	(0)	2	(100)
	≥18	0	(0)	0	(0)	2	(100)
Ireland	**2-17**	0	(0)	21	(7.69)	252	(92.31)
	≥18	0	(0)	167	(48.83)	175	(51.17)
Israel	**2-17**	0	(0)	9	(60.00)	6	(40.00)
	≥18	0	(0)	22	(61.11)	14	(38.89)
Italy	**2-17**	0	(0)	259	(57.30)	193	(42.70)
	≥18	0	(0)	184	(29.35)	443	(70.65)
Latvia	**2-17**	0	(0)	16	(100)	0	(0)
	≥18	0	(0)	8	(100)	0	(0)
Lithuania	**2-17**	0	(0)	3	(100)	0	(0)
	≥18	0	(0)	6	(100)	0	(0)
Luxembourg	**2-17**	0	(0)	3	(37.50)	5	(62.50)
	≥18	0	(0)	1	(100)	0	(0)
Rep of Moldova	**2-17**	0	(0)	18	(100)	0	(0)
	≥18	0	(0)	1	(100)	0	(0)
The Netherlands	**2-17**	0	(0)	102	(34.00)	198	(66.00)
	≥18	0	(0)	322	(68.08)	151	(31.92)
North Macedonia	**2-17**	0	(0)	41	(100)	0	(0)
	≥18	0	(0)	18	(100)	0	(0)
Norway	**2-17**	0	(0)	32	(84.21)	6	(15.79)
	≥18	0	(0)	31	(56.36)	24	(43.64)

[table 9.2 continued]

Country	Age at follow-up (years)	Use of Lumacaftor/Ivacaftor this year number (%)					
		Missing/unknown		No		Yes	
Poland	**2-17**	1	(0.32)	300	(94.63)	16	(5.05)
	≥18	2	(1.40)	136	(95.10)	5	(3.50)
Portugal	**2-17**	0	(0)	76	(82.61)	16	(17.39)
	≥18	1	(1.79)	37	(66.07)	18	(32.14)
Romania	**2-17**	0	(0)	94	(100)	0	(0)
	≥18	0	(0)	3	(100)	0	(0)
Russian Federation	**2-17**	20	(4.05)	474	(95.95)	0	(0)
	≥18	109	(68.55)	50	(31.45)	0	(0)
Serbia	**2-17**	0	(0)	47	(100)	0	(0)
	≥18	0	(0)	32	(100)	0	(0)
Slovak Republic	**2-17**	0	(0)	26	(52.00)	24	(48.00)
	≥18	1	(2	31	(62.00)	18	(36.00)
Slovenia	**2-17**	0	(0)	30	(85.71)	5	(14.29)
	≥18	0	(0)	20	(100)	0	(0)
Spain	**2-17**	0	(0)	166	(59.29)	114	(40.71)
	≥18	1	(0.38)	247	(92.85)	18	(6.77)
Sweden	**2-17**	0	(0)	8	(6.30)	119	(93.70)
	≥18	0	(0)	41	(27.15)	110	(72.85)
Switzerland	**2-17**	0	(0)	136	(80.00)	34	(20.00)
	≥18	0	(0)	175	(73.84)	62	(26.16)
Turkey	**2-17**	0	(0)	193	(100)	0	(0)
	≥18	0	(0)	32	(100)	0	(0)
Ukraine	**2-17**	0	(0)	47	(100)	0	(0)
	≥18	0	(0)	8	(100)	0	(0)
United Kingdom	**2-17**	0	(0)	873	(43.37)	1140	(56.63)
	≥18	0	(0)	2315	(91.68)	210	(8.32)
Total	**2-17**	125	(1.52)	4227	(51.51)	3854	(46.97)
	≥18	200	(2.18)	6339	(69.00)	2647	(28.82)

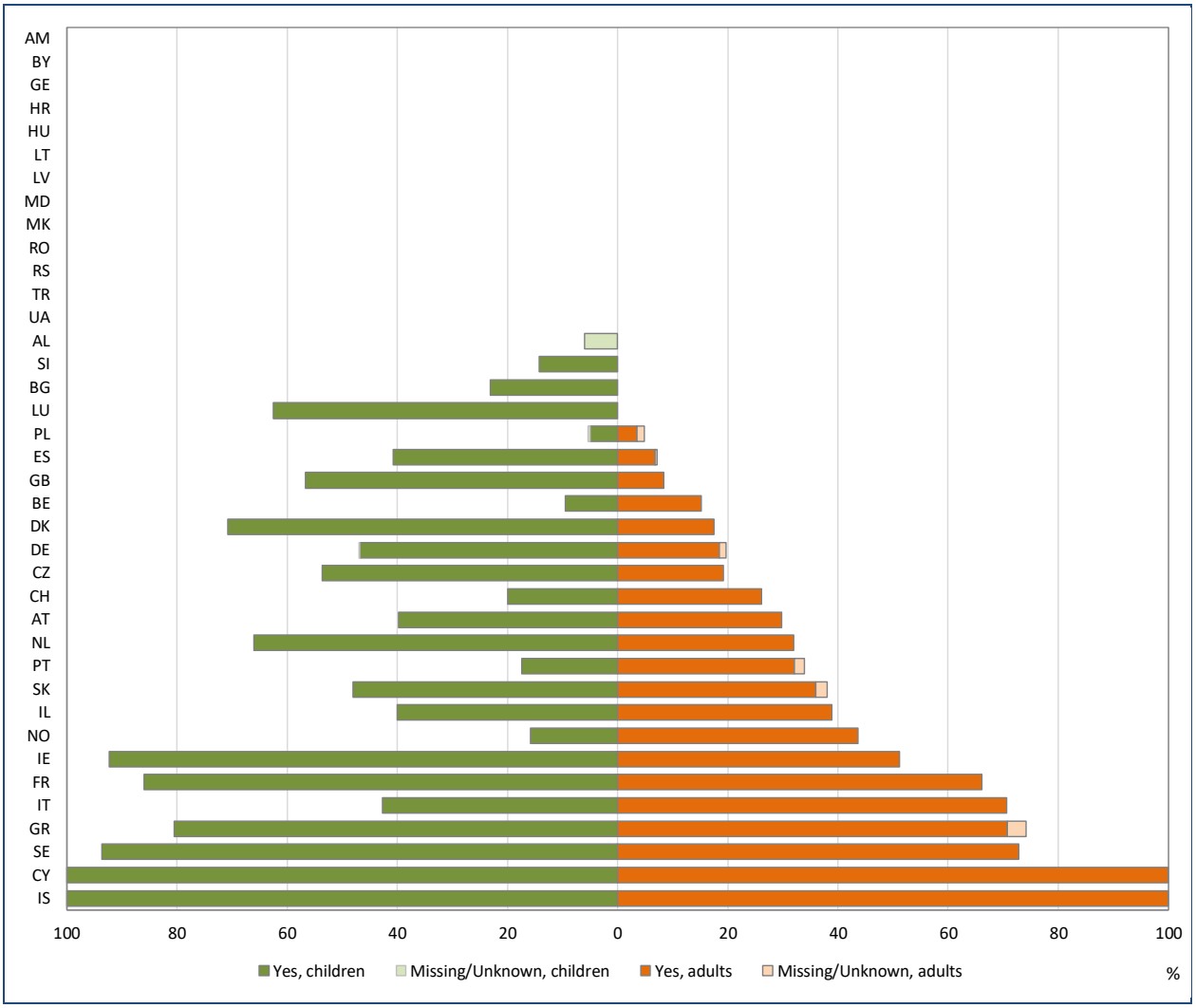
Note: Countries that do not have patients who are eligible for Lumacaftor/Ivacaftor are not included in the table.

We adopted the eligibility criteria of the European Medicine Agency (EMA) criteria for the countries in and outside Europe. Exceptions are Israel and Switzerland where specific eligibility criteria have been applied according to the national regulatory authorities.

The eligibility criteria for Lumacaftor/Ivacaftor in 2020 are:
The patient must be 2 years (6 years in Israel) or older and is F508del homozygous.

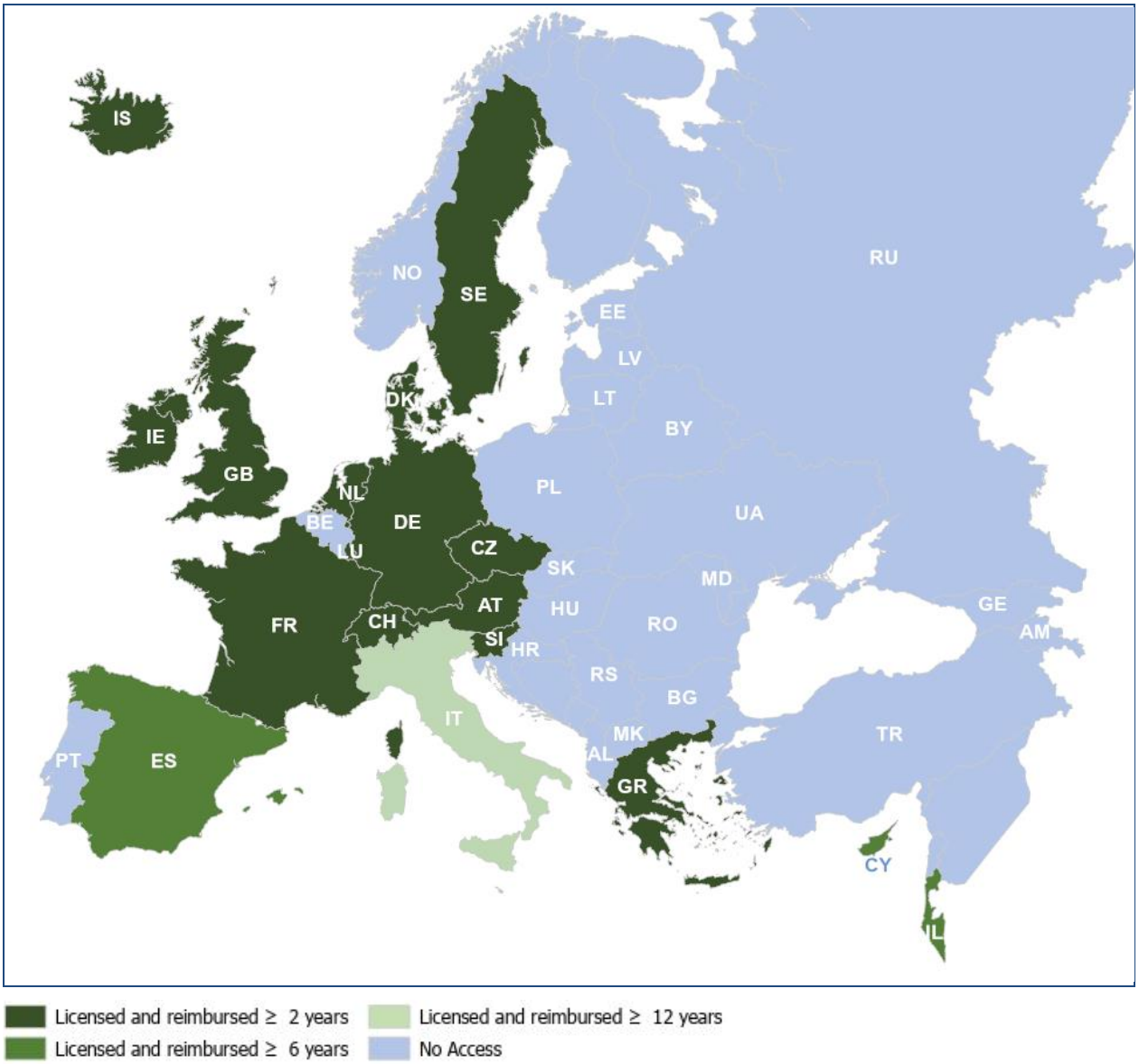
In countries where the therapy is licensed but not reimbursed, or not licensed nor reimbursed, eligible patients may sometimes have access to the therapy because of a clinical trial or a compassionate use programme.

Figure 9.3 Use of Lumacaftor/Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.



Note: We excluded from the graph the countries for which the information on Lumacaftor/Ivacaftor use is missing for more than 10% of the patients.

Figure 9.4 Countries where Lumacaftor/Ivacaftor is reimbursed in year 2020.



In this graph we highlighted the countries where Lumacaftor/Ivacaftor was licensed and reimbursed in 2020.

Table 9.3 Use of Tezacaftor/Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.

Country	Age at follow-up (years)	Use of Tezacaftor/Ivacaftor this year number (%)					
		Missing/unknown		No		Yes	
Albania	**12-17**	0	(0)	16	(100)	0	(0)
	≥18	0	(0)	2	(100)	0	(0)
Austria	**12-17**	0	(0)	53	(85.48)	9	(14.52)
	≥18	0	(0)	132	(68.04)	62	(31.96)
Belarus	**12-17**	0	(0)	11	(100)	0	(0)
Belgium	**12-17**	0	(0)	71	(94.67)	4	(5.33)
	≥18	0	(0)	355	(98.34)	6	(1.66)
Bulgaria	**12-17**	0	(0)	13	(100)	0	(0)
	≥18	0	(0)	28	(100)	0	(0)
Croatia	**12-17**	0	(0)	15	(100)	0	(0)
	≥18	0	(0)	34	(100)	0	(0)
Cyprus	**12-17**	0	(0)	3	(100)	0	(0)
Czech Republic	**12-17**	0	(0)	44	(81.48)	10	(18.52)
	≥18	0	(0)	105	(84.00)	20	(16.00)
Denmark	**12-17**	0	(0)	19	(34.55)	36	(65.45)
	≥18	0	(0)	61	(33.15)	123	(66.85)
France	**12-17**	517	(99.61)	0	(0)	2	(0.39)
	≥18	1633	(99.57)	0	(0)	7	(0.43)
Germany	**12-17**	2	(0.47)	326	(77.07)	95	(22.46)
	≥18	20	(1.10)	963	(53.15)	829	(45.75)
Greece	**12-17**	0	(0)	12	(85.71)	2	(14.29)
	≥18	1	(0.93)	79	(73.14)	28	(25.93)
Hungary	**12-17**	0	(0)	41	(100)	0	(0)
	≥18	0	(0)	67	(100)	0	(0)
Iceland	**12-17**	0	(0)	1	(100)	0	(0)
	≥18	0	(0)	2	(100)	0	(0)
Ireland	**12-17**	0	(0)	100	(95.24)	5	(4.76)
	≥18	0	(0)	207	(57.82)	151	(42.18)
Israel	**12-17**	0	(0)	3	(25.00)	9	(75.00)
	≥18	0	(0)	16	(29.09)	39	(70.91)
Italy	**12-17**	0	(0)	190	(95.96)	8	(4.04)
	≥18	0	(0)	845	(91.55)	78	(8.45)
Latvia	**12-17**	0	(0)	7	(100)	0	(0)
	≥18	0	(0)	8	(100)	0	(0)
Lithuania	**12-17**	0	(0)	1	(100)	0	(0)
	≥18	0	(0)	11	(100)	0	(0)
Luxembourg	**12-17**	0	(0)	1	(100)	0	(0)
	≥18	0	(0)	1	(100)	0	(0)
Rep of Moldova	**12-17**	0	(0)	5	(100)	0	(0)
	≥18	0	(0)	1	(100)	0	(0)
The Netherlands	**12-17**	0	(0)	26	(19.55)	107	(80.45)
	≥18	0	(0)	330	(54.91)	271	(45.09)
North Macedonia	**12-17**	0	(0)	16	(100)	0	(0)
	≥18	0	(0)	20	(100)	0	(0)
Norway	**12-17**	0	(0)	17	(100)	0	(0)
	≥18	0	(0)	78	(100)	0	(0)

[table 9.3 continued]

Country	Age at follow-up (years)	Use of Tezacaftor/Ivacaftor this year number (%)					
		Missing/unknown		No		Yes	
Poland	**12-17**	0	(0)	125	(98.43)	2	(1.57)
	≥18	2	(1.16)	170	(98.26)	1	(0.58)
Portugal	**12-17**	0	(0)	41	(100)	0	(0)
	≥18	1	(1.47)	67	(98.53)	0	(0)
Romania	**12-17**	0	(0)	37	(100)	0	(0)
	≥18	0	(0)	3	(100)	0	(0)
Russian Federation	**12-17**	5	(2.99)	160	(95.81)	2	(1.20)
	≥18	154	(72.64)	58	(27.36)	0	(0)
Serbia	**12-17**	0	(0)	17	(100)	0	(0)
	≥18	0	(0)	34	(100)	0	(0)
Slovak Republic	**12-17**	0	(0)	20	(100)	0	(0)
	≥18	1	(1.52)	65	(98.48)	0	(0)
Slovenia	**12-17**	0	(0)	4	(100)	0	(0)
	≥18	0	(0)	20	(100)	0	(0)
Spain	**12-17**	0	(0)	24	(16.33)	123	(83.67)
	≥18	2	(0.55)	111	(30.49)	251	(68.96)
Sweden	**12-17**	0	(0)	54	(100)	0	(0)
	≥18	0	(0)	161	(93.60)	11	(6.40)
Switzerland	**12-17**	0	(0)	37	(64.91)	20	(35.09)
	≥18	0	(0)	148	(58.50)	105	(41.50)
Turkey	**12-17**	0	(0)	66	(100)	0	(0)
	≥18	0	(0)	41	(100)	0	(0)
Ukraine	**12-17**	0	(0)	14	(100)	0	(0)
	≥18	0	(0)	9	(90.00)	1	(10.00)
United Kingdom	**12-17**	0	(0)	247	(30.88)	553	(69.13)
	≥18	0	(0)	665	(23.10)	2214	(76.90)
Total	**12-17**	565	(16.89)	1793	(53.60)	987	(29.51)
	≥18	1881	(17.24)	4833	(44.29)	4197	(38.47)

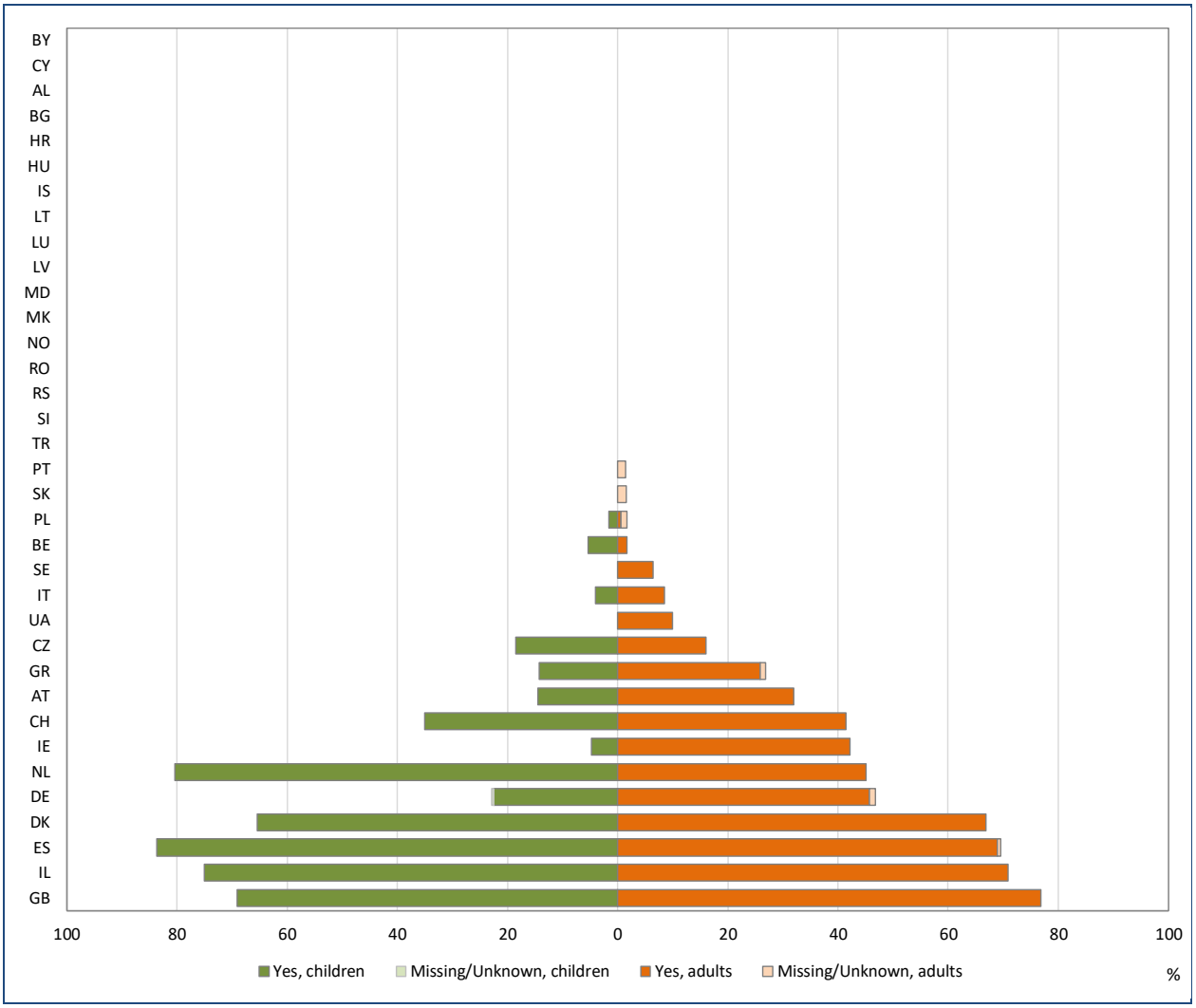
Note: Countries that do not have patients who are eligible for Tezacaftor/Ivacaftor are not included in the table.

We adopted the eligibility criteria of the European Medicine Agency (EMA) criteria for the countries, in and outside Europe. Exceptions are Israel and Switzerland where specific eligibility criteria have been applied according to the national regulatory authorities.

The eligibility criteria for Tezacaftor/Ivacaftor in 2020 are:
The patient is 12 years or older, and from 27 November 2020 6 years and older (12 years in Switzerland), and is F508del homozygous, or F508del heterozygous with one of the following mutations: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G, or 3849+10kbC→T.

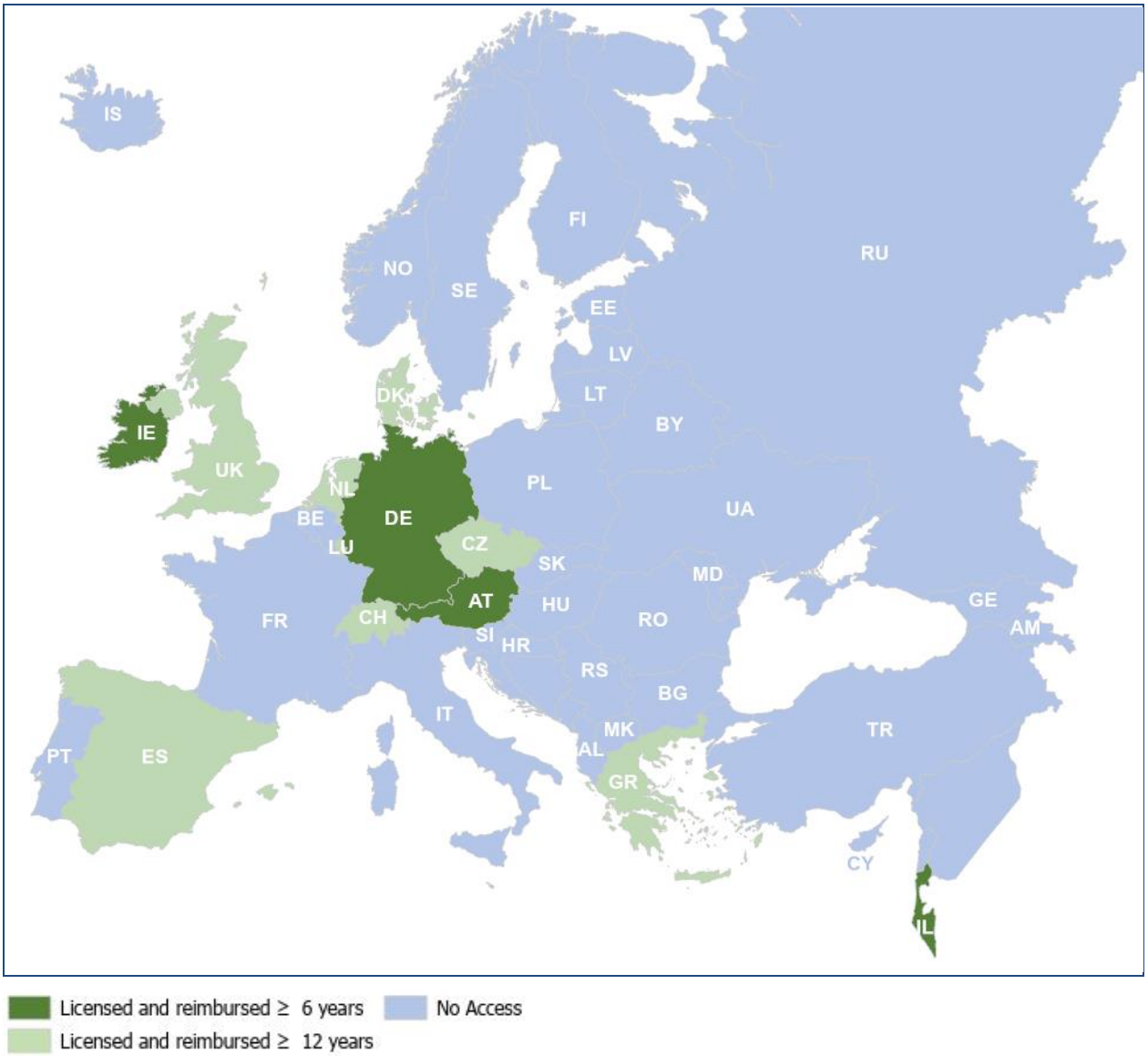
In countries where the therapy is licensed but not reimbursed, or not licensed nor reimbursed, eligible patients may sometimes have access to the therapy because of a clinical trial or a compassionate use programme.

Figure 9.5 Use of Tezaftor/Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.



Note: We excluded from the graph the countries for which the information on Tezacaftor/Ivacaftor use is missing for more than 10% of the patients.

Figure 9.6 Countries where Tezacaftor/Ivacaftor is reimbursed in year 2020.



Note: The Netherlands: only for patients with the mutation F508del homozygous.

In this graph we highlighted the countries where Tezacaftor/Ivacaftor was licensed and reimbursed in 2020.

Table 9.4 Use of Elexacaftor/Tezacaftor/Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.

Country	Age at follow-up (years)	Use of Elexacaftor/Tezacaftor/Ivacaftor this year number (%)					
		Missing/unknown		No		Yes	
Albania	**12-17**	0	(0)	17	(100)	0	(0)
	≥18	0	(0)	4	(100)	0	(0)
Austria	**12-17**	0	(0)	86	(89.58)	10	(10.42)
	≥18	0	(0)	205	(77.65)	59	(22.35)
Belarus	**12-17**	0	(0)	25	(100)	0	(0)
Belgium	**12-17**	0	(0)	93	(89.42)	11	(10.58)
	≥18	1	(0.24)	309	(75.55)	99	(24.21)
Bulgaria	**12-17**	0	(0)	26	(100)	0	(0)
	≥18	0	(0)	47	(97.92)	1	(2.08)
Croatia	**12-17**	0	(0)	23	(100)	0	(0)
	≥18	0	(0)	41	(100)	0	(0)
Cyprus	**12-17**	0	(0)	2	(100)	0	(0)
	≥18	0	(0)	2	(100)	0	(0)
Czech Republic	**12-17**	0	(0)	73	(96.05)	3	(3.95)
	≥18	0	(0)	160	(98.16)	3	(1.84)
Denmark	**12-17**	0	(0)	18	(29.51)	43	(70.49)
	≥18	0	(0)	50	(21.93)	178	(78.07)
France	**12-17**	0	(0)	722	(97.17)	21	(2.83)
	≥18	0	(0)	1742	(83.83)	336	(16.17)
Georgia	**12-17**	0	(0)	2	(100)	0	(0)
Germany	**12-17**	3	(0.44)	545	(80.39)	130	(19.17)
	≥18	39	(1.57)	1711	(69.08)	727	(29.35)
Greece	**12-17**	0	(0)	20	(100)	0	(0)
	≥18	0	(0)	151	(83.43)	30	(16.57)
Hungary	**12-17**	0	(0)	62	(100)	0	(0)
	≥18	0	(0)	102	(100)	0	(0)
Iceland	**12-17**	0	(0)	2	(100)	0	(0)
	≥18	0	(0)	4	(100)	0	(0)
Ireland	**12-17**	0	(0)	86	(62.32)	52	(37.68)
	≥18	0	(0)	241	(56.18)	188	(43.82)
Italy	**12-17**	0	(0)	371	(95.87)	16	(4.13)
	≥18	0	(0)	1149	(79.41)	298	(20.59)
Latvia	**12-17**	0	(0)	8	(100)	0	(0)
	≥18	0	(0)	11	(100)	0	(0)
Lithuania	**12-17**	0	(0)	3	(100)	0	(0)
	≥18	0	(0)	8	(100)	0	(0)
Luxembourg	**12-17**	0	(0)	1	(50.00)	1	(50.00)
	≥18	0	(0)	1	(100)	0	(0)
Rep of Moldova	**12-17**	0	(0)	6	(100)	0	(0)
	≥18	0	(0)	4	(100)	0	(0)
The Netherlands	**12-17**	0	(0)	155	(96.27)	6	(3.73)
	≥18	2	(0.33)	535	(88.14)	70	(11.53)
North Macedonia	**12-17**	0	(0)	25	(100)	0	(0)
	≥18	0	(0)	27	(100)	0	(0)
Norway	**12-17**	0	(0)	26	(100)	0	(0)
	≥18	0	(0)	109	(100)	0	(0)

[table 9.4 continued]

Country	Age at follow-up (years)	Use of Elexacaftor/Tezacaftor/Ivacaftor this year number (%)					
		Missing/unknown		No		Yes	
Poland	**12-17**	1	(0.53)	184	(97.87)	3	(1.60)
	≥18	2	(0.95)	208	(98.58)	1	(0.47)
Portugal	**12-17**	0	(0)	48	(97.96)	1	(2.04)
	≥18	1	(1.16)	84	(97.68)	1	(1.16)
Romania	**12-17**	0	(0)	50	(100)	0	(0)
	≥18	0	(0)	7	(100)	0	(0)
Russian Federation	**12-17**	6	(2.17)	269	(97.47)	1	(0.36)
	≥18	218	(70.78)	90	(29.22)	0	(0)
Serbia	**12-17**	0	(0)	24	(100)	0	(0)
	≥18	0	(0)	41	(100)	0	(0)
Slovak Republic	**12-17**	0	(0)	28	(100)	0	(0)
	≥18	1	(1.33)	72	(96.00)	2	(2.67)
Slovenia	**12-17**	0	(0)	2	(33.33)	4	(66.67)
	≥18	0	(0)	6	(22.22)	21	(77.78)
Spain	**12-17**	0	(0)	232	(95.87)	10	(4.13)
	≥18	2	(0.38)	469	(87.99)	62	(11.63)
Sweden	**12-17**	0	(0)	81	(100)	0	(0)
	≥18	0	(0)	222	(90.61)	23	(9.39)
Turkey	**12-17**	0	(0)	96	(100)	0	(0)
	≥18	0	(0)	60	(100)	0	(0)
Ukraine	**12-17**	0	(0)	33	(100)	0	(0)
	≥18	0	(0)	27	(100)	0	(0)
United Kingdom	**12-17**	0	(0)	593	(57.46)	439	(42.54)
	≥18	0	(0)	1423	(40.11)	2125	(59.89)
Total	**12-17**	72	(1.50)	3975	(82.85)	751	(15.65)
	≥18	368	(2.66)	9220	(66.76)	4224	(30.58)

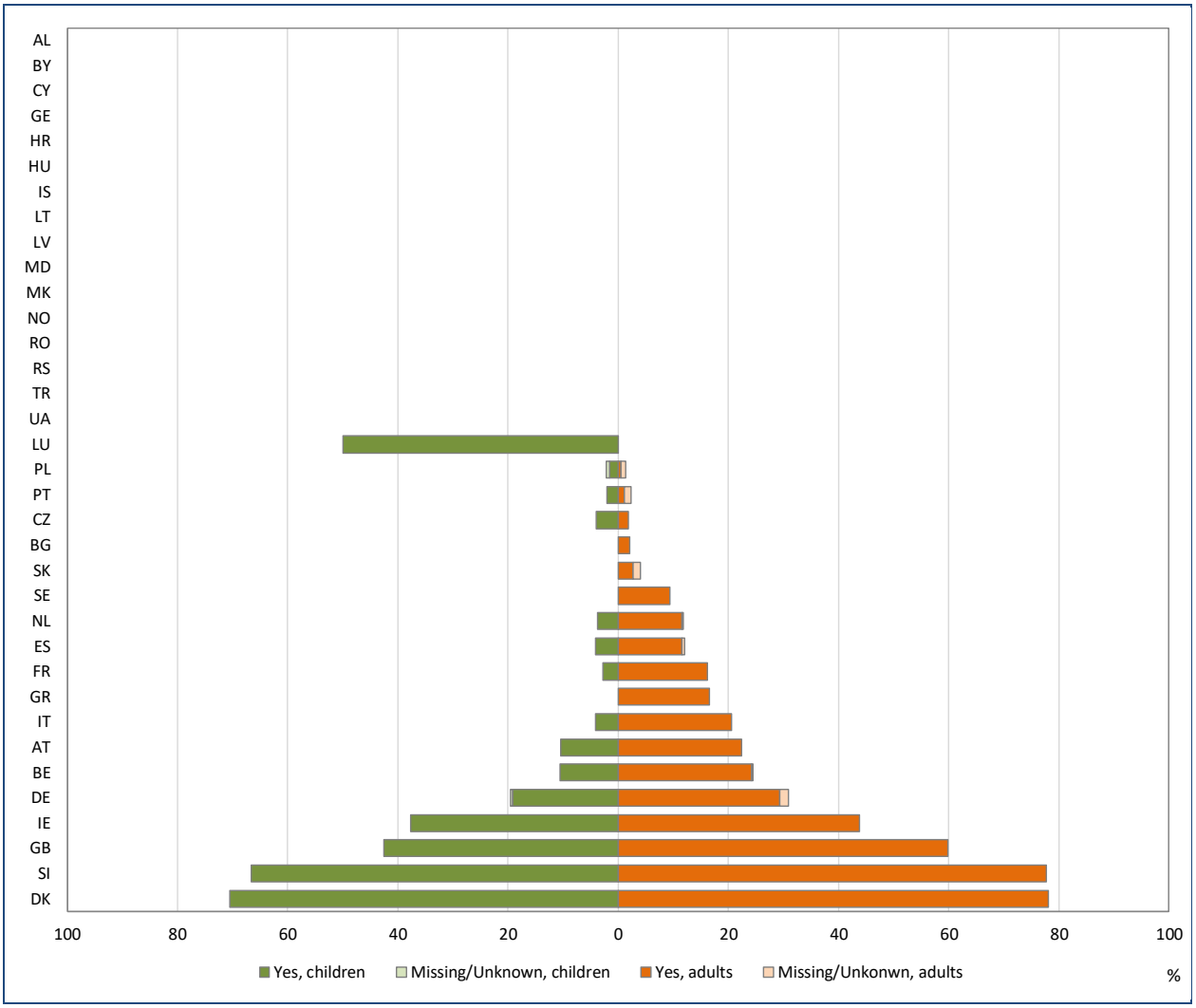
Note: Countries that do not have patients who are eligible for Elexacaftor/Tezacaftor/Ivacaftor are not included in the table.

We adopted the eligibility criteria of the European Medicine Agency (EMA) criteria for the countries, in and outside Europe. Exceptions are Israel and Switzerland where specific eligibility criteria have been applied according to the national regulatory authorities.

The eligibility criteria for Elexacaftor/Tezacaftor/Ivacaftor in 2020 are:
The patient is 12 years or older and is F508del homozygous or F508del heterozygous.

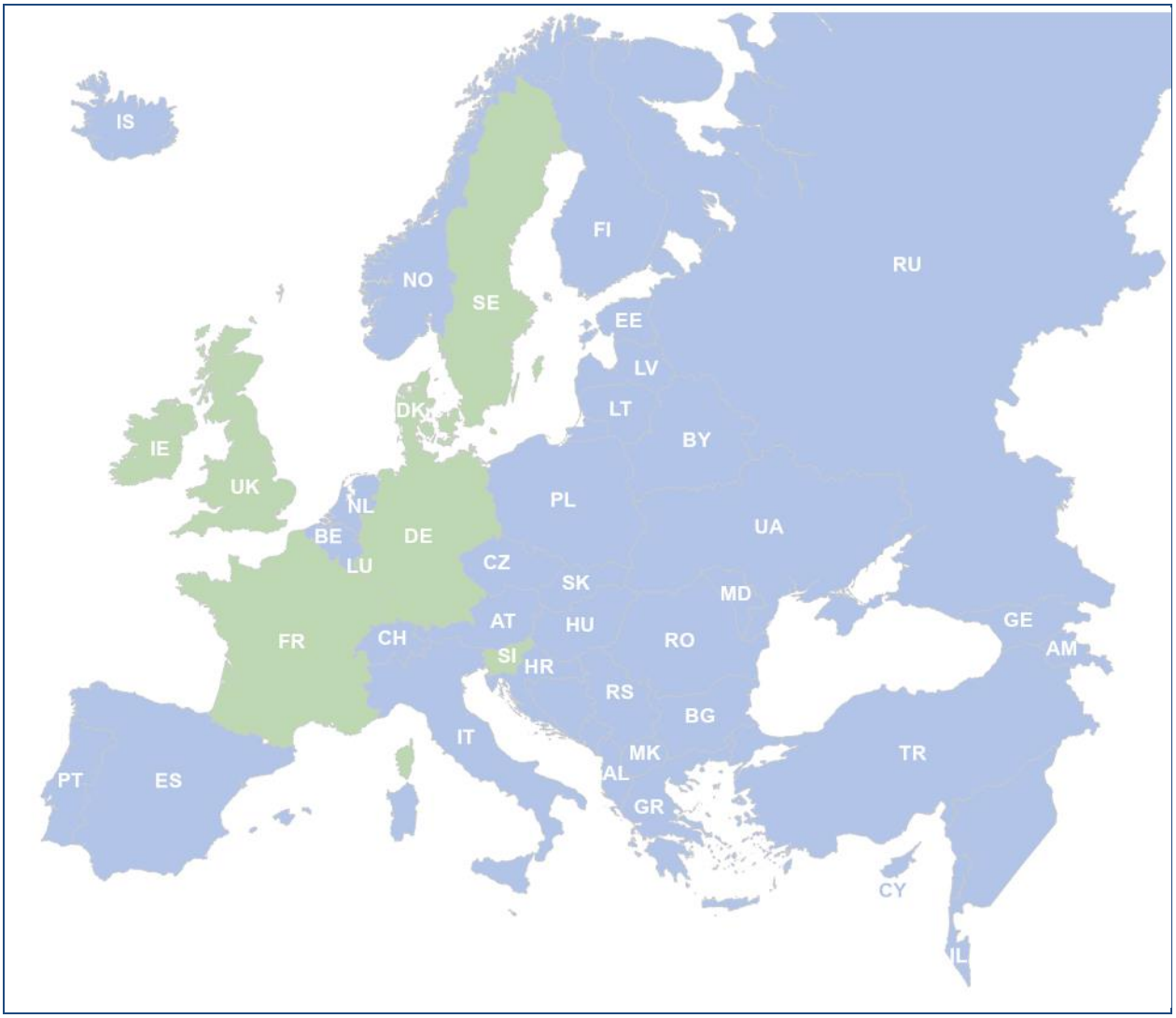
In countries where the therapy is licensed but not reimbursed, or not licensed nor reimbursed, eligible patients may sometimes have access to the therapy because of a clinical trial or a compassionate use programme.

Figure 9.7 Use of Elexacaftor/Tezaftor/Ivacaftor in all eligible patients seen in 2020 who had never had a transplant, by country and age group.



Note: We excluded from the graph the countries for which the information on Elexacaftor/Tezacaftor/Ivacaftor use is missing for more than 10% of the patients.

Figure 9.8 Countries where Elexacaftor/Tezacaftor/Ivacaftor is reimbursed in year 2020.



Note: France and Sweden: the therapy is available in compassionate use only.

In this graph we highlighted the countries where Elexacaftor/Tezacaftor/Ivacaftor was licensed and reimbursed in 2020.

10. Transplantation

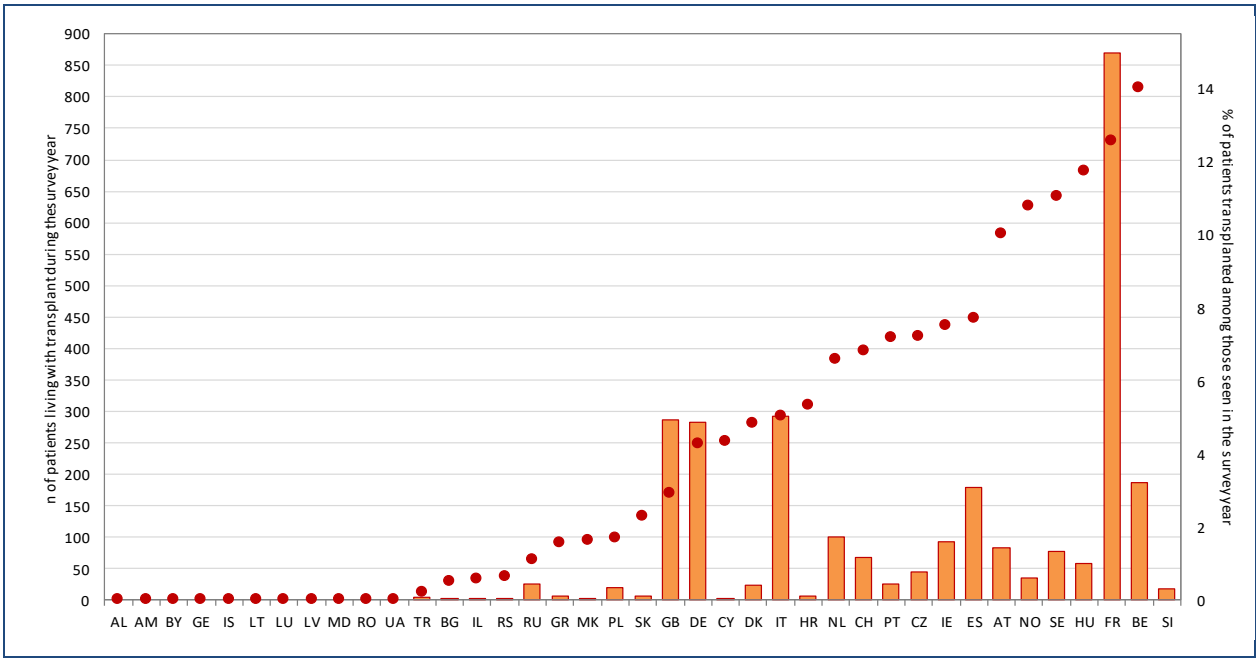
We ask the countries whether their patients are transplanted or not (lung, liver, other transplant), and if they are, in which year they had their (latest) transplant. In some countries transplanted patients are no longer registered in the database of the CF centres or the national CF registry because the patients have been transferred to a transplant centre. For this reason, the figures below may report a lower number of transplanted patients than the true number, but it has not been possible to acquire more accurate data.

Table 10.1 Number of patients living in 2020 with transplanted lung(s), by age and sex.

Age	Males	Females	Total	Transplants carried out in 2020
5-9	1	2	3	0
10-14	3	9	12	5
15-19	31	47	78	8
20-24	74	127	201	19
25-29	171	208	379	12
30-34	243	272	515	22
35-39	297	267	564	20
40-44	217	227	444	10
45+	336	267	603	9
Total	1373	1426	2799	105

This table shows the number of patients alive in 2020 who have had one or more lung transplant(s) at some time in their life, by age group, as well as the number of patients transplanted during 2020.

Figure 10.1 Number of patients living in 2020 with transplanted lungs, by country.



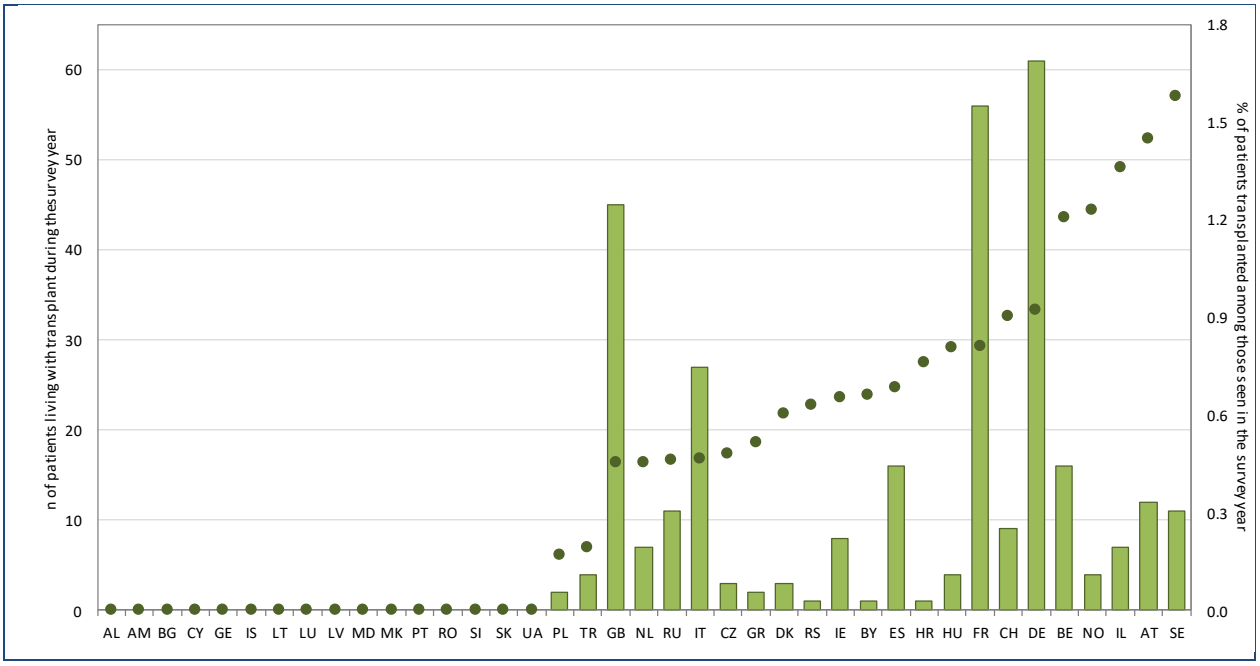
This graph shows the number of patients alive at 31/12/2020 who have had one or more lung(s) transplant (orange bars) at some point in their life. The red dots (right axis) show the percentage of patients that are living with transplant lungs in 2020 among the patients that were seen in 2020.

Table 10.2 Number of patients living in 2020 with transplanted liver, by age and sex.

Age	Males	Females	Total	Transplants carried out In 2020
0-4	2	0	2	1
5-9	3	0	3	1
10-14	10	4	14	3
15-19	31	18	49	3
20-24	34	18	52	2
25-29	32	16	48	1
30-34	40	22	62	2
35-39	26	9	35	1
40-44	15	8	23	0
45+	16	7	23	0
Total	209	102	311	14

This table shows the number of patients alive in 2020 who have had a liver transplant at some time in their life, by age group, as well as the number of patients transplanted during 2020.

Figure 10.2 Number of patients living in 2020 with transplanted liver, by country.



This graph shows the number of patients alive at 31/12/2020 who have had a liver transplant (green bars) at some point in their life. The dark green dots (right axis) show the percentage of patients that are living with transplanted liver in 2020 among the patients that were seen in 2020. Note that on the vertical axis the number of patients who had a liver transplant is much lower than the number who had a lung transplant. The main reason for this is that liver disease is only found in a subset of CF patients, whereas lung disease affects almost all patients.

Table 10.3 Number of patients living in 2020 with transplanted kidney, by age and sex.

Age	Males	Females	Total	Kidney transplants carried out in 2020
5-9	1	0	1	0
10-14	1	0	1	0
15-19	1	0	1	0
20-24	1	0	1	0
25-29	4	5	9	2
30-34	8	15	23	3
35-39	15	16	31	1
40-44	21	18	39	2
45+	25	21	46	2
Total	77	75	152	10

Note: Hungary does not collect information on kidney transplant.

This table shows the number of patients alive in 2020 who have had a kidney transplant at some time in their life, by age group, as well as the number of patients transplanted during 2020.

Table 10.4 Number of patients living in 2020 with other transplanted organs (not lung, liver, kidney), by age and sex.

Age	Males	Females	Total	Other Transplants carried out in 2020
0-4	0	1	1	0
10-14	0	2	2	0
15-19	0	1	1	0
20-24	4	2	6	0
25-29	6	6	12	2
30-34	3	5	8	0
35-39	6	3	9	0
40-44	7	7	14	1
45+	9	7	16	0
Total	35	34	69	3

Note: Hungary and Sweden do not collect information on other organ transplant.

This table shows the number of patients alive in 2020 who have had an organ transplant different from lung, liver or kidney at some time in their life, by age group, as well as the number of patients transplanted during 2020.

11. Mortality

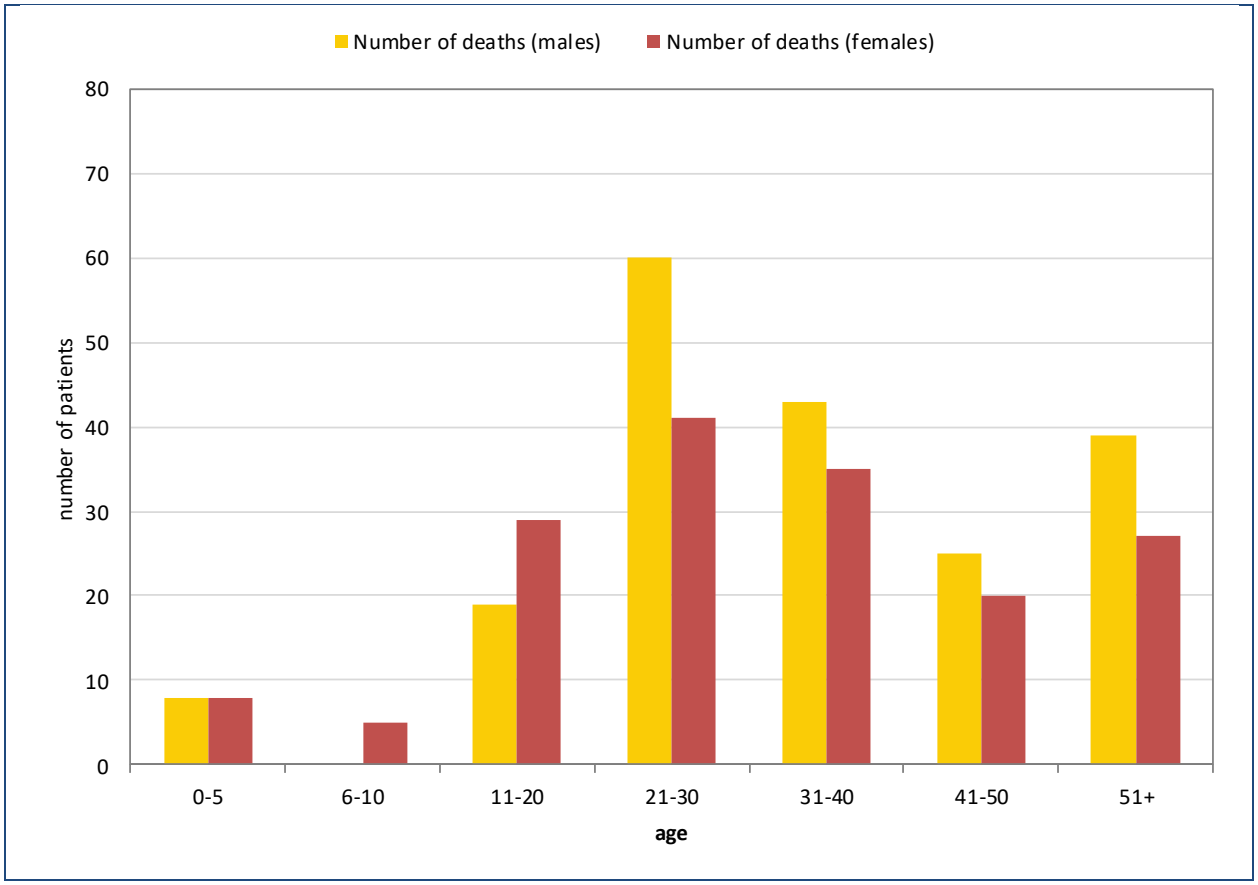
Table 11.1 Number of deaths in 2020, by age and sex.

Age at death	Number of male patients	% of deaths in this age group (of all male deaths)	Number of female patients	% of deaths in this age group (of all female deaths)	Total	% Total
0-5	8	4.12	8	4.85	16	4.46
6-10	0	0.00	5	3.03	5	1.39
11-20	19	9.79	29	17.58	48	13.37
21-30	60	30.93	41	24.85	101	28.14
31-40	43	22.17	35	21.21	78	21.73
41-50	25	12.89	20	12.12	45	12.53
51+	39	20.10	27	16.36	66	18.38
Total	194	100	165	100	359	100

Note: For the United Kingdom, all patients with a confirmed diagnosis of CF were included (N=10,837). The total number of patients presented is 50,026.

This table shows the number of deaths in 2020 by age group and sex. Death in small children is very rare, and the most frequent range of age at death for both sexes is 21-30 years. It is possible that the number of deceased patients is under reported because some of the patients were not seen at the centre during the year, and therefore the information may not have been recorded.

Figure 11.1 Age at death distribution of patients deceased in 2020, by sex.



This graph shows the distribution of age at death of patients who died in 2020, separately by males (yellow) and females (red).

Table 11.2 Cause of death distribution of deaths in 2020.

Cause of death	Number of deaths	Percentage of all deaths
Respiratory	204	56.82
Transplantation	44	12.26
Cancer	25	6.96
Other CF related	24	6.69
Unknown	23	6.41
Non-CF related	22	6.13
Liver-GI	14	3.90
Suicide	2	0.56
Trauma	1	0.28
Total	359	100.00

Note: For the United Kingdom, all patients with a confirmed diagnosis of CF were included (N=10,837). The total number of patients presented is 50,026.
Note: Germany and the United Kingdom record Cause of death as “cardio/respiratory”.
Note: The Netherlands does not record “Cancer” and “Other-CF related” as cause of death.

The table shows cause of death for the deceased patients. The most frequent cause of death is respiratory disease.

Data Quality

For the first time in the ECFSPR Annual Data Report, we present an overview of the activities undertaken by the Registry to ensure that the approved data used in reports and studies are of the highest possible quality.

Data quality measures deployed by the ECFSPR

Quality has always been at the centre of our activities. The following measures are all taken to demonstrate our ongoing commitment to quality, and support the contributing centres and national registries:

Clear guidance documentation including variable descriptions, parameters options and references ; training (live, recorded webinars) and expert help provided by the ECFSPR Service Desk; a secure, custom built data collection platform that highlights errors and inconsistencies from data input/upload, additional rigorous checks applied by the statisticians, and final data approval by the Registry Director and by the country representative.

To enhance and complete existing efforts, we launched a new initiative in 2018, whereby members of the ECFSPR staff visit participant centres to verify and validate data at source.

Why do we need to validate source data?

The availability of verified, high-quality data from consenting people with CF is essential for the ECFSPR to pursue and fulfil its aims. Registry data are used to improve and promote better understanding of many aspects of CF, they are employed in pharmacovigilance and other research studies, and also as an instrument to monitor and review a range of patient outcomes. It is vital that the data is of the highest quality possible. The ECFSPR on-site validation visits not only provide an overview of the health of the source data, they offer a valuable opportunity for the Registry and its participants to collaborate on ways to improve quality, relevance and reliability in the ECFSPR data.

The aims of the on-site validation visits

The aims of the on-site validation visits are i) to quantify data completeness, consistency and the accuracy of data-input at source level; ii) to verify, in accordance with current local and European legislation, that the centre obtained the informed consent of the patient to include his/her data in the Registry. “Consistency” means: adherence by the centre to the variable definitions, options, and parameters used by the Registry. “Accuracy” of data-input is defined as the proportion of values recorded in the ECFSPR software that match the medical records.

Under the programme, from all of the countries that submit data to the ECFSPR, 20% per year are to be visited, with a maximum of 5 countries per year. In a selected country, the aim is to visit at least 10% of the centres and visits are limited to centres with ≥50 patients. In each centre, a subset of variables is checked for 15-20% of the total number of patients in a given follow-up year (the most recent data approved by the ECFSPR).

What data is checked?

The variables to be checked are the same for each centre and they were chosen because they satisfied one or both of the following criteria: they are more challenging to collect and/or more open to misinterpretation or misrepresentation (based on ECFSPR experience and participant feedback); they are significant because they are used in reported Registry outcomes. They cover demographics, diagnosis, transplantation, anthropometric and lung function measurements, bacterial infections, selected

medications and defined complications. In the tables in this section, you can see the variables in the subset, together with the results for completeness and accuracy per country.

Results of the validation visits

We present a synopsis of the overall quality of the ECFPSR data based on the above-mentioned factors, completeness and accuracy. In this report overall results are shown to highlight and areas of improvement are highlighted. In the coming years we intend to further increase the amount of information and to present it into more detail.

Completeness

We calculated the percentage completeness of data, for a subset of variables for the year 2020, for all countries participating in the Registry, and the overall result is presented in Table 12.1.

Table 12.1 Data completeness in follow-up year 2020, overall results by variable.

DNA test	Liver/ lung transplantation	Height	Weight	FEV1 %pp	Chron. Pseudomonas aeruginosa	Chron. Burkholderia cepacia
99	100	96	96	92	97	97

Inhal. antibiotics	Pancreatic enzymes	rhDNase	Diabetes mellitus	Liver disease	Haemoptysis	Completeness of 2020 data by country
98	99	98	98	97	96	97

>95% 90-95% <90%

Note: FEV1%pred. is the best FEV1%predicted measurement from the year of follow-up.

Note: Completeness of 2020 data from all countries of the ECFSPR is represented as follows: Blue: > 95%; Grey: 90% - 95%; Red: < 90%.

Table 12.1 displays data completeness for 2020, by variable, for all countries participating in the ECFSPR. The countries are sorted by cohort size. The three colours used indicate, as a percentage range, how complete a particular variable was for a country, in the data that had been submitted to the Registry. Exact percentages are also displayed. Blue is used for all variables that were more than 95% complete. Note that transplant data is at 100% for all countries and genotyping is at more than 95%. Grey represents completion up to 95%; chronic infection falls into this category for some countries. For some variables, in some countries, completion rates were lower: lung function measurement (FEV1), and the associated weight and height measurements, were below 90% completeness, as can be seen in light red. The COVID-19 pandemic affected data completeness in 2020 and had a significant impact on CF care, but despite these challenges, centres and countries still managed to send their annual clinical data to the Registry.

Accuracy

The ECFSPR visited 10 countries up to the beginning of 2020: Austria, Greece, Latvia, Poland, Portugal, Serbia, Slovakia, Slovenia, Spain, and Switzerland. When borders opened again in 2022, Austria, Denmark, Norway, Slovenia, and Sweden were visited. Each time, a list of patients was randomly generated by the ECFSPR statistician for checking on-site. 50% of the selected patients were aged 18 or older, 40% of patients were aged 6-17 years and 10% were younger than 6. As mentioned previously, source data was checked only for a selection of variables. The exactness of the values and thereby data consistency was determined by comparing the ECFSPR data and the data in the patient medical record at source. The number of validated annual patient data were taken into account for the number of patients checked for the corresponding year.

The accuracy results of the validated data from onsite visits for the follow-up years 2016, 2017 and 2020, are presented here as percentages.

Table 12.2 Data accuracy for the follow-up years 2016, 2017 and 2020 from countries visited, overall results by variable.

DNA test	Liver/lung transplantation	Height	Weight	FEV1%pp	Chron. Pseudomonas aeruginosa	Chron. Burkholderia cepacia
81	99	91	89	86	95	97

Inhaled antibiotics	Pancreatic enzymes	rhDNase	Diabetes mellitus	Liver disease	Haemoptysis	Accuracy of 2016, 2017, 2020 data
95	98	96	97	92	96	93

>95% 90-95% <90%

Note: Accuracy of 2016, 2017 and 2020 data from all countries of the ECFSPR is represented as follows: Blue: > 95%; Grey: 90% - 95%; Red: < 90%.

Note: data of 993 patients were checked during the visits between 2018, 2019, 2020 and 2022, representing 2% of the total number of patients seen in year 2020.

Note: FEV1%pred. is the best FEV1%predicted measurement from the year of follow-up.

Data accuracy is directly influenced by the availability, at the centres, of the original patient medical records and by local interpretation and understanding of the ECFSPR variable definitions. Variables such as genotype, height, weight and FEV1 measurements, and liver disease, are more challenging for data providers than are other variables collected by the ECFSPR. The accuracy of the mutation data could not be verified without the original genetic report, and the percentages of DNA testing data validated as accurate varied across centres; reasons included transplantation and follow-up in another centre, patient transfer to another centre or to adult care, shared care, other cases where genotyping reports are not forwarded. However, many centres had repeated genotyping since the introduction of CFTR modulators and did have new genetic reports. Overall, the percentage of anomalies was very small (5%). The lower accuracy of lung function and liver disease data was influenced by differences in the methods used by the centre or country to collect data and/or in the interpretation of parameters. Height and weight measurement accuracy was also negatively affected if the submitted values corresponded to a FEV1 measurement which was not the highest FEV1% predicted of the year, or if it corresponded to a date other than the last height and weight measurements of the year when there was no FEV1.

Conclusion

Despite the challenges faced by the CF community in general, and particularly in 2020, the results depict a positive picture of the overall completeness of the data submitted to the ECFSPR. The on-site validation visits have allowed us to identify specific variables where accuracy is high but also where data accuracy can be improved, meaning we can focus efforts on where they will have the highest impact. Already, preliminary results from follow-up visits in 2022 indicate significant improvements in data accuracy in certain areas. Also, national registries have been encouraged to continue to apply data quality measures in their countries, and, consequently, several countries have launched national data quality activities following the ECFSPR programme.

We are confident that together with all participating centres and national registries, we are on the right path to ensuring and improving on the high quality of the Registry data.

Publications

The ECFSPR database is a useful source for research and the data is actively used. Applications for data are conscientiously handled in accordance with the ECFSPR guidelines. More information on the data application process you will find on the website www.ecfs.eu/projects/ecfs-patient-registry/data-request-application.

In the period from January 2011 to April 2022 we received 101 applications to use Registry data. The majority of these requests, 83%, originated from researchers from the European Cystic Fibrosis Society and other institutes, and 17% of the applications derived from Industry.

Several of these research projects have resulted in publications and other publications are in the pipeline. A complete overview of publications using ECFSPR data is available on www.ecfs.eu/projects/ecfs-patient-registry/articles.

Sponsors

The ECFSPR is grateful to the following organisations for the support of our work, by means of an unrestricted grant:

National Patient Organisations

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LIFC
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Fibrosi Cistica

association luxembourgeoise
de lutte contre la mucoviscidose

Schweizerische Gesellschaft
für Cystische Fibrose (CFCH)

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Appendix 1: List of contributing centres and national registries

List of individual centres and national registries that contributed to the ECFSPR. In larger print: the name of the country representative in the ECFSPR Steering Group; underlined: the name of the database manager for the national registry; in Italics: new participants with 2020 data.

Country	Centre/National Registry name	Contact
Albania	1 individual centre:	Irena Kasmi
	”Mother Thereza” Hospital Centre, Department of Paediatrics, Tirana	Irena Kasmi Evda Vevecka
Armenia	1 individual centre:	Satenik Harutyunyan
	Yerevan State Medical University, Muratsan University Hospital, Cystic Fibrosis Centre, Yerevan	Satenik Harutyunyan
Austria	14 individual centres:	Andreas Pfleger
	Medizinische Universität Graz, Universitätsklinik für Kinder- und Jugendheilkunde, Klinische Abteilung für Pädiatrische Pulmonologie und Allergologie und CF Zentrum für Kinder, Jugendliche und Erwachsene, Graz	Ernst Eber Andreas Pfleger Maria Gaber Manfred Modl Doris Malle-Scheid
	Medizinische Universität Innsbruck, Zertifiziertes CF Zentrum für Kinder, Jugendliche und Erwachsene, Innsbruck	Helmut Ellemunter Johannes Eder
	Klinikum Klagenfurt am Wörthersee, Abteilung für Kinder- und Jugendheilkunde, Pädiatrische Pulmologie/ Allergologie, Klagenfurt	Franz Hubert Wadlegger
	Kepler Universitätsklinikum, Universitätsklinik für Kinder- und Jugendheilkunde, Linz	Adrienne Molnar Julia Pichler Christina Thir
	Kepler Universitätsklinikum, Klinik für Lungenheilkunde/ Pneumologie, Linz	Martin Stadlinger Viktoria Reinelt Katrin Scheich
	Kardinal Schwarzenberg Klinikum, Abteilung für Kinder- und Jugendmedizin, Schwarzach im Pongau	Josef Riedler Christoph Seelbach
	Salzburger Landeskliniken, Universitätsklinik für Pneumologie, Salzburg	Michael Studnicka Natalie Firlei-Fleischmann
	PEK Klinikum Steyr, Abteilung für Kinder- und Jugendheilkunde und Abteilung für Lungenheilkunde, Steyr	Alexander Ebner Margit Kallinger Monika Pell
	Medizinische Universität Wien, Allgemeines Krankenhaus Wien für Thoraxchirurgie, Vienna	Peter Jaksch Dagmar Liebhart
	Medizinische Universität, Allgemeines Krankenhaus Wien, Universitätsklinik für Kinder-und Jugendheilkunde, Klinische Abteilung für Pädiatrische Pneumologie, Allergologie und Endokrinologie, Zentrum für Cystische Fibrose, Vienna	Sabine Renner Saskia Gruber Brigitte Mersi
	Klinik Ottakring, Abteilung für Kinder- und Jugendheilkunde mit Ambulanz, Vienna	Thomas Frischer Kerstin Tiringer Katharina Kainz
	Klinik Hietzing, Abteilung für Atmungs- und Lungenkrankheiten, Vienna	Andrea Lakatos–Krepcik

Country	Centre/National Registry name	Contact
	Klinikum Wels-Grieskirchen, Abteilung für Kinder- und Jugendheilkunde, Wels	Beatrix Wintersteiger Vera Karin Bauer
	Klinikum Wels-Grieskirchen, Abteilung für Lungenkrankheiten, Wels	Alexander Leitner Matthäus Ploder Thomas Tempelmayer Andrea Ringl
Belarus	1 individual centre:	Svetlana Keegan
	Belarusian Republic Children's Centre of Pulmonology and Cystic Fibrosis, Pulmonary Department, 3rd City Children's Clinical Hospital, Minsk	Vladimir Bobrovnichiy Svetlana Keegan
Belgium	Belgian Cystic Fibrosis Registry	Géraldine Daneau Simeon Wanyama
Bulgaria	2 individual centres:	Guergana Petrova
	Alexandrovska University Hospital, Pediatric Clinic, Sofia	Guergana Petrova
	University Hospital St. Marina, 2nd Paediatric Clinic, Varna	Miglena Georgieva Nataliya Dobrudzhanska Margarita Nikolova Ruzha Pancheva
Croatia	1 individual centre:	Duska Tjesic-Drinkovic Andrea Vukić Dugac
	University Hospital Centre Zagreb, Cystic Fibrosis Centre – Paediatrics and Adults, Zagreb	Duska Tjesić-Drinković Dorian Tjesić-Drinković Andrea Vukic Dugac
	On behalf of the Croatian CF Patient Database	Ivan Bambir Ivona Markelic
Cyprus	1 individual centre:	Panayiotis Yiallouros
	Medical School, University of Cyprus, children and adults	Panayiotis Yiallouros Andreas Matthaiou Panayiotis Kouis Pinelopi Anagnostopoulou
Czech Republic	Cystic Fibrosis Registry of the Czech Republic	Pavel Drevinek Alena Bilkova Milan Macek Marek Turnovec
Denmark	Cystic Fibrosis Registry Denmark	Hanne Vebert Olesen Tania Pressler
France	Registre Français de la Mucoviscidose	Lydie Lemonnier Clémence Dehillotte
Germany	German Cystic Fibrosis Registry	Lutz Naehrlich Julia Wosniok
Greece	2 individual centres:	Elpis Hatziagorou
	Sismanoglio General Hospital of Attica, Adult Cystic Fibrosis Unit, Athens	Filia Diamantea Margarita Gkotsina
	Aristotle University of Thessaloniki, Cystic Fibrosis Centre, Thessaloniki	John Tsanakas Elpis Hatziagorou Aikaterini Manika Maria Sionidou Maria Fotoulaki

Country	Centre/National Registry name	Contact
Georgia	1 individual centre:	Ia Khurtsilava
	I. Tsitsishvili Children's Clinic, CF Centre, Tblisi	Ia Khurtsilava Tsitsino Parulava
Hungary	Cystic Fibrosis Registry of Hungary	Andrea Párniczky Géza Marsal
Iceland	*1 individual centre:*	*Helga Elidottir*
	Children´s Medical Center Landspitali – The National University Hospital of Iceland, Reykjavik, Iceland	*Helga Elidottir*
Ireland	Cystic Fibrosis Registry of Ireland	Godfrey Fletcher Laura Kirwan
Israel	6 individual centres:	Meir Mei-Zahav
	Soroka Medical Centre, Ben Gurion University, Beer Sheva	Micha Aviram
	Carmel Medical Centre, Haifa	Galit Livnat
	Ruth Rappaport Children's Hospital, Rambam Medical Centre, Haifa	Michal Gur
	Hadassah Medical Centre, Mount Scopus, Jerusalem	Malena Cohen-Cymberknoh
	Schneider Children's Medical Centre of Israel, Petach Tikvah	Meir Mei-Zahav
	Safra Children's Hospital, Sheba Medical Centre, Ramat Gan	Ori Efrati
Italy	Italian Cystic Fibrosis Registry	Rita Padoan Marco Salvatore Annalisa Amato Gianluca Ferrari
Latvia	1 individual centre:	Elina Aleksejeva
	Rīga Stradinš University, Children's Clinical University Hospital, Department of Pneumology, Riga	Elina Aleksejeva Dita Gaidule-Logina
Lithuania	2 individual centres:	Kęstutis Malakauskas
	Hospital of Lithuanian University of Health Sciences Kauno Klinikos, Adult Cystic Fibrosis Centre, Kaunas	Kęstutis Malakauskas Virginija Kalinauskaitė - Žukauskė
	Hospitalof Lithuanian University of Health Sciences Kauno Klinikos, Centre of Pediatric Chronic Respiratory Diseases, Kaunas	Valdone Misevičiene
Luxembourg	1 individual centre:	Anna-Maria Charatsi
	Centre Hospitalier de Luxembourg	Romain Nati Anna-Maria Charatsi Meriem Mastouri Flore Nzuangue
Rep. of North Macedonia	2 individual centres:	Stojka Fustik, Tatjana Jakovska-Maretti
	Institute for respiratory diseases in children Kozle, Centre for cystic fibrosis, Children and adults, Kozle	Tatjana Jakovska-Maretti Ivana Arnaudova Danevska
	University Children's Hospital, Centre for Cystic Fibrosis, Skopje	Stojka Fustik Ana Stamatova

Country	Centre/National Registry name	Contact
Rep. of Moldova	Outpatient Centre for Cystic Fibrosis and Other Rare Diseases	Oxana Turcu
Netherlands	Dutch Cystic Fibrosis Registry	Vincent Gulmans Domenique Zomer
Norway	Norwegian Cystic Fibrosis Patient Registry	Egil Bakkeheim Anita Senstad Wathne
Poland	13 individual centres:	Łukasz Woźniacki
	Voivodeship Children's Hospital, Dept. of Paediatric Pneumology and Allergology, Bydgoszcz	Radoslawa Staszak – Kowalska Mikolaj Kowalski
	Cystic Fibrosis Centre, Polanki Paediatric Hospital, Gdansk	Maria Trawinska-Bartnicka Ewa Sapiejka
	Centrum Medyczne Karpacz, Children/Adults' Hospital, Karpacz	Grzegorz Gaszczyk Monika Rams
	John Paul II Upper Silesian Child Health Centre, The independent Public Clinical Hospital no 6 of the Medical University of Silesian in Katowice, Katowice	Urszula Grzybowska-Chlebowczyk Bozena Kordys-Darmolinska
	St. Louis Regional Specialised Children's Hospital, Krakow	Stanislaw Stepniewski Daria Dziecichowicz-Latala
	Wojewódzkie Wielospecjalistyczne centrum Onkologii i Traumatologii im. M. Kopernika w Lodzi, Ośrodek Pediatryczny im. J. Korczak, Lodz	Iwona Stelmach Agnieszka Koniarek-Maniecka
	University Hospital of Lords Transfiguration, Dept. of Pulmonology, Allergology and Pulmonary Oncology, Poznan	Szczepan Cofta Agata Nowicka
	Karol Jonscher University Hospital of Poznan University of Medical Sciences, Poznan	Irena Wojsyk-Banaszak
	Institute of Tuberculosis and Lung Diseases, Rabka-Zdrój Branch, Dept. of Pneumology and Cystic Fibrosis, Rabka Zdroj	Henryk Mazurek Lidia Pawlik
	Provincial Clinical Hospital no. 2, Dept of Allergology and Cystic Fibrosis, St Jadwigi Krolowej in Rzeszow	Marta Rachel
	Szczecin Hospital "Zdroje" Dep. Of Pediatrics, Allergology and Pulmonology	Pawel Gonerko Pawel Fabisiak
	Dziekanow Paediatric Hospital, Cystic Fibrosis Centre, Institute of Mother and Child, Warsaw	Dorota Sands Łukasz Woźniacki
	Institute of Tuberculosis and Lung Diseases, Adult CF Centre, Warsaw	*Wojciech Skorupa* *Sylwia Ziernik*
Portugal	Cystic Fibrosis Registry of Portugal	Luísa Pereira
Romania	7 individual centres:	Liviu Pop
	Regional Cystic Fibrosis Centre, Clinical Emergency Children's Hospital of Brasov, Brasov	Laura Larisa Dracea
	Children Emergency Hospital "Maria S. Curie", Bucharest	Maria Brustan
	Clinical Children's Hospital Grigore Alexandrescu, Bucharest	Simona Mosescu
	Mother & Child Health Institute, Bucharest	Iustina Stan
	Regional Cystic Fibrosis Centre Cluj, Emergency Clinical Children's Hospital of Cluj-Napoca, Cluj-Napoca	Radu Sorin Șerban Szabo Csilla-Enikő

Country	Centre/National Registry name	Contact
	"Sf. Maria" Children Emergency Hospital Iasi, Iasi	Dana-Teodora Anton-Paduraru
	National Cystic Fibrosis Centre, Timişoara	Liviu Pop Ioana Ciuca
Russian Federation	Cystic Fibrosis Registry of the Russian Federation	Elena Kondratyeva Elena Amelina Marina Starinova Stanislav Krasovskiy Anna Voronkova Nataliya Kashirskaya
Serbia	1 individual centre:	Milan Rodic
	National Centre for Cystic Fibrosis, Mother and Child Health Institute of Serbia "Dr Vukan Čupić", Belgrade	Predrag Minić Milan Rodić Aleksandar Sovtić
Slovakia	6 individual centres:	Hana Kayserova
	Childrens CF Centre, DFN Banská Bystrica, Banská Bystrica	Branko Takáč
	Centrum cystickej fibrozy pre dospelych FNSP FDR, Banská Bystrica	Eva Bérešova
	Centrum cystickej fibrozy pre dospelych, Klinika pneumologie l.SZU a Univerzitna nemocnica, Bratislava	Marta Hajkova
	Klinika detskej pneumologie SZU UN Bratislava, pracovisko Podunajské Biskupice, Bratislava	Hana Kayserova Nina Bližňáková
	CF Adult centre, University Hospital L Pasteura, Košice	Lenka Kopčová
	Centrum cystickej fibrozy detí, Detská fakultná nemocnica Košice, Košice	Anna Fetekeova Zuzana Hribíková
Slovenia	3 individual centres:	Uroš Krivec
	University Clinic of Pulmonary and Allergic Diseases, Golnik	Matjaž Fležar Julij Šelb Urška Hribar
	University Medical Centre Ljubljana, Department of Pulmonology and Allergy, Ljubljana	Izidor Kos Barbara Salobir
	University Medical Centre Ljubljana, University Children`s Hospital, Unit for pulmonary diseases, Ljubljana	Uroš Krivec Jasna Rodman Berlot Majda Oštir
Spain	26 individual centres:	Mª Dolores Pastor Vivero
	Parc Taulí Hospital Universitario, Hospital de Sabadell, Unitat de Pneumologia Pediátrica i Unitat de Fibrosi Quística, Sabadell, Barcelona	Oscar Asensio de la Cruz Miguel Garcia Gonzàlez Xavier Pomares Amigó Concepción Montón Soler
	Hospital Sant Joan de Déu, Unitat de Pneumologia Pediàtrica i Fibrosi Quística, Barcelona	Maria Cols i Roig Jordi Costa i Colomer
	Hospital Universitari Vall d'Hebron, Unidad de Fibrosis Quística del Adulto, Barcelona	Antonio Alvarez Fernández
	Hospital Universitari Vall d'Hebron, Unidad Fibrosis Quística y Neumología Pediátrica, Barcelona	Silvia Gartner

Country	Centre/National Registry name	Contact
	Hospital Universitario Cruces, Unidad de Fibrosis Quística, Bizkaia	Mª Dolores Pastor Vivero Ainhoa Gómez Bonilla Beatriz Gómez Crespo Estibaliz Catediano Sainz
	Hospital Universitario Reina Sofia, Dpto. Especialidades Médico-quirúrgicas, Área de Pediatría, Unidad de Alergia y Neumología Pediátricas, Unidad de Gestión Clínica de Pediatría y sus Especialidades, Cordoba	Javier Torres Borrego Noelia Sancho Montero
	Complejo Hospitalario Universitario Insular Materno Infantil, Las Palmas de Gran Canaria	Antonio José Aguilar Fernández
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Sweden	Cystic Fibrosis Registry of Sweden	Isabelle de Monestrol Anders Lindblad
Switzerland	20 individual centres:	Andreas Jung
	Kinderspital Aarau, Kantonsspital Aarau AG, Abteilung pädiatrische Pneumologie, Allergologie und Immunologie, Aarau	Dominik Müller-Suter Peter Eng Rachel Kusche
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	UKBB Universitäts-Kinderspital beider Basel, Abteilung Intensivmedizin & Pneumologie, Basel	Jürg Hammer Daniel Trachsel Anja Jochmann Diana Reppucci
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	Lindenhofspital Quartier Bleu, Bern	Reta Fischer Iris Schmid Bernhard Schwizer Patrizia Bevilacqua
	Universitätsklinik für Kinderheilkunde, Zentrum für Cystische Fibrose und Pulmonologie, Inselspital, Bern	Philipp Latzin Romy Rodriguez Florian Singer
	Hôpital Cantonal Fribourg, Pädiatrie, Fribourg	Denise Herzog Maxime Hensen Johannes Wildhaber
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Country	Centre/National Registry name	Contact
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	Luzerner Kantonsspital, Abteilung für Pneumologie, Luzern	Christian Murer Natascha Sidler
	Hôpital Neuchâtelois – Pourtales, Consultation de Mucoviscidose Adulte, Neuchâtel	Alain Sauty Jean Marc Fellrath Marie Hofer
	Children's Hospital of Eastern Switzerland, Division of Paediatric Pulmonology & CF Centre, St Gallen	Jürg Barben Christine Baumgartner
	Kantonsspital St. Gallen, Lungenzentrum, Zentrum für Cystische Fibrose für Erwachsene, St. Gallen	Martin Brutsche Otto Schoch Anna-Lena Walter Rebekka Kleiner
	Kantonsspital Winterthur, Klinik für Pneumologie und Klinik für Innere Medizin, Adulte Cystische Fibrose, Winterthur	Markus Hofer Sieghart Filippi
	Universitäts-Kinderspital Zürich, Abteilung für Pneumologie, Zürich	Andreas Jung Alexander Möller Demet Inci Eugènie Collaud
	Universitätsspital Zürich, Klinik für Pneumologie, Adultes CF Zentrum, Zürich	Macé Schuurmans Thomas Kurowski
Turkey	Cystic Fibrosis Registry of Turkey	Deniz Dogru
	Marmara University Faculty of Medicine, Division of Pediatric Pulmonology, Istanbul	Bülent Karadağ Yasemin Gökdemir Ela Erdem Eralp
	Medipol University Faculty of Medicine, Division of Pediatric Pulmonology, Istanbul	Sedat Öktem Füsun Ünal
	Medeniyet University, Faculty of Medicine, Division of Pediatric Pulmonology, Istanbul	Saniye Girit Yetkin Ayhan
Ukraine	2 individual centres:	Halyna Makukh
	Ivano-Frankivsk Regional Children's Clinical Hospital of Ivano-Frankivsk Regional Council, Department of Pulmonology, Ivano-Frankivsk	*Sirun Makian* *Olha Fedynska*
	Cystic Fibrosis Centre of Western Ukrainian Specialized Children's Medical Centre, Lviv	Lyudmyla Bober Halyna Makukh
United Kingdom	UK Cystic Fibrosis Registry	Rebecca Cosgriff Susan Charman Elaine Gunn Siobhán Carr Sarah Clarke

Appendix 2: Inclusion criteria and technical notes

Patient inclusion criteria

The ECFSPR registers patients diagnosed with CF in accordance with agreed definitions:

1. **Two sweat tests value > 59 mmol/L chloride**: CF diagnosis accepted.
2. **One sweat test value > 59 mmol/L chloride and DNA Analysis/Genotyping – two identified disease-causing CF mutations**: CF diagnosis accepted.
3. **Sweat value ≤ 59 mmol/L chloride**:
   If the sweat value is less than or equal to 59 mmol/L chloride or not reported, then at least 2 of these must be fulfilled:
   a. DNA Analysis/Genotyping: two identified disease-causing CF mutations;
   b. Transepithelial (Nasal) Potential Difference or Intestinal current measurement: result consistent with a diagnosis of CF;
   c. Clinical Presentation: typical features of CF.
4. **Diagnosis reversal**:
   If the patient's CF diagnosis was reversed during the year, must be due to one of the options listed:
   a. DNA Analysis: unable to identify two disease causing CF mutations;
   b. Transepithelial (Nasal) Potential Difference and/or Intestinal current measurement: result not consistent with a diagnosis of CF;
   c. Repeated normal values from sweat tests and confirmed by the clinical team.

Data of patients without a CF diagnosis according to the agreed definitions are accepted in the database but not included in the analyses.

Data manipulation

To ensure that data was anonymous, we collected only year and month of birth and the day of birth was set to the 15th of the month.
For prenatal diagnoses, we set age at diagnosis equal to 0.
We checked for outliers and, whenever possible, we corrected the values according to the instructions of the national registries / individual centres. If, after the data quality controls, aberrant values were still present in the database, we set them to missing.

Software used for data management and statistical analyses

SAS software, Version 9.4. Copyright, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

Explanation of statistical terms

Max: maximum. It is the highest value.

Mean: it is the average value of a set of measurements. For example, if the mean age at diagnosis is 3 years, it means that, on average, the patients are diagnosed when they are 3 years old.

Median: the value that separates the set of measurements in two halves, so that 50% of measurements are below the median value and the other 50% of measurements are above the median value. For example, if median age at diagnosis is 5 months, it means that half of the patients are diagnosed before 5 months of age, and the other half of the patients are diagnosed after 5 months of age.

Min: minimum. It is the lowest value.

N: the number of patients in a group for whom the information is not missing.

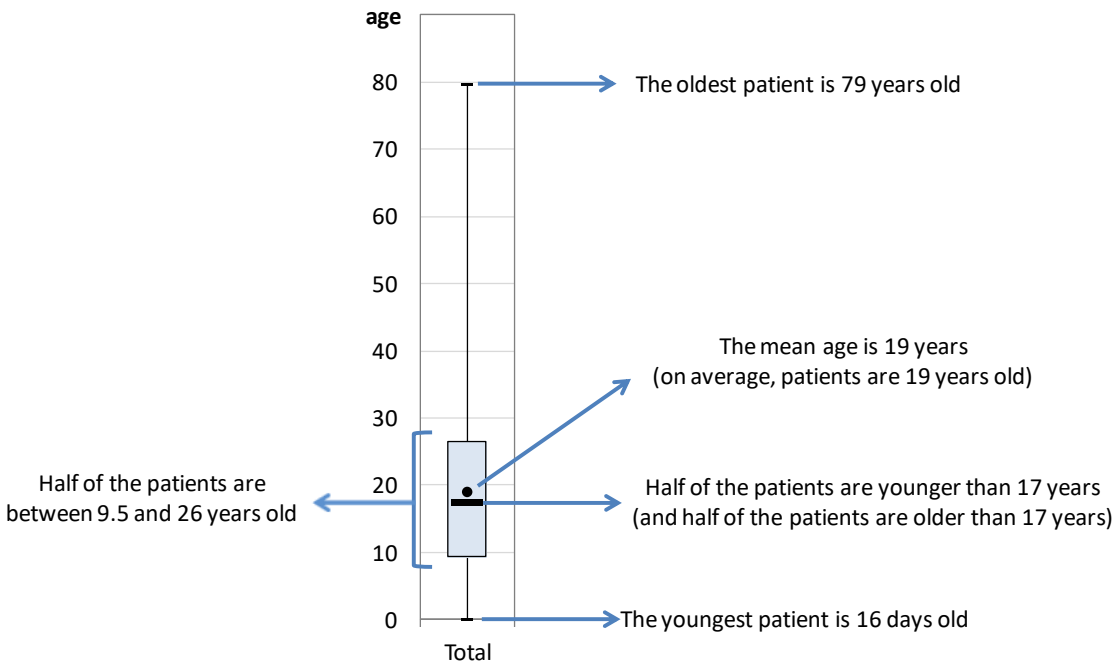
N miss: number of missing values. It is the number of patients for whom the information is missing.

Quartiles: The 25th percentile, the median (the 50th percentile) and the 75th percentile are collectively called quartiles, because they divide the set of measurements into quarters.

25th Pctl: 25th percentile, also called first quartile. It is the value that separates the set of measurements in two parts, so that one quarter (25%) of the measurements is below it and the other three quarters are above it. For example, if the 25th percentile for age at diagnosis is 1 month, it means that a quarter of the patients were diagnosed before they were a month old, and the other three quarters were diagnosed after they were a month old.

50th Pctl: 50th percentile, also called second quartile or median (please refer to definition of Median).

75th Pctl: 75th percentile, also called third quartile. It is the value that separates the set of measurements in two parts, so that three quarters (75%) are below it and the other quarter is above it. For example, if the 75th percentile for age at diagnosis is 3 years, it means that three quarters of the patients are diagnosed before they were 3 years old, and the remaining quarter was diagnosed after they reached 3 years of age.



Note: This is an example of how to read a boxplot. The numbers used in this figure are not real.

Appendix 3: List of variables and definitions used by the ECFSPR

Variables

Demographics

CF centre code
Patient code
Year of follow-up
Date of birth (year and month)
Gender
Status of patient
Cause of death
Date of death

Diagnosis

Diagnosis status
Age at diagnosis
Sweat test type and value
Electrolytes
Chloride value
Meconium Ileus
Nasal Potential Difference (NPD)
CF-typical NPD
Date of NPD
Intestinal current measurement (ICM)
CF-typical ICM
Date of ICM
Neonatal screening

Genotype

First mutation
Second mutation

Therapy

Inhaled continuous hypertonic NaCl ≥3% this year
Inhaled continuous Mannitol this year
Inhaled continuous antibiotic this year
Inhaled continuous bronchodilators this year
Oxygen therapy ≥ 3 months during the year
Use of continuous Non-invasive positive pressure ventilation (NIPPV) this year
Use of continuous rhDNase this year
Use of continuous Inhaled steroids this year
Use of continuous Oral steroids this year
Use of continuous azithromycin (or other macrolide) this year
Use of continuous ursodeoxycholic acid this year
Use of continuous pancreatic enzymes this year
Use of continuous proton pump inhibitors (PPI)
Use of CFTR Modifier Therapy
Start and stop dates CFTR Modulator Therapy (start date & stop date x 2 per kind of modulator)
Sweat chloride values (before CFTR modulator and during CFTR modulator)

Complications

Allergic broncho-pulmonary aspergillosis this year
Diabetes treated this year
Pneumothorax this year
Distal intestinal obstruction syndrome (DIOS)
Salt depletion this year
Liver disease this year
Haemoptysis major (volume of expectorate ≥250ml in a day)
Pancreatic status: faecal fat
Occurrence of malignancy this year

Microbiology

(positive, chronic / positive, not chronic)

Pseudomonas aeruginosa
Staphylococcus aureus
Burkholderia cepacia complex
Stenotrophomonas maltophilia this year
Nontuberculous mycobacteria this year
Achromobacter spp this year
Haemophilus influenza this year
MRSA this year
Total days on iv antibiotics at home and in hospital this year
Total days on iv antibiotics in hospital this year
Total days in hospital this year

Follow-up

Date of best FEV_{1*} recorded this year
Value of best FEV_{1**} recorded this year
Value of best FVC recorded this year
Date of lowest LCI 2.5% this year
Value of lowest LCI 2.5% this year
Type of device
Height measured at date of best FEV_1 (or in case of no FEV_1 last height of the year)
Weight measured at date of best FEV_1 (or in case of no FEV_1 last height of the year)

Transplant

Liver transplant
Year of latest liver transplant (before or during this year)
Lung transplant
Year of latest lung transplant (before or during this year)
Kidney transplant
Year of latest lung transplant (before or during this year)
Other transplant
Year of latest other transplant (before or during this year)

*FEV1 of highest FEV1% predicted
**FVC at time of best FEV1

Definitions used by the ECFSPR

SWEAT TEST

1. Diagnostic standards: the quantity of sweat should indicate an adequate rate of sweat production.

2. a. The sweat sample should be processed immediately after sweat test collection;
   b. Chloride concentration measurement is the preferred analysis;
   c. Chloride value: the Chloride value should be measured in millimols per litre (mmol/L); if duplicate tests were completed on the same day, report **the highest positive value**;
   d. A sweat chloride value > 59 mmol/L is consistent with a diagnosis of CF;
   e. A sweat chloride value < 30 mmol/L makes the diagnosis of CF unlikely (However, specific CF causing mutations can be associated with a sweat test value of below 30 mmol/L).

   Note: The acceptable range for Chloride values is 1-160 mmol/L. Anyone who has a Chloride value above 160 mmol/L must be re-tested.

3. The ECFSPR considers only Titration/Chloride values in the analyses.

References:

- ECFS Standards of Care Best Practices Guidelines, Smyth AR et al. J Cyst. Fibros. 13 (2014) S23-S42.
- Standards of Care for Cystic Fibrosis ten years later. Castellani C, Conway S, Smyth AR, Stern M, Elborn JS. J Cyst. Fibros. 13 (2014) S1-S2.

NUTRITION

Measurements: Weight and height should be measured in accordance with the EuroCareCF guidelines:

a. weight: removal of outer clothing, shoes and socks;
b. height: without shoes and socks; stadiometer: top of head in contact with headboard, slight pressure;
c. date: the recorded height and weight should be the measurements taken the same day as the best FEV1 (FEV1 of the highest FEV1% predicted). If spirometry was not done the last weight and height measurements of the year, and the date they were measured, should be recorded.

Reference populations used for computing z-scores

The value of a z-score depends on the anthropometric reference chart: if different reference values are used, the same value of height (or weight or BMI) will result in different values of z-scores, and these differences might be of clinical importance. In order to compare the nutritional status of CF patients with that of healthy individuals an appropriate reference population must be used: ideally, a fair comparison requires that CF patients and healthy individuals belong to the same population. This implies the availability of a national reference.

The lack of a national reference for most countries participating in the ECFSPR obliged us to use an inter-national reference to compute z-scores for height, weight and BMI. We decided to use the CDC 2000 reference charts (Kuczmarski et al, 2002), which were derived from samples of healthy individuals from the USA[1]. The choice of CDC charts as a reference, although not necessarily the most suitable to assess the nutritional status of European CF patients, is justified by the widespread use of these charts at international level.

References:

- Percentiles of body mass index in children and adolescents evaluated from different regional German studies. Kromeyer-Hauschild K, Wabitsch M, Kunze D, Geller F, Geiss HC, Hesse V et al. Monatsschr Kinderheilkd 2001; 149:807-818.
- Comparison of growth status of patients with cystic fibrosis between the United States and Canada. Lai H-C, Corey M, FitzSimmons S, Kosorok MR, Farrell M. Am J Clin Nutr 1999; 69:531-538.
- Public Use File BGS98, German National Health Interview and Examination Survey 1998, Robert-Koch-Institut, Berlin, Germany, 2000.
- Evaluation of body mass index percentiles for assessment of malnutrition in children with cystic fibrosis. Wiedemann B, Paul KD, Stern M, Wagner TO, Hirche TO, on behalf of the German CFQA Group. Eur J Clin Nutr 2007; 61, 759-768.

- 2000 CDC Growth Charts for the United States: methods and development. National Centre for Health Statistics. Kuczmarski RJ, Ogden CL, Guo SS et al. 2000. Vital Health Stat 2002; 11(246): 1-190.

[1] For details on the target population, please see www.cdc.gov/growthcharts/2000growthchart-us.pdf.

SPIROMETRY

The ECFS Patient Registry collects data on spirometry values in order to obtain standardized data for comparison with other centres/countries and for use in epidemiological studies. Some of the conditions for this (see below) may not be met at every clinical visit for all patients, and, for the ECFSPR, only spirometry tests fulfilling the criteria must be recorded by centres or extracted by the National Registries.

All spirometry tests must be carried out in accordance with the ATS/ERS guidelines: www.thoracic.org/statements/resources/pfet/PFT2.pdf.

For the spirometry values reported to the ECFSPR the following criteria must be met:

1. Pre-test:
    a. date of birth, gender and height must be recorded for calculation of predicted values;
    b. all recorded spirometry tests must be pre-bronchodilator* values
        i. short-acting bronchodilators: at least 4 hours pre-test;
        ii. long-acting bronchodilators: at least 12 hours pre-test.
2. Values to report:
    a. FEV1 value to report: value of FEV1, in litres (up to 2 decimals), of the highest FEV1% predicted of the year, in accordance with local reference values;
    b. The FEV1 and FVC measurements must be reported in litres (L), to max 2 decimal points;
    c. The FVC measurement is the FVC from the same test as the recorded FEV1 and it must be greater than or equal to the FEV1 measurement;
    d. For the reported spirometry value, the date of the test and the patient's height and weight at that date must also be recorded so that the percentage of predicted values can be calculated;
    e. Only tests deemed valid according to ATS/ERS guidelines to be reported.
3. Calculation of percent of predicted values:
    A common set of reference values is used: Global Lung Function Initiative equations described by Quanjer PH et al.

References:

- Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J 2012; 40: 1324–1343.
- Standardisation of spirometry. Miller et al. Eur Respir J 2005; 26: 319–338.
- General considerations for lung function testing. Miller et al. Eur Respir J 2005; 26: 153–161.
- Cystic Fibrosis Foundation Patient Registry User's Guide, Version 4.0. 2006.
- Task Force to Evaluate Choice of Spirometric Reference Equations for the National Patient Registry: Summary and Recommendations. Rosenfeld et al. Cystic Fibrosis Foundation Registry Committee, 2005.

CHRONIC INFECTION IN THE LOWER AIRWAYS

1. Chronic Pseudomonas aeruginosa infection:

    A patient should be considered chronically infected if the modified Leeds criteria are met (a) below, and/or anti-pseudomonas antibodies are detected (b) below.

    A patient should be defined as chronically infected if he/she fulfils the criteria now, or has done so in recent years, and the physician has no reason to think that the status has changed:

    a. Modified Leeds criteria, chronic infection: >50% of the samples (sputum/other) collected during the last 12 months should be positive; at least 4 samples collected.
    b. Significantly raised anti-pseudomonas antibodies according to local laboratories.
2. Chronic infection with other gram-negative bacteria should meet the same criteria as described above.

References:

- Evaluation of a new definition for chronic Pseudomonas aeruginosa in cystic fibrosis patients. Lee TWR, Brownlee KG, Conway SP, Denton M, Littlewood JM. J Cyst Fibros. 2003 Mar;2(1):29-34.
- Evaluating the "Leeds criteria" for Pseudomonas aeruginosa infection in a cystic fibrosis centre. Proesmans M, Balinska-Miskiewiscz, Dupont L et al. Eur Resp J 2006;27:937-943.

- Antibiotic therapy against Pseudomonas aeruginosa in cystic fibrosis: a European consensus. Döring G, Conway SP, Heijerman HG, et al. Eur Respir J 2000;16:749-767.

ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS (ABPA)

ABPA is an allergic lung disease characterised by an excessive response to the mould *Aspergillus fumigatus.*

Diagnostic criteria:

1. Acute or subacute clinical deterioration (cough, wheeze, exercise intolerance, exercise-induced asthma, change in pulmonary function, or increased sputum production) not attributable to another etiology.
2. Total IgE > 500 IU/ml.
3. Positive skin prick test for Aspergillus antigen (> 3 mm) or positive specific IgE for *A. fumigatus*.
4. Either:
   a. precipitins to *A. fumigatus* or in vitro demonstration of IgG antibody to *A. fumigatus*;
   b. or new or recent abnormalities on chest radiography (infiltrates or mucus plugging) or chest CT (characteristic changes) that have not cleared with antibiotics and standard physiotherapy.

References:

Allergic bronchopulmonary aspergillosis in cystic fibrosis—state of the art: Cystic Fibrosis Foundation Consensus Conference. Stevens DA, Moss RB, Kurup VP, Knutsen AP, Greenberger P, Judson MA, Denning DW, Crameri R, Brody AS, Light M, Skov M, Maish W, Mastella G; Participants in the Cystic Fibrosis Foundation Consensus Conference. Clin Infect Dis. 2003 Oct 1;37 Suppl 3:S225-64.

LIVER DISEASE

The ECFSPR has adopted the definitions for Liver Disease used by the Cystic Fibrosis Registry in the United Kingdom.

These definitions discriminate patients with severe liver disease (with portal hypertension) from milder cases (cirrhosis without portal hypertension).

Cirrhosis with Hypertension: scarring of the liver related to underlying CF, typically in a biliary pattern.
Severe liver disease may include portal hypertension and/or hypersplenism;

Cirrhosis without Hypertension: scarring of the liver related to underlying CF;

Liver disease without cirrhosis: this includes fatty liver or viral hepatitis but not biliary cirrhosis.

PANCREATIC STATUS

To define pancreatic insufficiency two determinations are mandatory:

- Young children: Stool fat (van de Kamer) > 4-5 g/d;
- Children older than 10 years and adults: Stool fat (van de Kamer) >7g/d and/or faecal pancreatic elastase-1 < 200 ug/g.

Note: Faecal fat excretion values of infants below 3 months are contradictory.
Other than pancreatic causes of steatorrhoea must have been excluded.

For the ECFSPR, pancreatic status is assessed as follows:
Pancreatic insufficiency: Faecal elastase <200 µg/g (twice), and faecal fat high* (twice);
Pancreatic sufficiency: Faecal elastase ≥200 µg/g (twice) and Faecal fat normal* (twice).

*See definition above.

References:

- Nutrition in patients with cystic fibrosis. A European consensus. Sinaasappel M, Stern M, Littlewood J, Wolfe S, Steinkamp G, Heijerman HGM, Robberecht E, Döring G. Nutrition J Cystic Fibros.K 2002; 1:51-75.
- Invited review: Indirect pancreatic function tests in children. Walkowiak J, Nousia-Arvanitakis S, Henker J, Stern M, Sinaasappel M, Dodge JA. J Pediatr Gastroenterol Nutr 2005; 40:107-114.
- Metabolic alkalosis with hypoelectrolytemia in infants with cystic fibrosis. Fustik S, Pop-Jordanova N, Slaveska N, Koceva S, Efremov G. Pediatr int 2002; 44: 289-92.

SALT LOSS SYNDROME

Primary metabolic alkalosis with blood pH > 7.45, serum sodium < 130 mmol/l and serum chloride < 90 mmol/l.

References:
Fustik S, Pop-Jordanova N, Slaveska N, Koceva S, Efremov G. Metabolic alkalosis with hypoelectrolytemia in infants with cystic fibrosis. Pediatr int 2002; 44: 289-92.

TRANSPLANTATION

1. For patients who had a transplant during the year of follow up:
   The best FEV1 (of the highest FEV1% predicted) before transplantation must be used;
   Therapy, complications and microbiology from before transplantation must be recorded.
2. For patients who had a transplant before the current follow-up year, record all information available.

Appendix 4: Explanation of terms

ABPA: allergic bronchopulmonary aspergillosis is an allergic lung disease characterised by an excessive response to the mould *Aspergillus fumigatus.*

BMI: body mass index: weight (kg) / [height (m)]^2.

Bronchodilator: medication that relaxes the muscles of the airways, used also for asthma.

CFRD: CF related diabetes.

CFTR: CF transmembrane conductance regulator is a protein at the cell surface that controls the salt and water balance across a cell. The gene that causes CF is the blueprint for the CFTR protein. Everyone has two copies of the gene for CFTR, but to be born with CF both CFTR genes must be affected by a CF-causing mutation.

CFTR modulator therapy: a range of CFTR modulators have been approved for use. They are designed to correct the malfunctioning CFTR protein: different mutations cause different defects in the structure of the protein and its functionality and the different CFTR modulators either correct or potentiate CFTR assembly or function; they can also be combined to become more efficient. Since the CFTR modulator therapies work specifically for certain mutation classes, those currently available are effective only in people with those mutations.

Compassionate use: is a treatment option that allows the use of an unauthorised medicine for patients who have no alternative treatment options and no access to clinical trials.

DIOS: distal intestinal obstruction syndrome is a condition, unique to people with CF. In DIOS, the intestines are blocked by thickened stool due to sticky mucus and other mechanisms, which leads to reduced stool flow through the intestines and abdominal pain and can result in an emergency.

FEV_1: the Forced Expiratory Volume of air in the first second of a forced exhaled breath.

FEV_1%: the FEV_1 as a percentage of the average value for healthy people of the same age, height and sex.

Haemoptysis: coughing up blood. This happens frequently in small amounts in CF, so the complication we asked for is major bleeding (major meaning when the volume of expectorate is 250 ml or more over the course of the day).

Homozygous: CF is caused by mutations of the CFTR gene, one on each allele. One is inherited from the mother and one from the father. If both mutations are the same, the person is said to be homozygous for this mutation.

Heterozygous: CF is caused by mutations of the CFTR gene, one on each allele. One is inherited from the mother and one from the father. If these are two different mutations, the person is considered to be heterozygous.

ICM: Intestinal current measurement is a method to diagnose or exclude CF in difficult situations (e.g. unclear relevance of CFTR mutations). CF is caused by abnormalities in the mechanism that carries salt into and out of cells. With ICM, the rate of salt transport is measured in tissue samples taken from the person (rectal biopsy) and measured against reference values of a healthy population. ICM can be carried out at any age.

LCI: Lung clearance index, measured by multiple breath washout (MBW); this is a test that measures non-homogeneity of lung ventilation. A tracer gas is inhaled, and the time to exhale a defined proportion of the gas is determined (LCI). MBW is very sensitive and particularly useful to measure lung function in children and people with milder forms of CF.

Macrolides: a type of antibiotic with anti-inflammatory properties. Azithromycin is a macrolide often used in people with CF who have chronic Pseudomonas aeruginosa lung infection.

Meconium ileus: small-bowel obstruction caused by unusual thick, sticky faeces (i.e. meconium, which is the first stool of newborn babies).

NaCl: sodium chloride. Here: inhaled hypertonic saline.

NIPPV: Non-invasive positive pressure ventilation; this refers to mechanical ventilation that helps patients with breathing difficulties. It is done with the help of a face mask and does not require the insertion of an artificial airway (tube). It can be one of two types: BiPaP (Bi-level positive air pressure) or CpaP (continuous positive air pressure).

NPD: Nasal Potential Difference; this is a method to diagnose or exclude CF in unclear cases and involves placing an electrode on the surface of the inside of the nose to measure the electrical potential difference across the nasal epithelium. The NPD is a result of the transport of ions such as sodium and chloride in and out of the cells, a mechanism that is affected by defects in the CFTR protein.

Pancreatic insufficiency: the absence of pancreatic enzymes in the gut leading to malnutrition if not treated (in the ECFSPR pancreatic insufficiency is therefore defined as the use of pancreatic enzyme supplementation).

Pneumothorax: collapsed lung. In CF usually because of severe lung damage.

PPI: Proton Pump Inhibitors, is medication that reduces stomach acid levels.

rhDNase: recombinant human DNase (marketed as Pulmozyme®).

Z-score (or standardised scores): a way to compare results with a "normal" population, the reference population (see Appendix 2 for details). Negative z-scores mean that the value is below the mean of values in the reference population, whereas positive z-scores mean that the value is above the mean. Z-score equal to 0 means that the value is equal to the mean of values in the reference population. For example, a z-score for weight of -2 means that the weight is 2 standard deviations below the mean of subjects of the same age and sex of the reference population. For example, if the z-score for BMI of a 10-year-old boy is -2, it means that the BMI for that boy is 2 standard deviations below the mean BMI of 10-year-old boys of the reference population.