

ECFS

PATIENT REGISTRY

REPORT

2007 DATA



This report contains data collected from existing national registries and from single centers in Europe. All known national registries were contacted and asked for their co-operation. The single centers represent countries that do not have a national registry yet, but still want to participate. Demographic and clinical data were collected through a common template.

The data were extracted from the local databases into the template by the representatives of national registries and centers. Discrepancies in definitions between local databases and ECFR are highlighted throughout this report.

All data were transferred anonymously (identified only by a patient code, gender, month/year of birth and country or center) according to the regulations of the Danish Data Protection agency, where the ECFR is registered. Data analysis was performed at the Università degli Studi di Milano (Dept. Medicina del Lavoro, Statistica Medica e Biometria).

Data were analyzed according to the guidelines given by ECFS Patient Registry Definition Consensus group*. We used international references for computation of FEV₁% of predicted and z-scores for height, weight and BMI.

Data were collected during year 2009 and were first presented at the 32nd European Cystic Fibrosis Conference in Brest, France.

*http://www.ecfs.eu/ecfs_supported_initiatives/european_cf_registry/patient_criteria

We would like to thank the participating countries for their patience and cooperation. Special thanks to the people involved in the data extraction and evaluation of final report:

Baroukh Maurice Assael, Italy
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People and ideas for innovation in healthcare
Chiesi Farmaceutici S.p.A. is proud to be the sole
pharmaceutical sponsor of the ECFS Patient Registry





DEMOGRAPHICS

Table 1 **Number of patients reported by each country**

country	abbreviation	n
Austria	(A)	116
Belgium*	(B)	1052
Bulgaria	(BG)	95
Czech Republic*	(CZ)	502
Denmark*	(DK)	447
France*	(F)	5147
Germany*	(D)	5039
Greece	(GR)	121
Hungary*	(H)	572
Israel	(IL)	507
Italy	(I)	774
Netherlands*	(NL)	1113
Portugal	(P)	116
Republic of Belarus	(BY)	145
Slovenia	(SI)	50
United Kingdom*^	(UK)	4408
<i>total</i>		<i>20204</i>

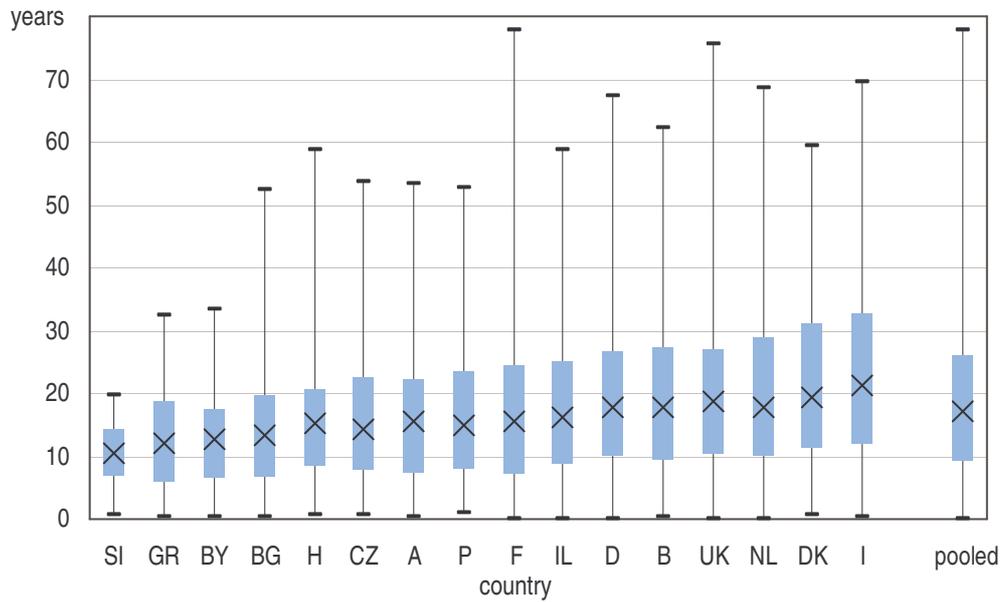
* These countries are represented by a national registry.

^ Data refer only to patients with complete data.

Table 2 Age (in years) on 31-12-2007

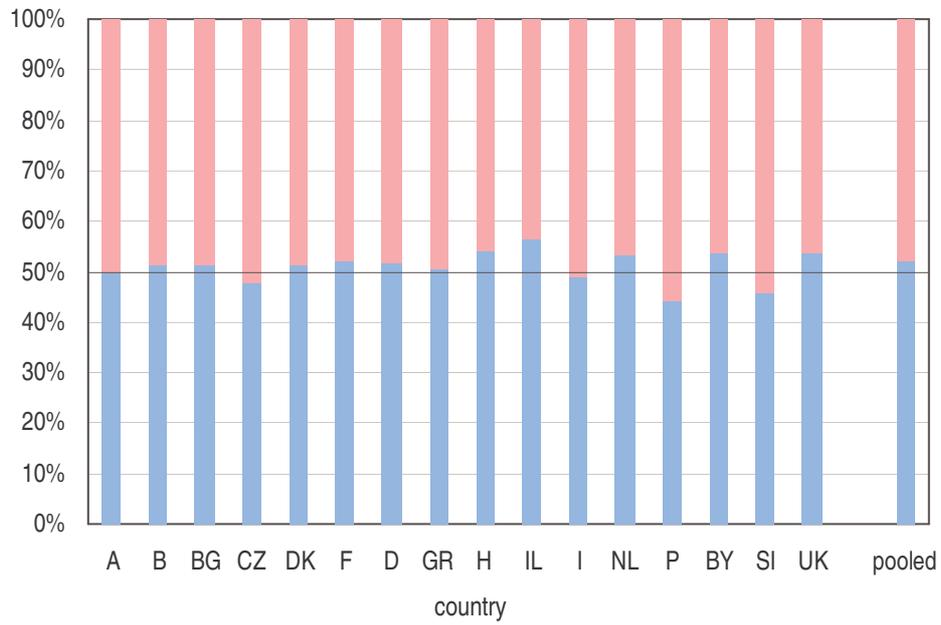
country	mean	min	25 th pctl	median	75 th pctl	max	% ≥18 years
SI	10.49	0.54	6.87	10.38	14.38	19.79	4.00
GR	12.85	0.21	5.96	12.04	18.79	32.29	27.27
BY	12.87	0.38	6.71	12.71	17.46	33.38	21.38
BG	14.20	0.21	6.54	13.42	19.79	52.29	31.58
H	15.44	0.54	8.46	15.21	20.63	58.87	35.84
CZ	16.14	0.63	8.08	14.33	22.59	53.54	38.05
A	16.49	0.21	7.38	15.46	22.38	53.46	41.38
P	16.89	1.04	8.08	14.92	23.38	52.54	40.52
F	17.21	0.13	7.46	15.71	24.46	77.63	42.06
IL	17.87	0.04	8.80	16.13	25.04	58.71	43.00
D	19.13	0.13	10.12	17.63	26.54	67.38	48.46
B	19.40	0.21	9.38	17.63	27.25	62.12	48.86
UK	19.91	0.13	10.46	18.71	27.04	75.71	52.13
NL	20.37	0.04	10.29	17.71	28.96	68.46	48.97
DK	21.18	0.54	11.29	19.29	30.96	59.29	54.14
I	22.29	0.21	12.13	21.13	32.63	69.46	57.88
<i>pooled</i>	<i>18.70</i>	<i>0.04</i>	<i>9.29</i>	<i>17.21</i>	<i>26.04</i>	<i>77.63</i>	<i>46.82</i>

Figure 1 Boxplot of age (in years) on 31-12-2007



Boxplots: cross represents median, box represents 25th to 75th percentiles, whiskers represent minimum and maximum.

Figure 2 Gender distribution (pink=females, light blue=males)



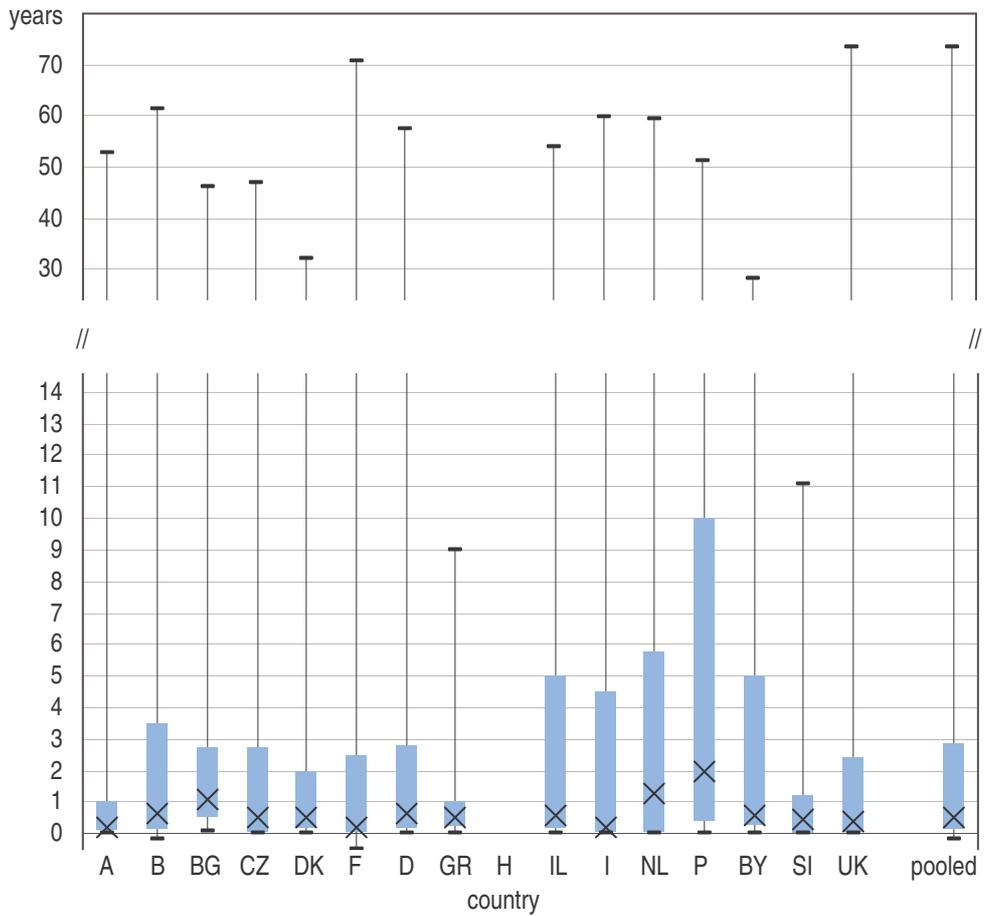
DIAGNOSIS

Table 3 Age (in years) at diagnosis

country	% missing values	mean	min	25 th pctl	median	75 th pctl	max	% ≥18 years	% <1 year
A	9.48	2.92	at birth	0.11	0.19	1.03	52.78	5.17	67.24
B	3.42	4.36	-0.18*	0.15	0.65	3.50	61.15	7.32	55.80
BG	0.00	2.57	0.10	0.50	1.10	2.70	46.00	2.11	47.37
CZ	0.00	2.72	at birth	0.10	0.50	2.70	46.90	2.39	59.96
DK	0.00	2.11	at birth	0.17	0.50	2.00	32.08	0.89	59.96
F	69.19	3.20	-0.49*	0.09	0.19	2.49	70.83	1.59	21.26
D	7.16	2.96	at birth	0.18	0.66	2.77	57.55	3.25	53.19
GR	38.84	1.07	0.04	0.25	0.50	1.00	9.00	0.00	40.50
H	100.00	-	-	-	-	-	-	-	-
IL	9.07	4.47	at birth	0.17	0.58	5.00	54.00	5.92	53.65
I	3.10	4.62	at birth	0.08	0.21	4.50	59.65	8.66	62.79
NL	74.39	6.03	at birth	0.08	1.25	5.75	59.42	3.05	11.95
P	0.86	6.53	at birth	0.40	2.00	10.00	51.00	11.21	35.34
BY	20.69	3.58	0.04	0.25	0.60	5.00	28.00	2.76	41.38
SI	0.00	1.28	at birth	0.04	0.44	1.21	11.10	0.00	66.00
UK	5.99	3.37	at birth	0.08	0.42	2.42	73.33	5.17	58.76
<i>pooled</i>	<i>28.61</i>	<i>3.38</i>	<i>-0.49*</i>	<i>0.10</i>	<i>0.48</i>	<i>2.83</i>	<i>73.33</i>	<i>3.58</i>	<i>43.14</i>

* Prenatal diagnosis.

Figure 3 Age (in years) at diagnosis



Boxplots: cross represents median, box represents 25th to 75th percentiles, whiskers represent minimum and maximum.

Table 4 Sweat chloride (mmol/L)

n	mean	min	25 th pctl	median	75 th pctl	max
6737	95.59	3.00	83.00	98.00	110.00	160.00

Figure 4 Sweat chloride (mmol/L)

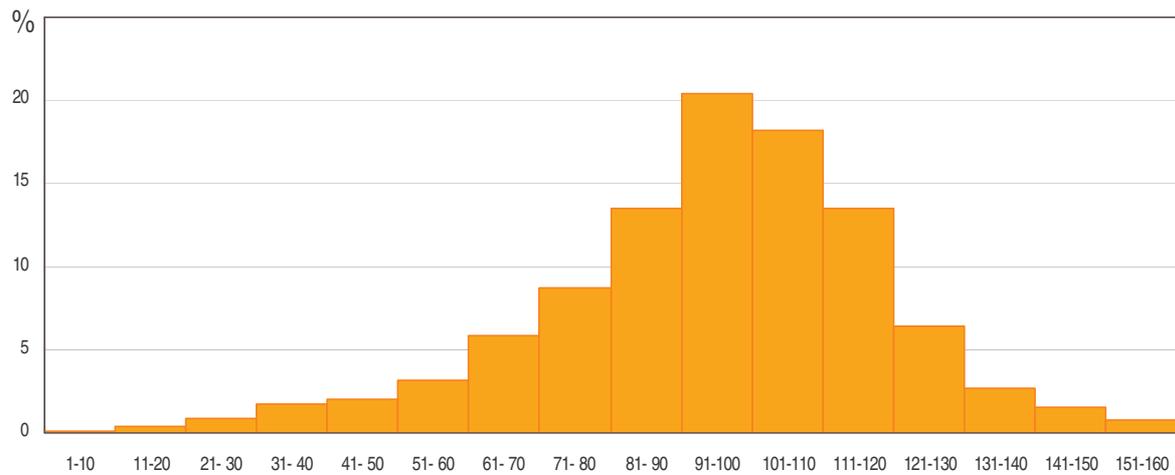
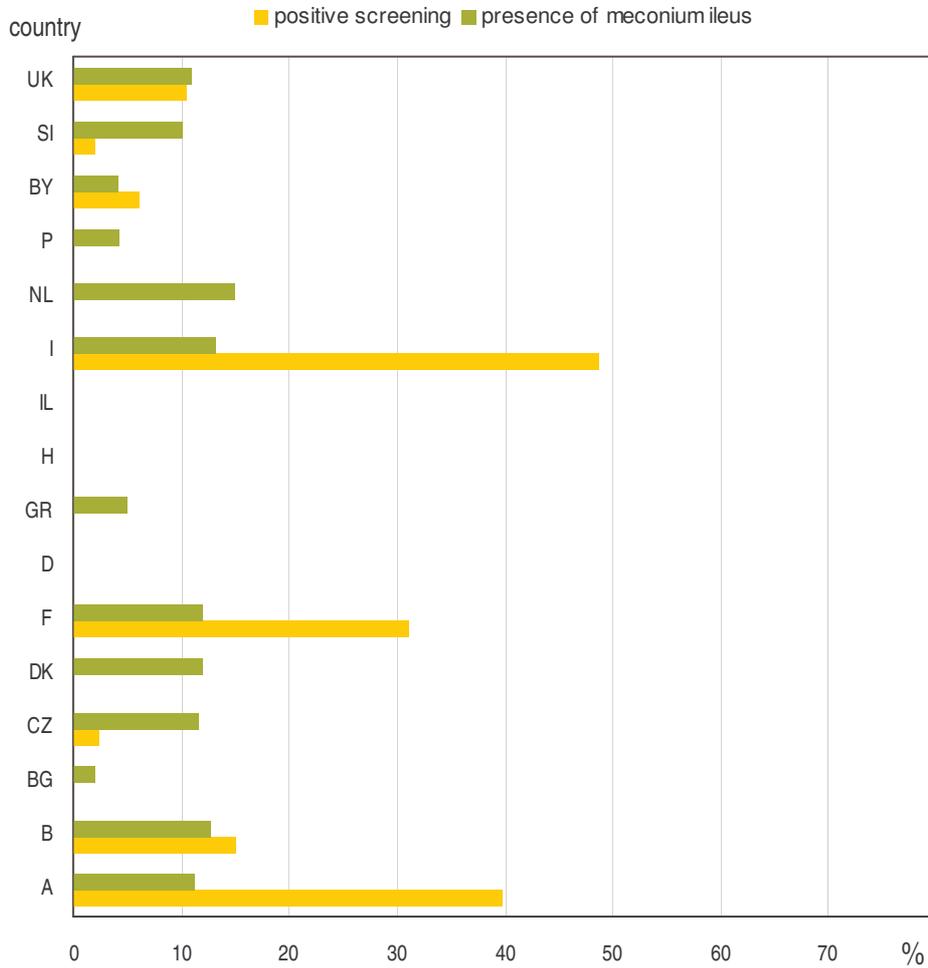


Table 5 Sweat chloride (mmol/L) by age at diagnosis (in years)

Age at diagnosis	n	mean	min	25 th pctl	median	75 th pctl	max
<1	3347	97.26	9.00	87.00	99.00	110.00	160.00
1-4	1223	99.70	10.00	87.00	102.00	115.00	160.00
5-17	740	90.41	9.00	71.00	94.00	110.00	160.00
≥18	315	79.07	5.00	60.00	82.00	99.00	160.00

Figure 5 Percentages of newborns positive at screening and newborns with meconium ileus for the whole population



Neonatal screening

Data not available for Germany and Hungary.

Due to high proportion of missing data for Italy (30%), France (65%), Czech Republic and United Kingdom (>85%), estimates are unreliable.

In Belgium no national screening is performed; information on positivity of a screening test is only given as one of the signs that lead to a diagnosis of CF.

Meconium ileus

Data not available for Germany, Hungary and Israel.

Due to high proportion of missing data for Netherlands (11%), Czech Republic (89%), Portugal, Republic of Belarus and United Kingdom (>40%), estimates are unreliable.



GENETICS

Figure 6 Allelic frequencies of unknown mutations

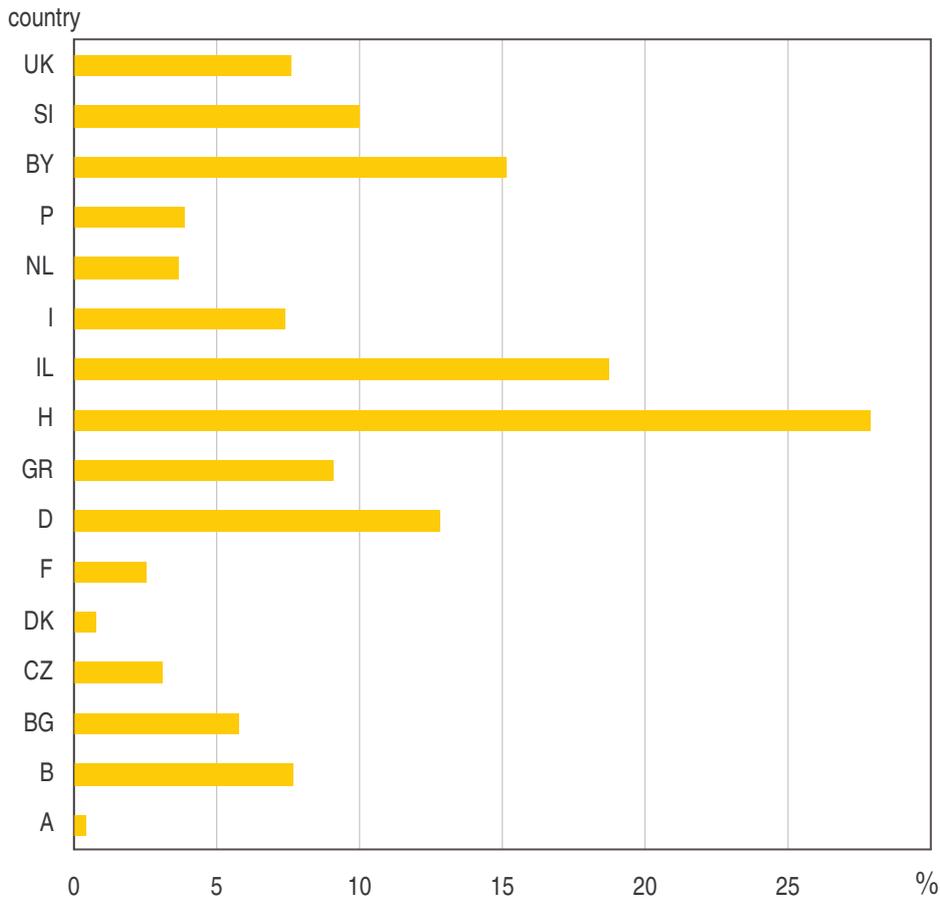
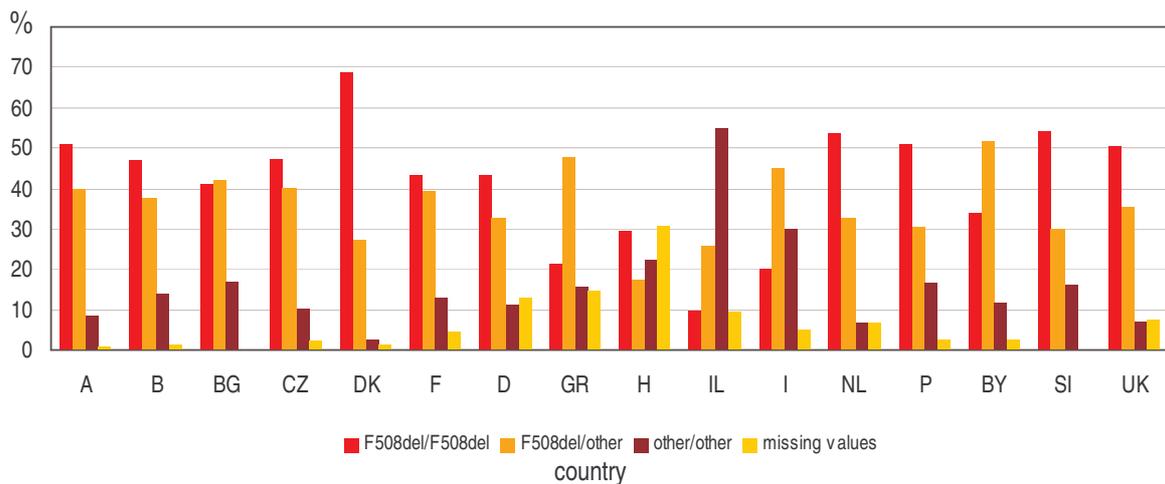
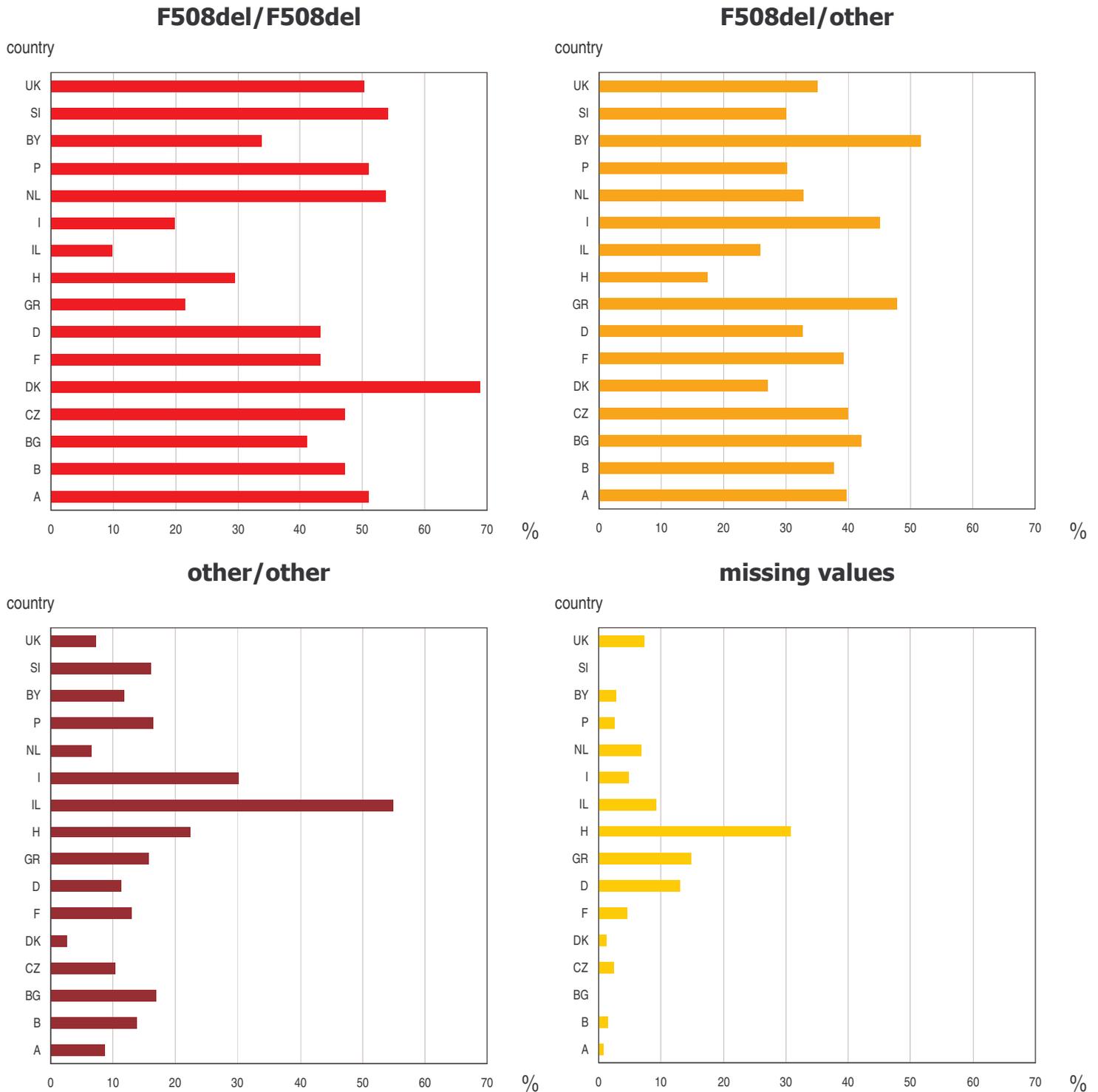


Figure 7.1 Genotype frequencies



The category "other" includes unknown mutations (i.e. remained unidentified after testing). The category "missing values" includes patients not undergone DNA testing.

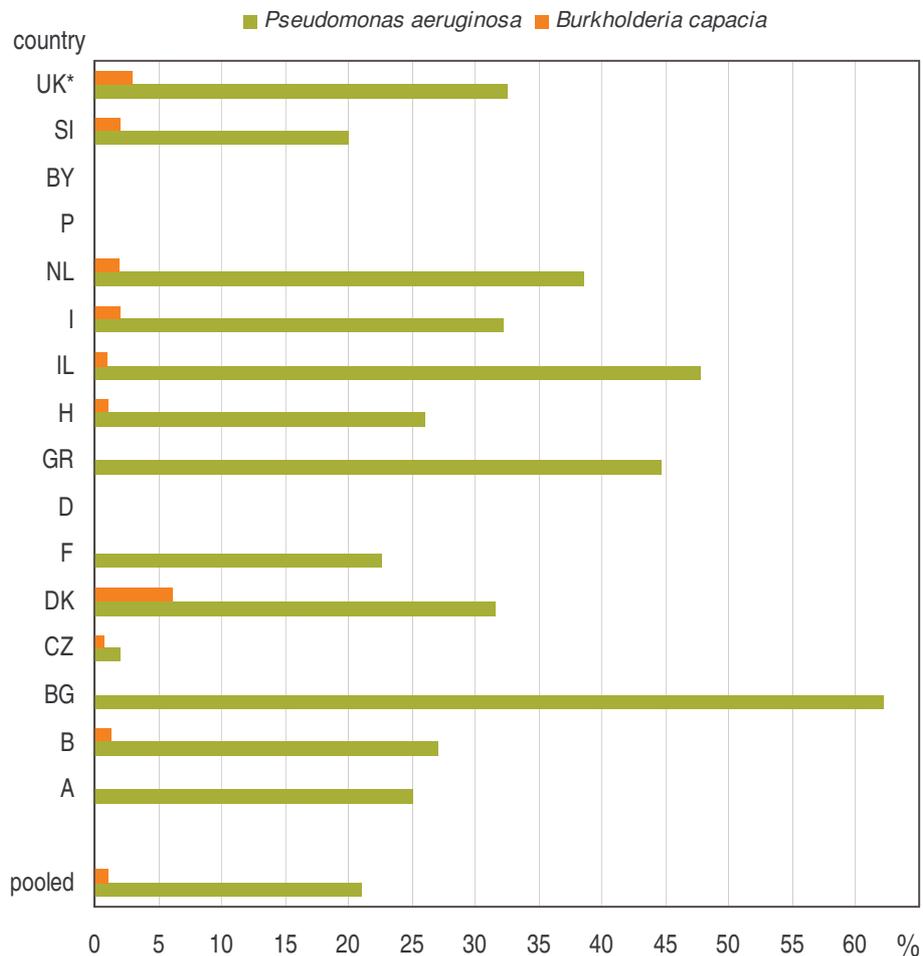
Figure 7.2 Genotype frequencies



The category "other" includes unknown mutations (i.e. remained unidentified after testing). The category "missing values" includes patients not undergone DNA testing.

MICROBIOLOGY

Figure 8.1 Percentages of chronic *Pseudomonas aeruginosa* and chronic *Burkholderia cepacia* infections



Chronic infection was defined by local physician according to modified Leeds criteria^a and/or antibodies^b. Patient was defined as chronically infected if he/she fulfils the criteria now or in recent years and the physician has no reason to think the status has changed.

^a Modified Leeds criteria: >50% of the sputum samples positive, collected during the last 12 months. At least 4 sputum samples during that period.

^b Significantly raised antibodies according to local laboratories.

* United Kingdom defined chronic infection when patients have 3 or more positive isolates during the last 12 months.

Chronic *Pseudomonas aeruginosa* infection

Data not available for Germany, Portugal and Republic of Belarus.

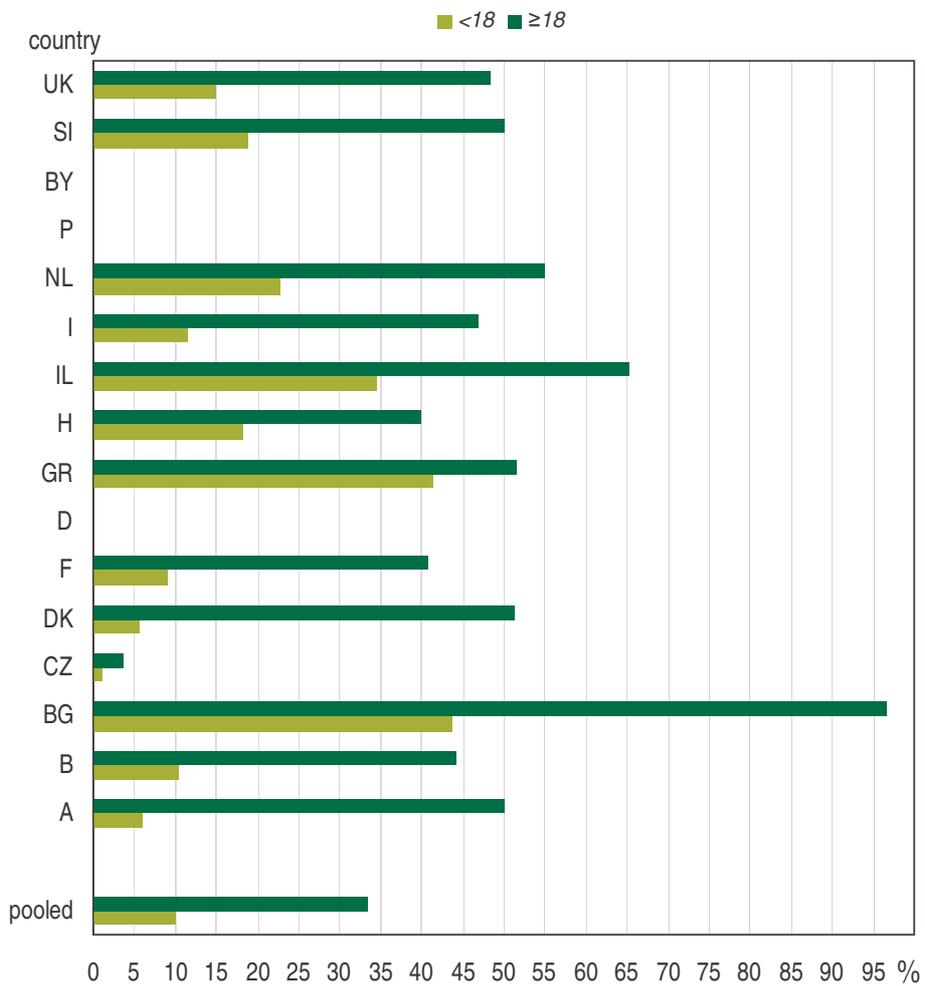
Due to high proportion of missing data (>10%), estimates for Bulgaria, Czech Republic, Greece and United Kingdom are unreliable.

Chronic *Burkholderia cepacia* infection

Data not available for Bulgaria, France, Germany, Portugal and Republic of Belarus.

Due to high proportion of missing data (>10%), estimates for Czech Republic and Greece are unreliable.

Figure 8.2 Percentages of chronic *Pseudomonas aeruginosa* infection by age (years)

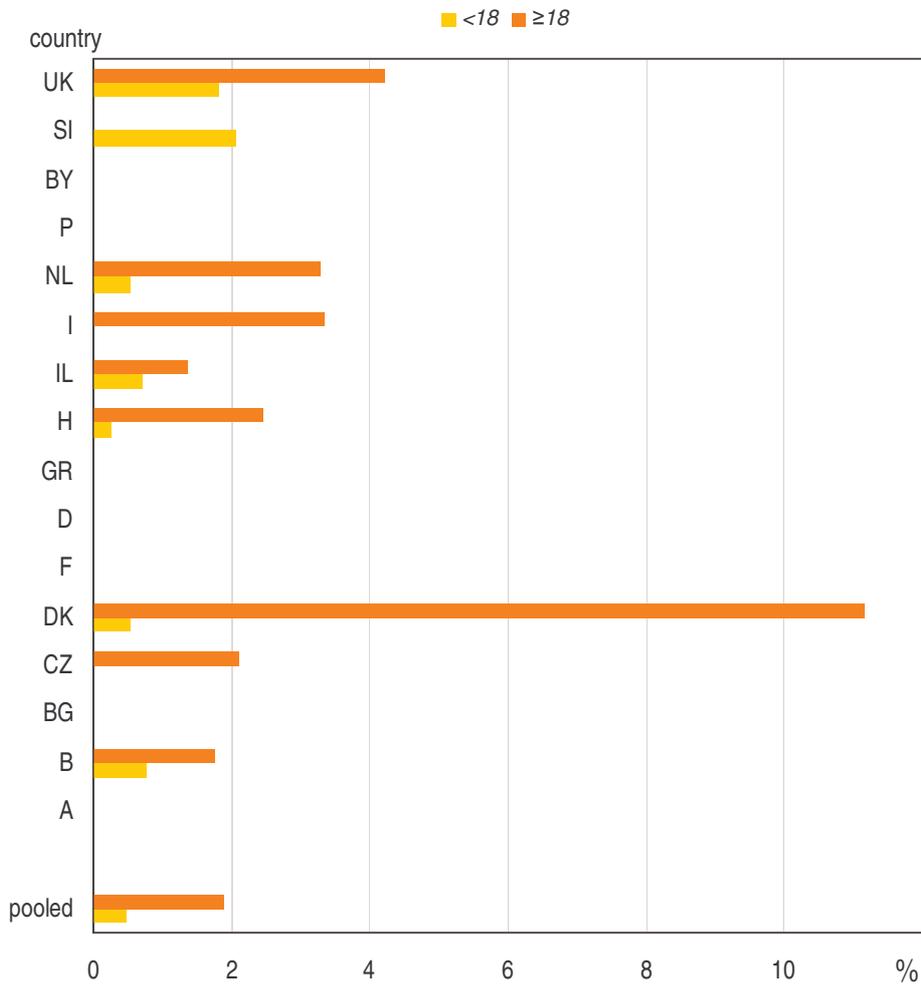


Chronic *Pseudomonas aeruginosa* infection

Data not available for Germany, Portugal and Republic of Belarus.

Due to high proportion of missing data (>10%), estimates for Bulgaria, Czech Republic, Greece and United Kingdom are unreliable.

Figure 8.3 Percentages of chronic *Burkholderia cepacia* infection by age (years)



Chronic *Burkholderia cepacia* infection

Data not available for Bulgaria, France, Germany, Portugal and Republic of Belarus. Due to high proportion of missing data (>10%), estimates for Czech Republic and Greece are unreliable.

Table 6 Other infections

	no		yes		missing values	
	N	%	N	%	N	%
<i>Nontuberculous mycobacteria</i>	12599	62.36	158	0.78	7447	36.86
<i>Chronic Staphylococcus aureus</i>	5524	27.34	1891	9.36	12789	63.30
<i>Stenotrophomonas maltophilia</i>	11957	59.18	634	3.14	7613	37.68

Chronic infection was defined by local physician according to modified Leeds criteria^a and/or antibodies^b. Patient was defined as chronically infected if he/she fulfils the criteria now or in recent years and the physician has no reason to think the status has changed.

^a Modified Leeds criteria: >50% of the sputum samples positive, collected during the last 12 months. At least 4 sputum samples during that period.

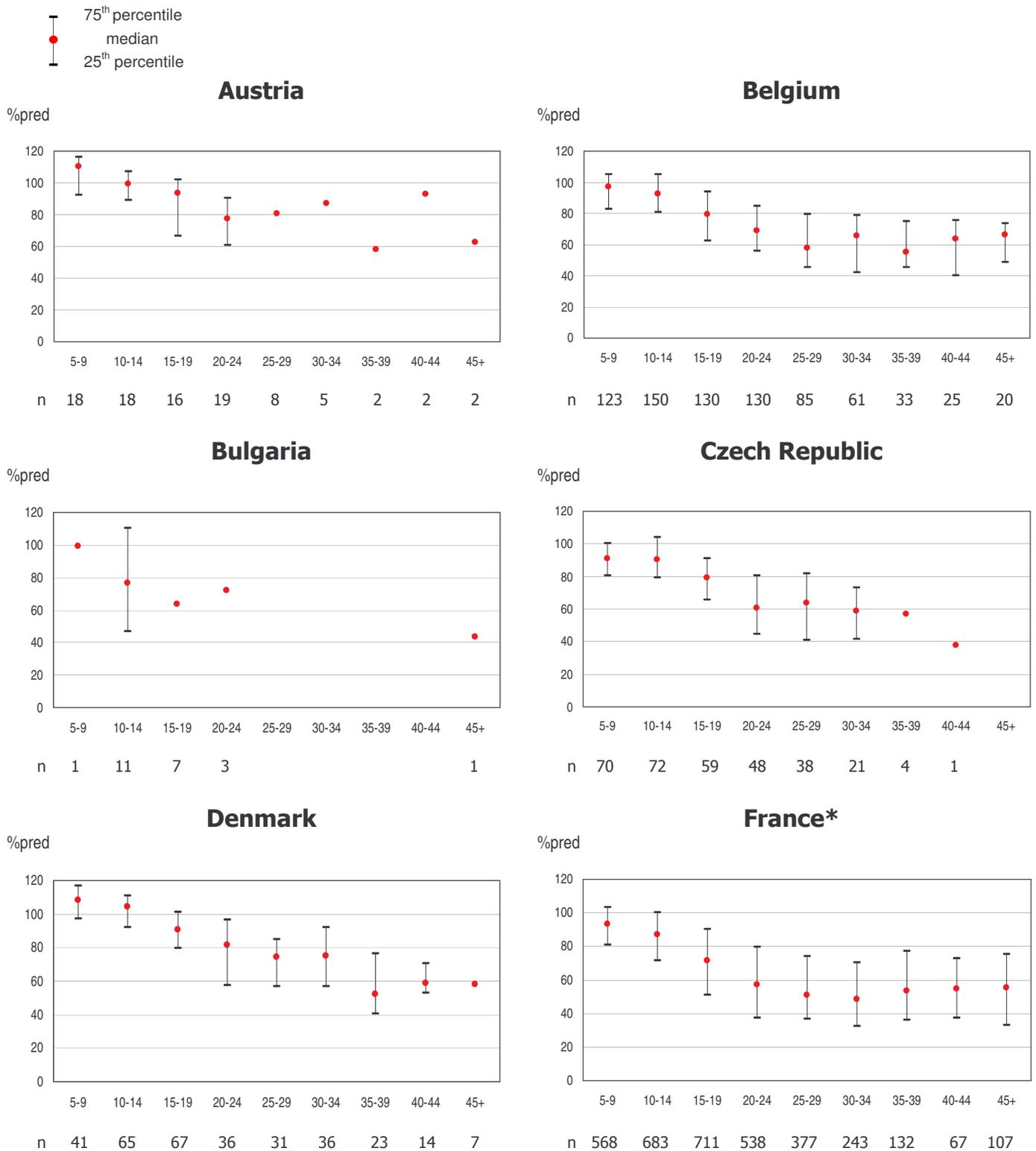
^b Significantly raised antibodies according to local laboratories.

Country breakdown is not shown due to small proportion of positive answers.

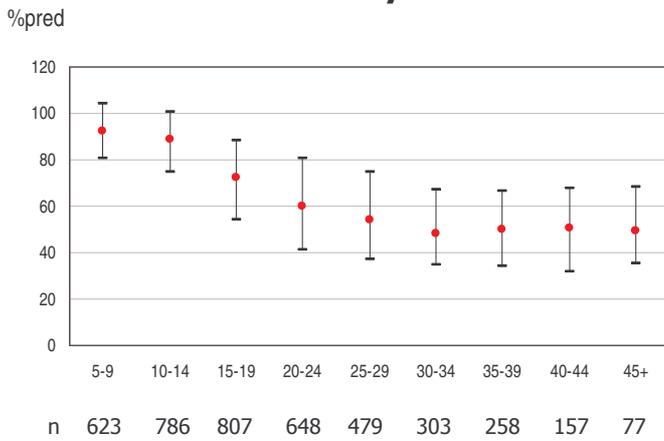
United Kingdom defined chronic infection when patients have 3 or more positive isolates during the last 12 months.

LUNG FUNCTION AND GROWTH

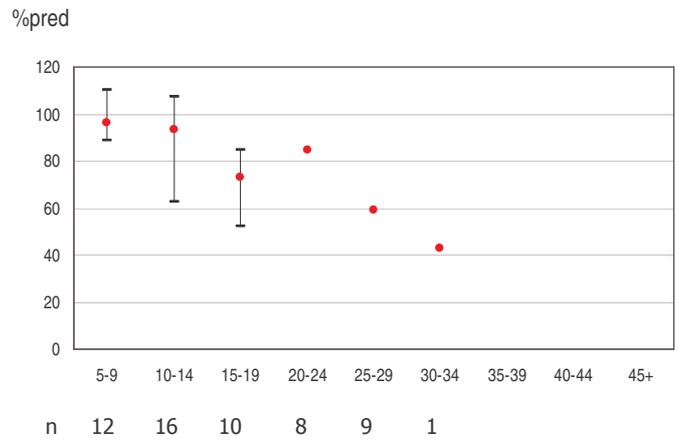
Figure 9 Quartiles of FEV₁% of predicted (best of the year), by age (years)



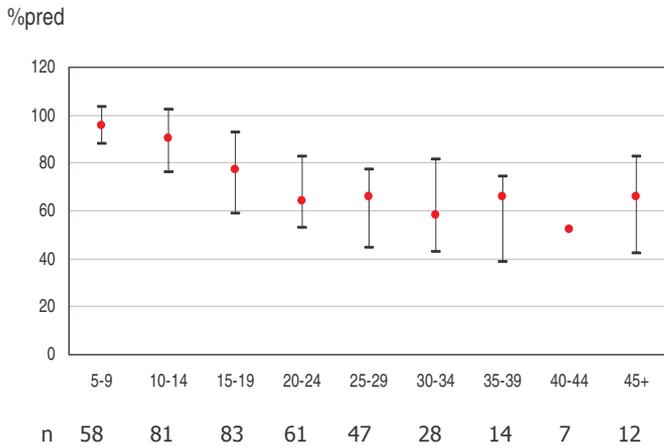
Germany**



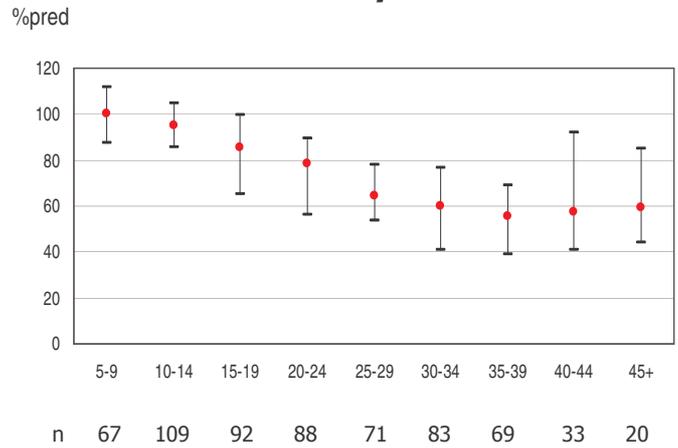
Greece



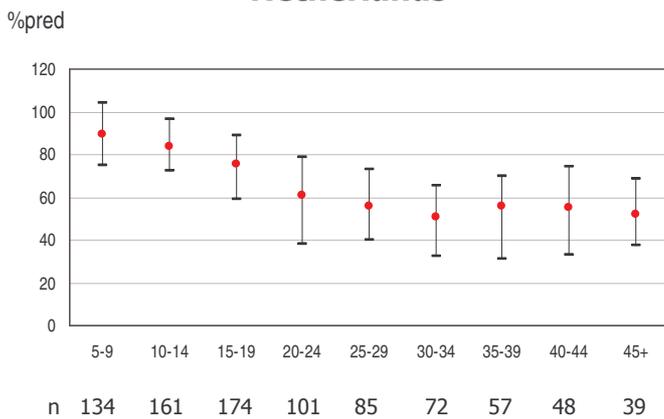
Israel



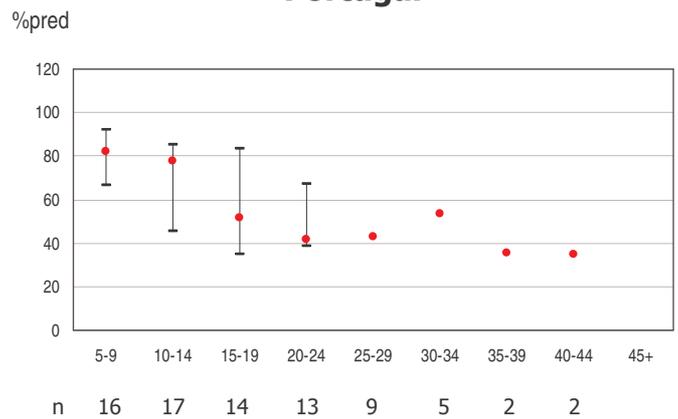
Italy



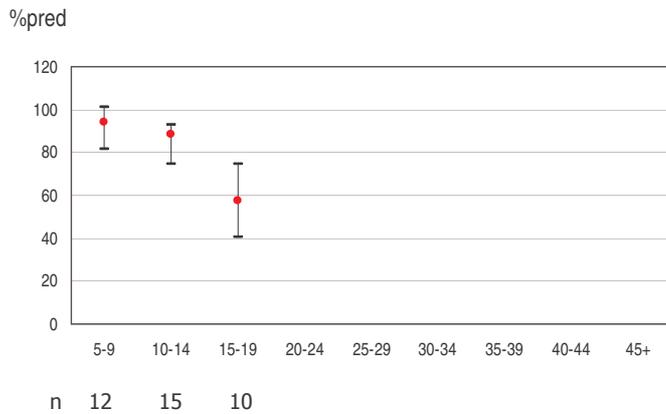
Netherlands



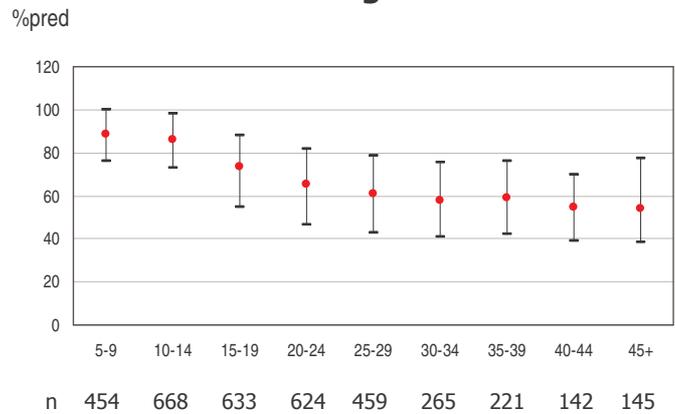
Portugal



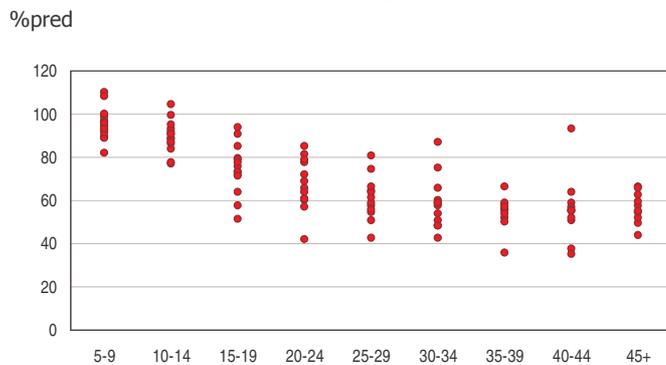
Slovenia



United Kingdom***



All countries



Patients below 6 years of age and transplanted patients were excluded from the analysis.

FEV₁% of predicted was computed through international references:

for male children (6-17 yrs) and female children (6-15 yrs): Wang *et al*¹

for male adults (≥ 18 yrs) and female adults (≥ 16 yrs): Hankinson *et al*².

For children (< 6 yrs), predicted values were not computed due to lack of valid reference equations.

For groups with n<10, 25th and 75th percentiles were not computed.

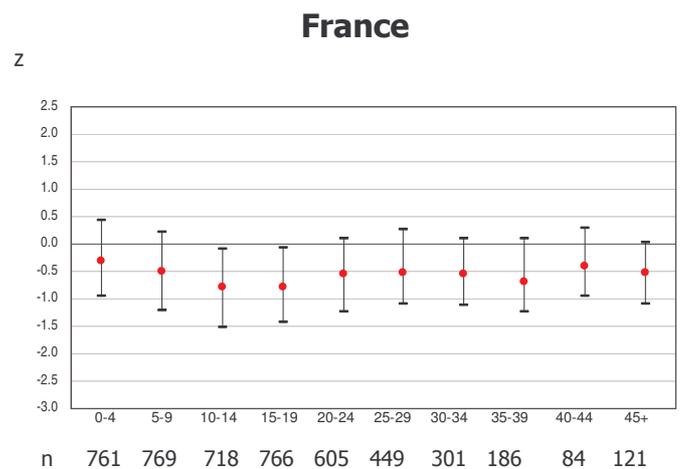
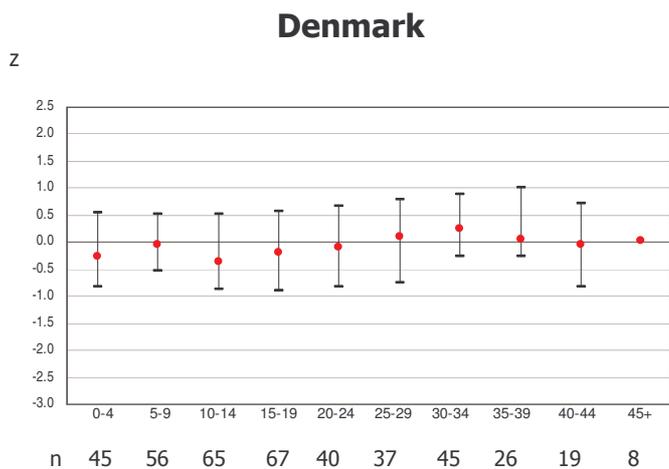
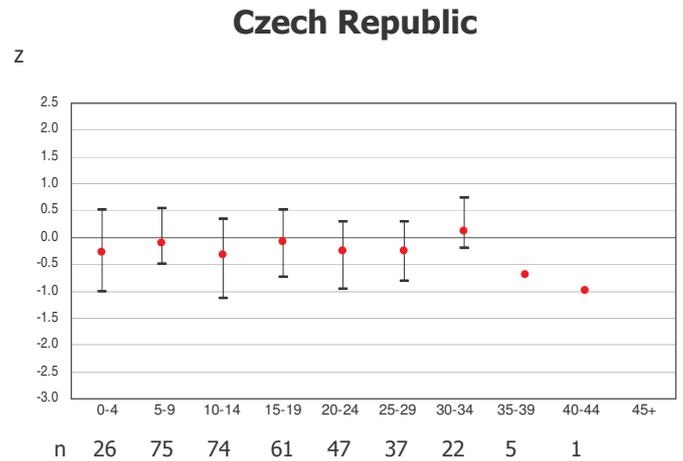
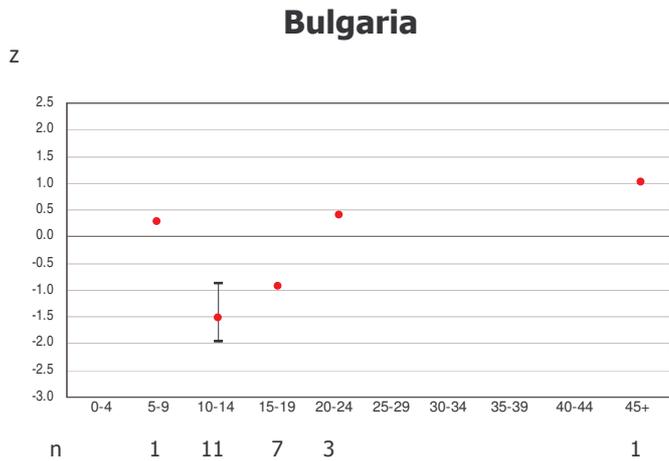
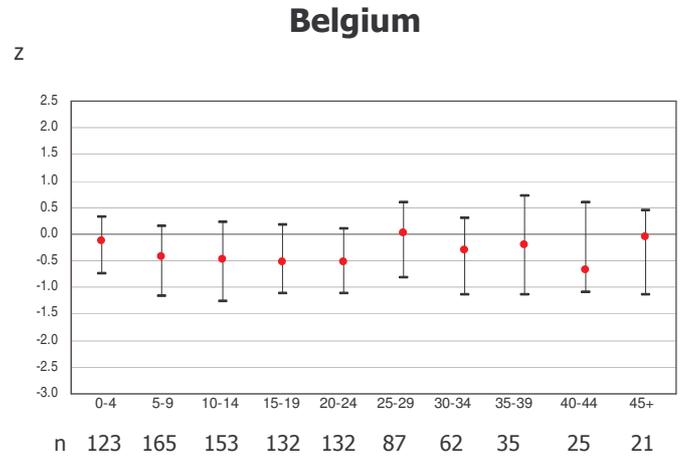
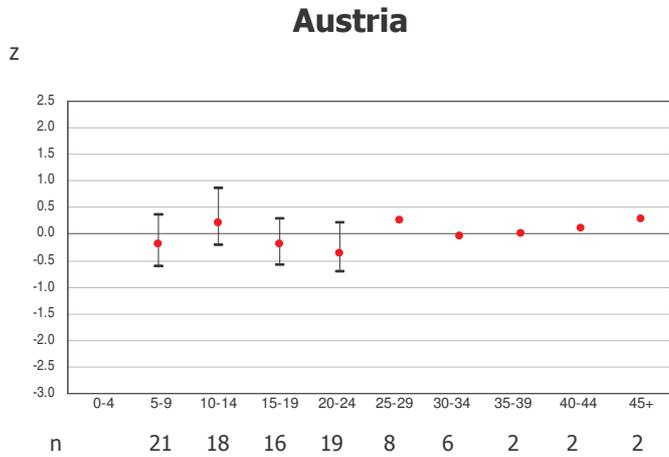
- * FEV₁ was the last of the year.
- ** FEV₁ was near the patient's birthday.
- *** FEV₁ referred to the annual visit.

¹ Wang X, Dockery DW, Wypij D, Fay ME, Ferris BG. Pulmonary function between 6 and 18 years of age. *Pediatr Pulmonol* 1993;15:75-88.

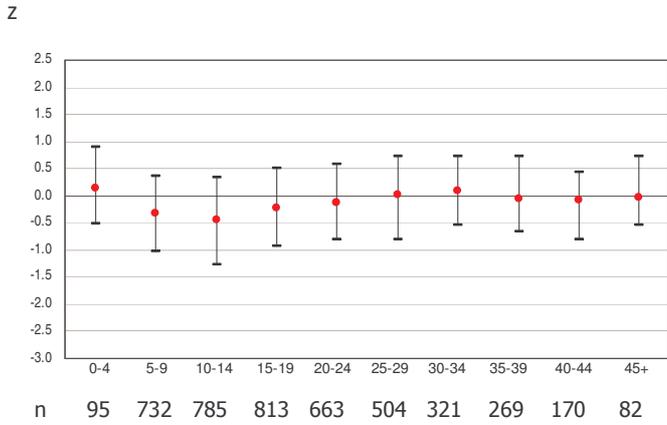
² Hankinson JL, Odencrantz RJ, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respr Crit Care Med* 1999;159:179-87.

Figure 10 Quartiles of z-scores for height, by age (years)

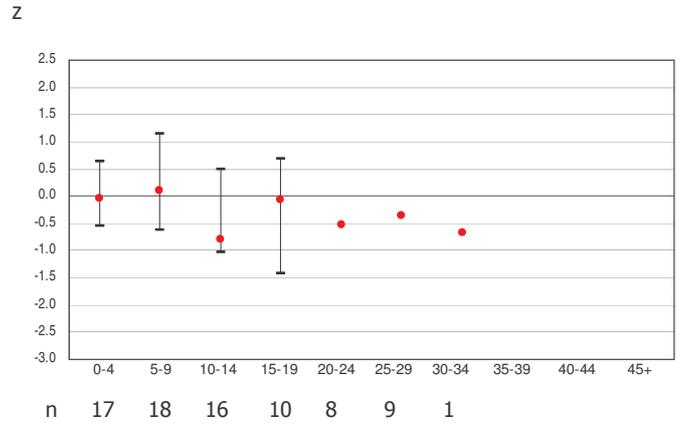
75th percentile
median
25th percentile



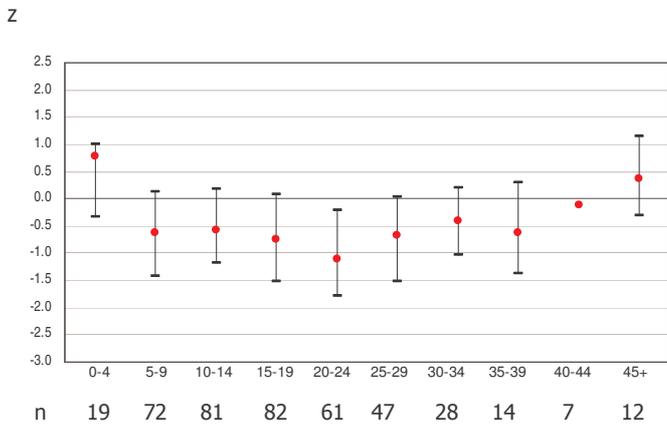
Germany



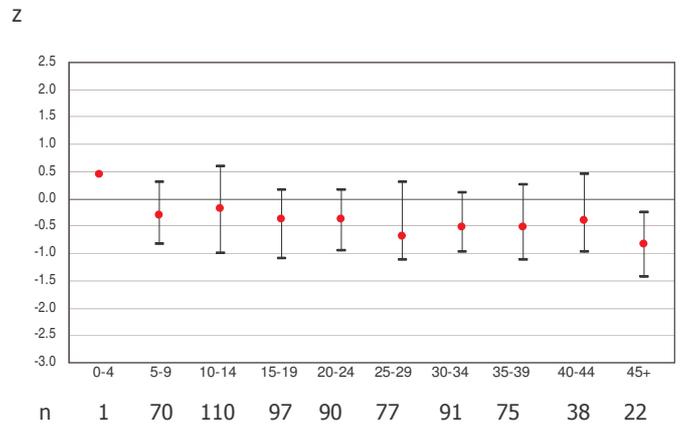
Greece



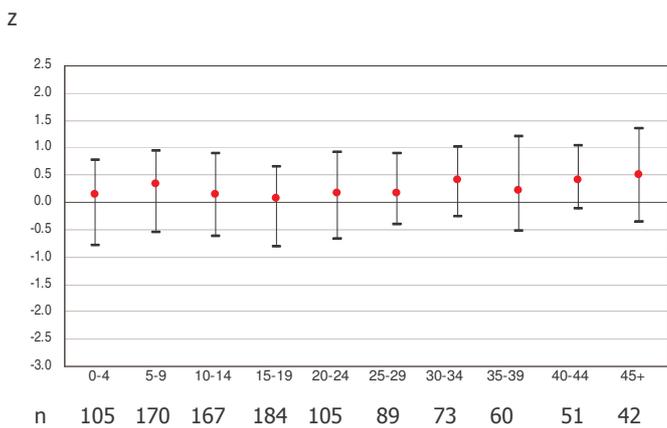
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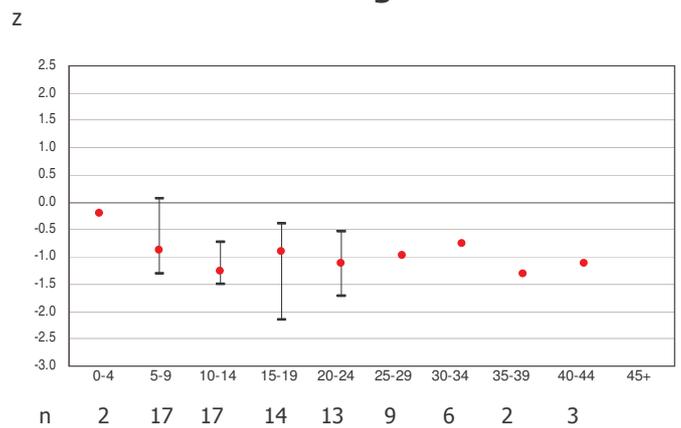
Italy



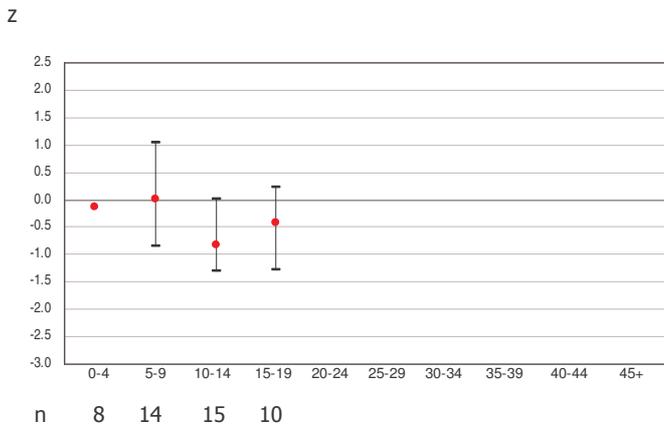
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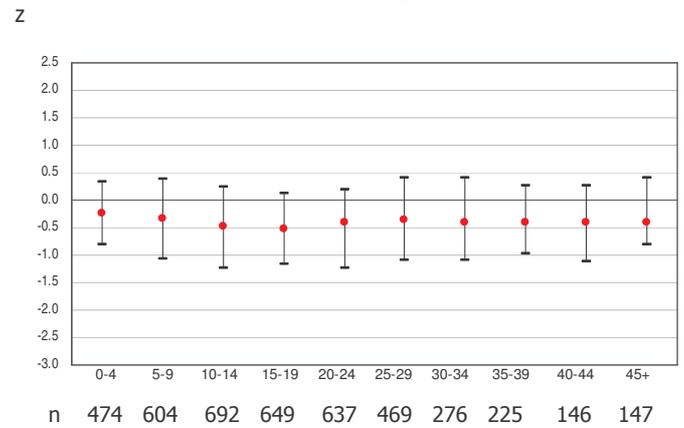
Portugal



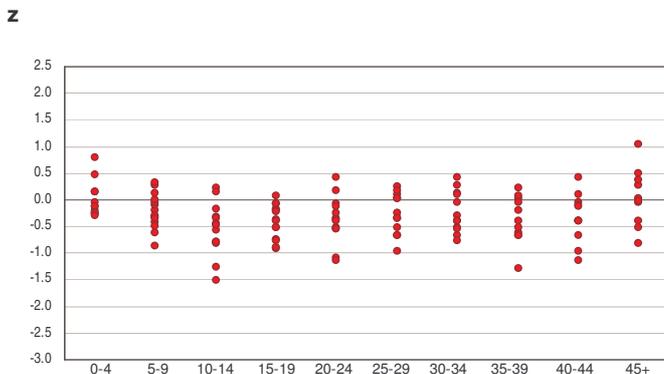
Slovenia



United Kingdom



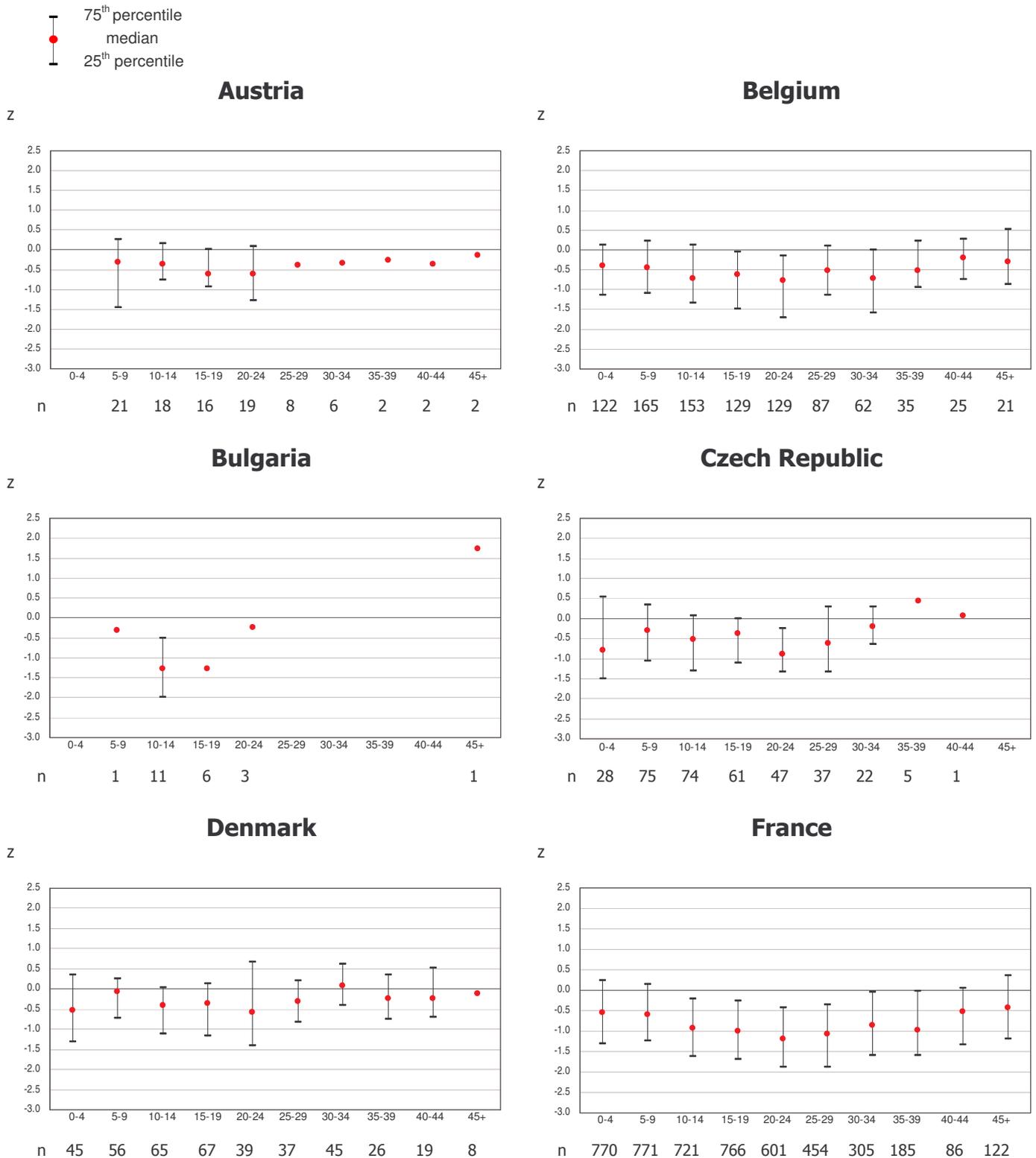
All countries



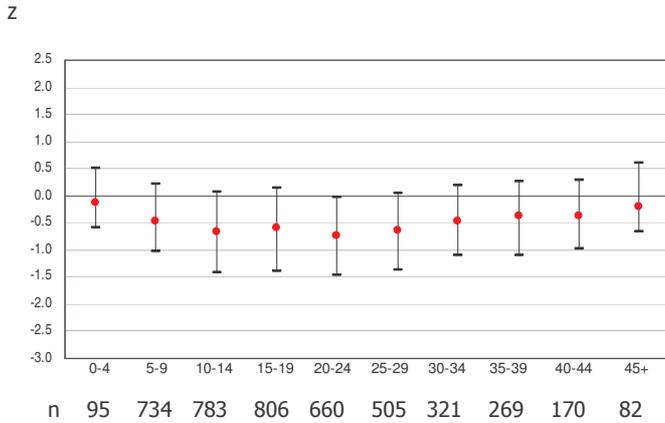
International references¹ were used to compute z-scores.
For groups with n<10, 25th and 75th percentiles were not computed.

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

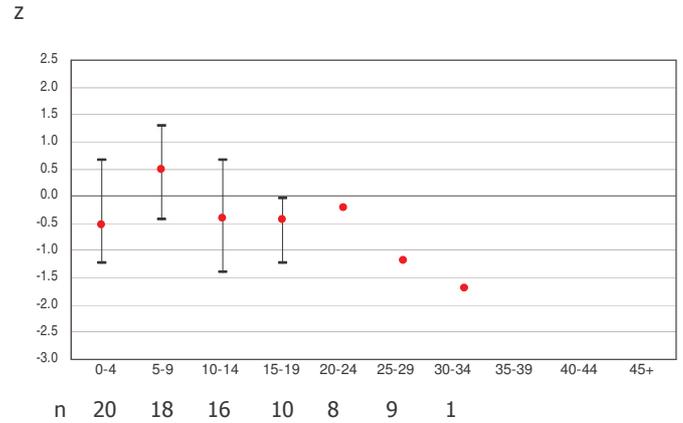
Figure 11 Quartiles of z-scores for weight, by age (years)



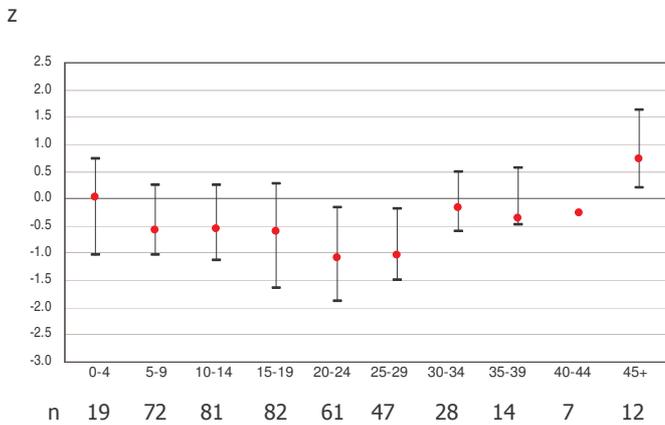
Germany



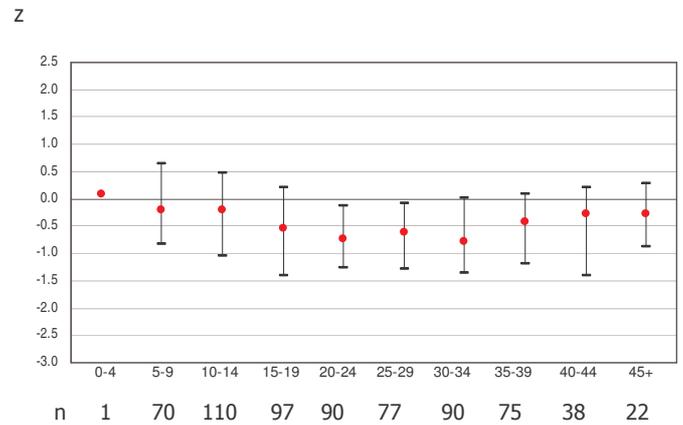
Greece



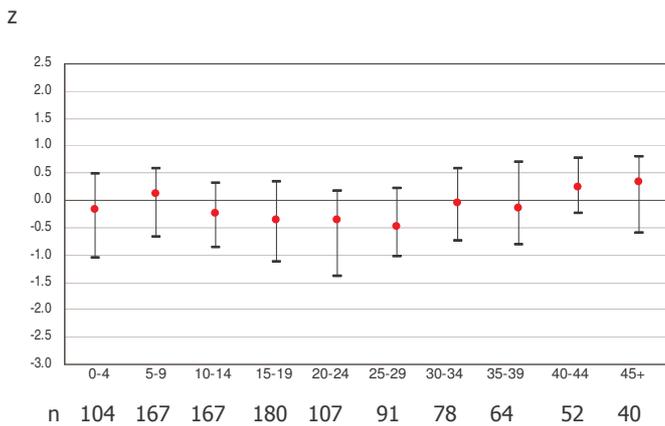
Israel



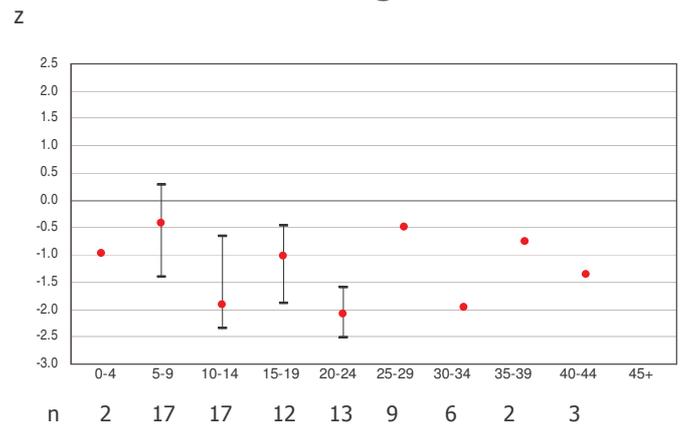
Italy



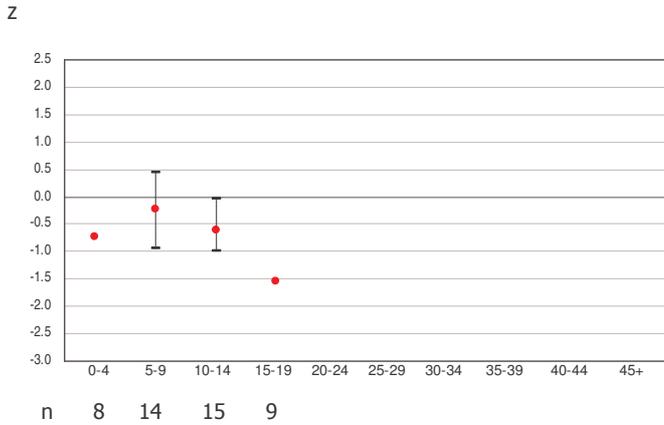
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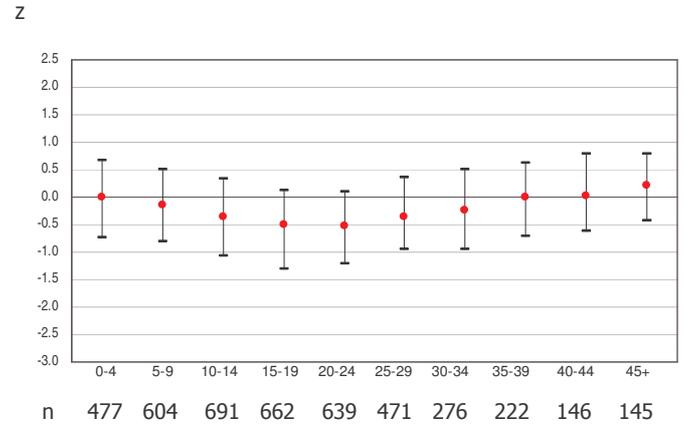
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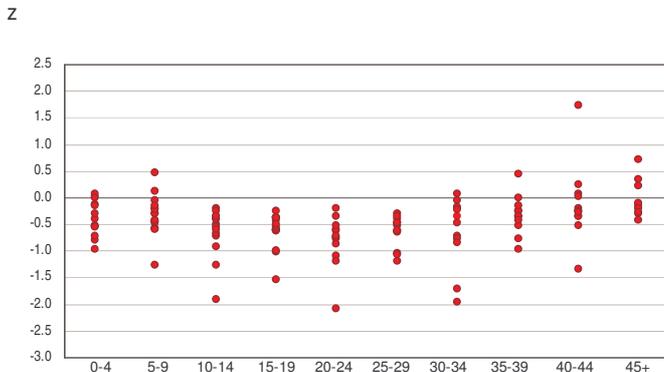
Slovenia



United Kingdom



All countries

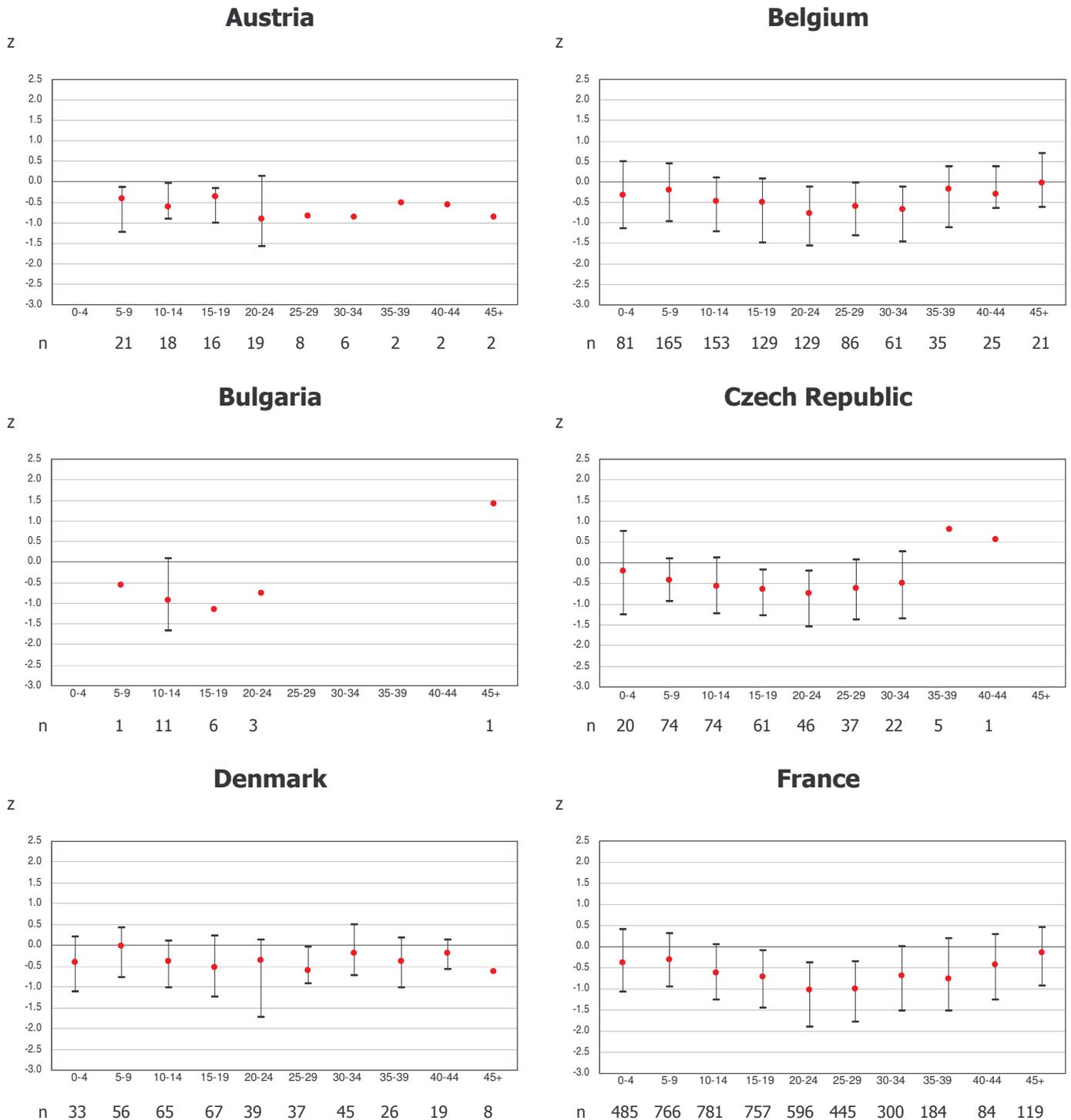


International references¹ were used to compute z-scores.
For groups with n<10, 25th and 75th percentiles were not computed.

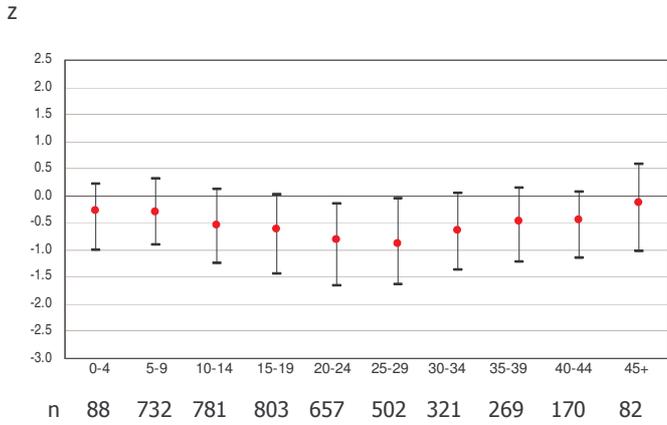
¹ Kuczmarski RJ, Ogden CL, Guo SS et al. 2000 CDC growth charts for the United States: Methods and development. National Center for Health Statistics. Vital Health Stat 2002;11(246):1-190.

Figure 12 Quartiles of z-scores for BMI, by age (years)

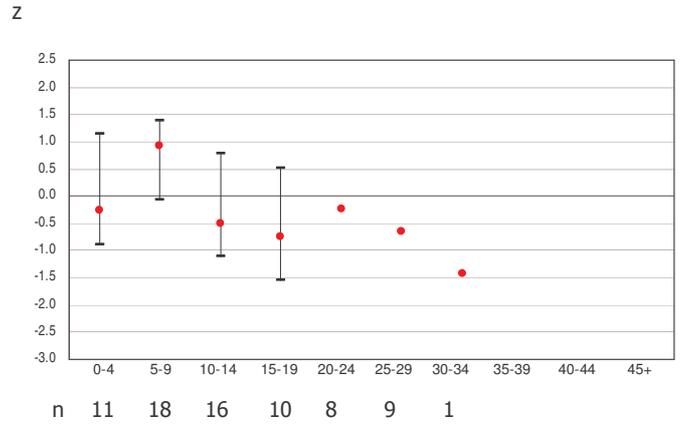
75th percentile
median
25th percentile



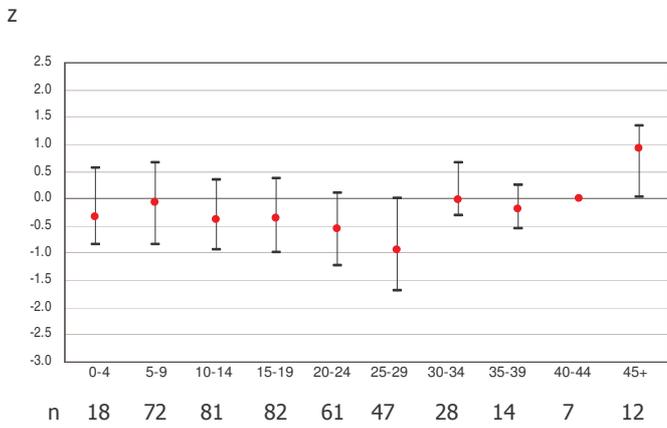
Germany



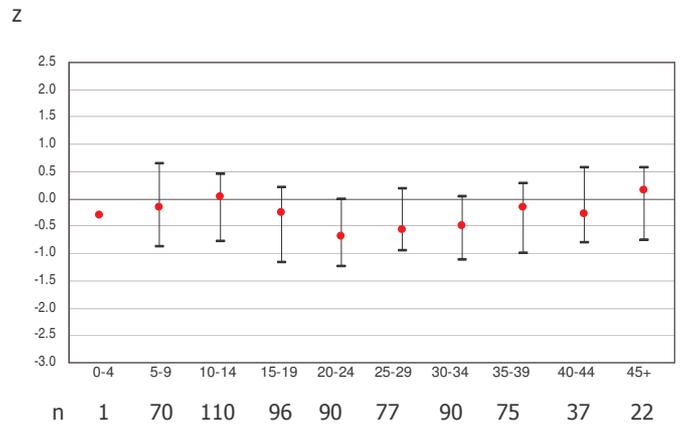
Greece



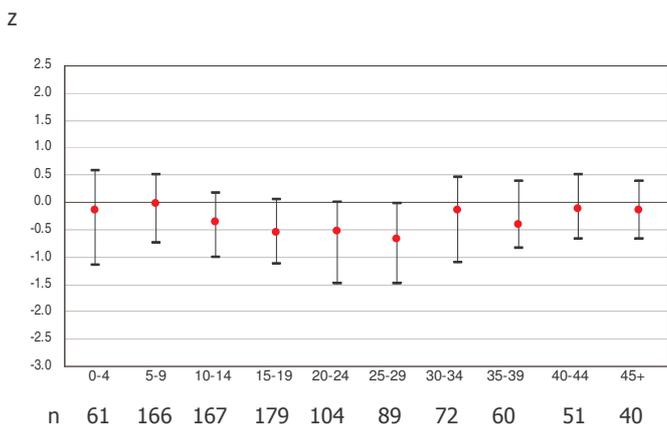
Israel



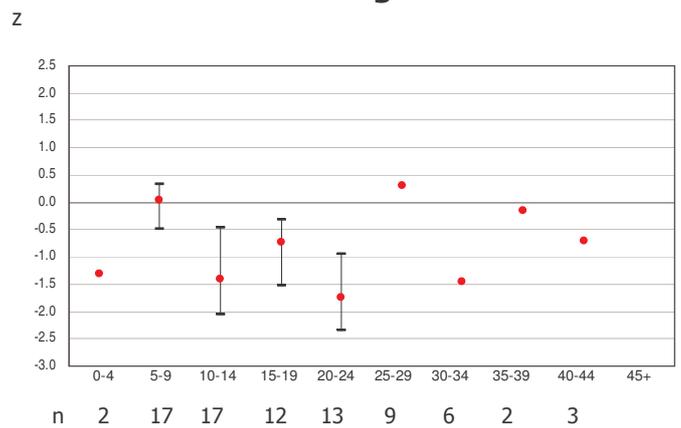
Italy



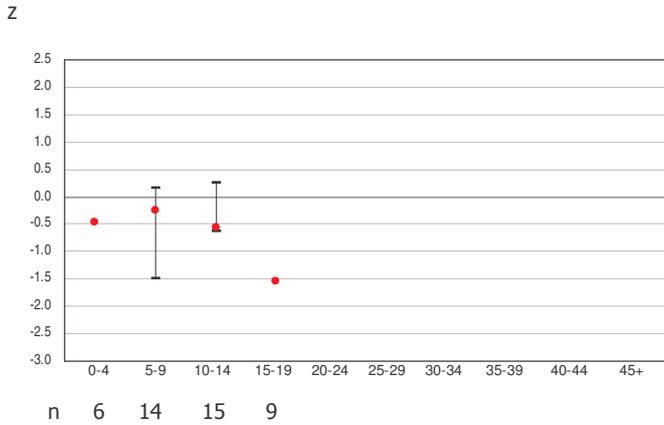
Netherlands



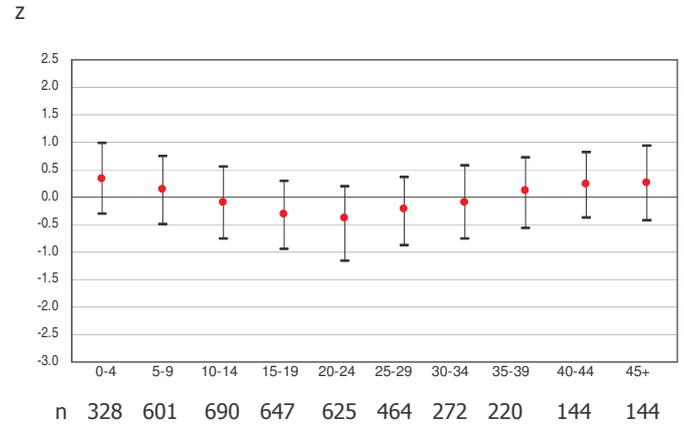
Portugal



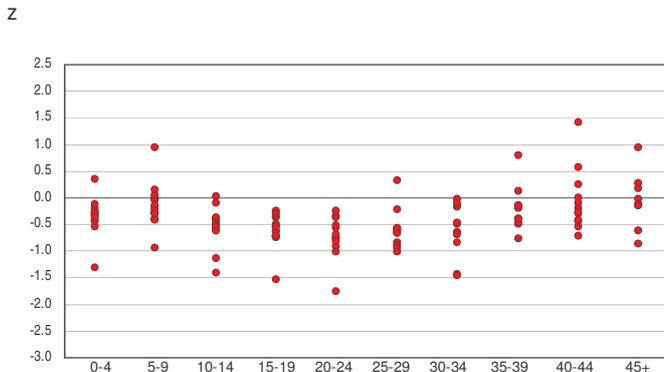
Slovenia



United Kingdom



All countries



Patients below 2 years of age were excluded from the analysis.
 International references¹ were used to compute z-scores.
 For groups with n<10, 25th and 75th percentiles were not computed.

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

THERAPY

Table 7.1 Therapy: use of drugs during 2007 (%)

	hypertonic NaCl		antibiotic		broncho-dilators		Oxygen		rhDNase		macrolide	
	missing values	yes	missing values	yes	missing values	yes	missing values	yes	missing values	yes	missing values	yes
A	-	50.0	-	35.3	-	81.0	-	4.3	-	60.3	-	12.9
B	-	21.5	4.9	50.4	-	62.6	0.1	3.3	100	-	-	34.0
BG	1.1	-	1.1	3.2	2.1	9.5	1.1	4.2	1.1	87.4	2.1	-
CZ	21.5	3.6	21.5	6.8	21.5	29.3	21.5	2.6	21.5	45.6	21.5	14.1
DK	100.0	-	100.0	-	100.0	-	100.0	-	100.0	-	100.0	-
F	-	2.0	-	37.3	-	42.7	-	5.6	-	41.5	-	38.1
D	100.0	-	2.5	39.2	100.0	-	0.5	6.2	100.0	-	100.0	-
GR	0.8	-	15.7	48.8	12.4	33.9	9.9	1.7	12.4	36.4	13.2	22.3
H	100.0	-	97.6	2.5	100.0	-	100.0	-	97.9	2.1	100.0	-
IL	100.0	-	100.0	-	100.0	-	100.0	-	100.0	-	100.0	-
I	100.0	-	-	39.4	-	58.0	-	3.5	-	25.5	100.0	-
NL	22.9	4.5	14.7	31.0	22.1	20.9	25.4	5.4	0.5	55.1	22.9	26.8
P	51.7	-	53.5	28.5	100.0	-	51.7	1.7	100.0	-	54.3	14.7
BY	100.0	-	100.0	-	100.0	-	100.0	-	100.0	-	100.0	-
SI	2.0	90.0	6.0	6.0	6.0	10.0	-	-	2.0	52.0	8.0	16.0
UK	-	3.7	-	46.4	-	42.5	20.1	3.5	-	28.8	-	25.4

Table 7.2 Therapy: use of drugs during 2007 (%)

	ursodeoxycholic acid		pancreatic enzymes	
	missing values	yes	missing values	yes
A	-	25.0	-	92.2
B	5.3	25.6	5.1	81.6
BG	2.1	2.1	2.1	95.8
CZ	21.5	30.1	100.0	-
DK	100.0	-	-	95.1
F	-	25.3	-	78.8
D	0.5	46.6	0.5	89.9
GR	13.2	36.4	14.1	83.5
H	100.0	-	100.0	-
IL	100.0	-	100.0	-
I	-	28.2	-	73.0
NL	36.0	17.4	11.1	78.5
P	100.0	-	-	80.2
BY	100.0	-	100.0	-
SI	4.0	54.0	-	96.0
UK	16.9	15.3	16.5	74.6

Figure 13 Inhaled continuous (>3 months) hypertonic NaCl during 2007

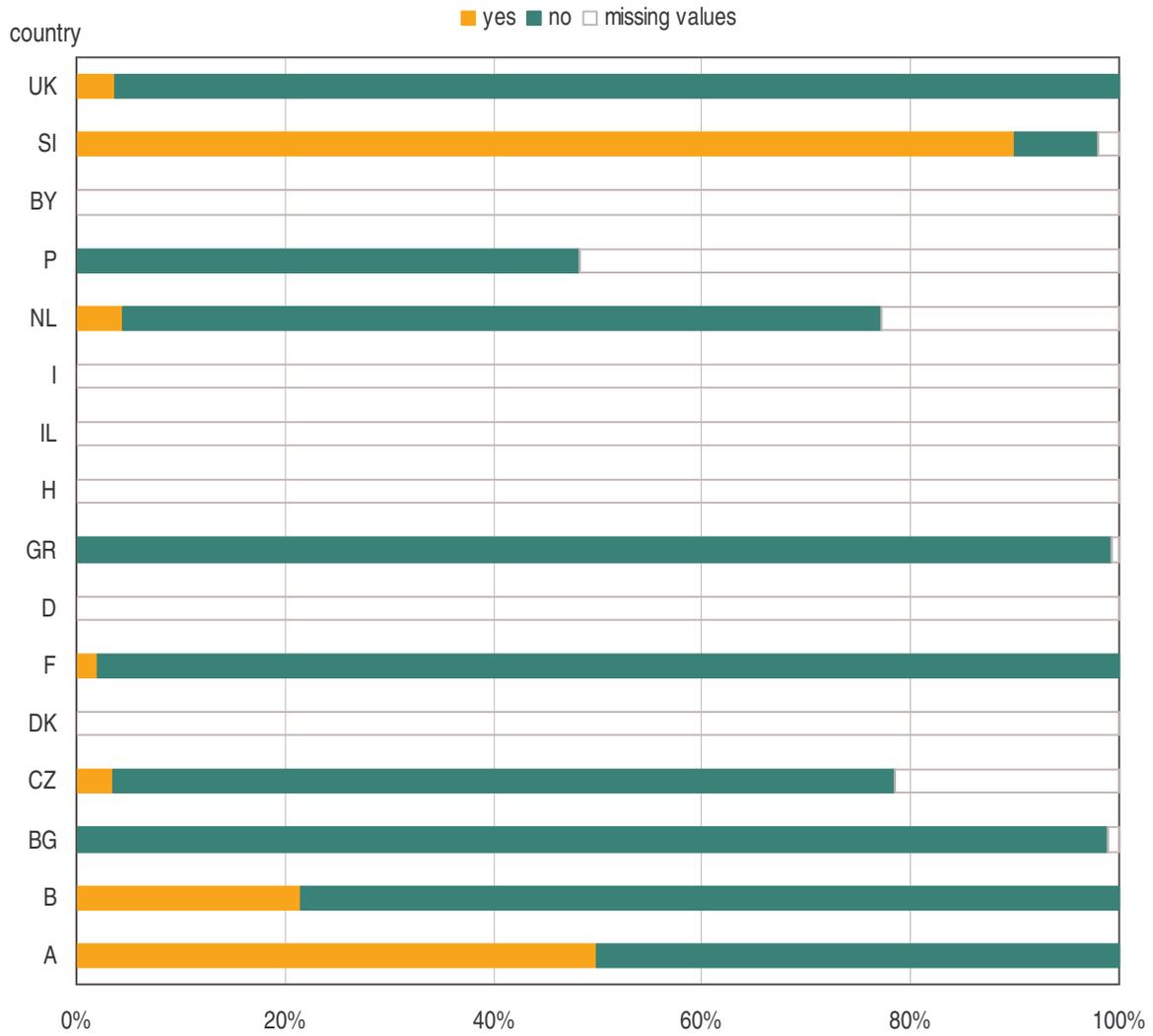


Figure 14 Inhaled continuous (>3 months) antibiotic during 2007

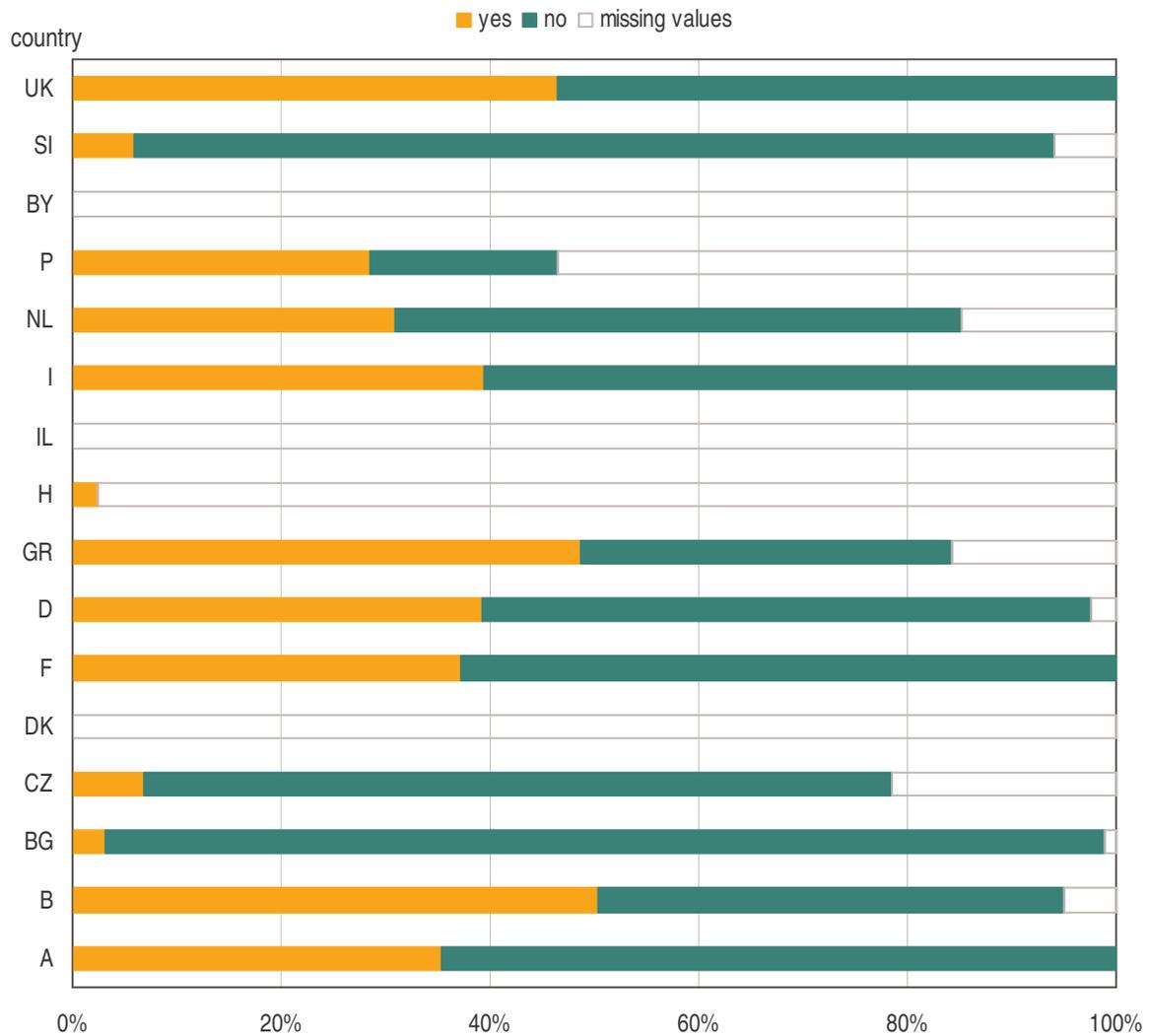


Figure 15 Inhaled continuous (>3 months) bronchodilators during 2007

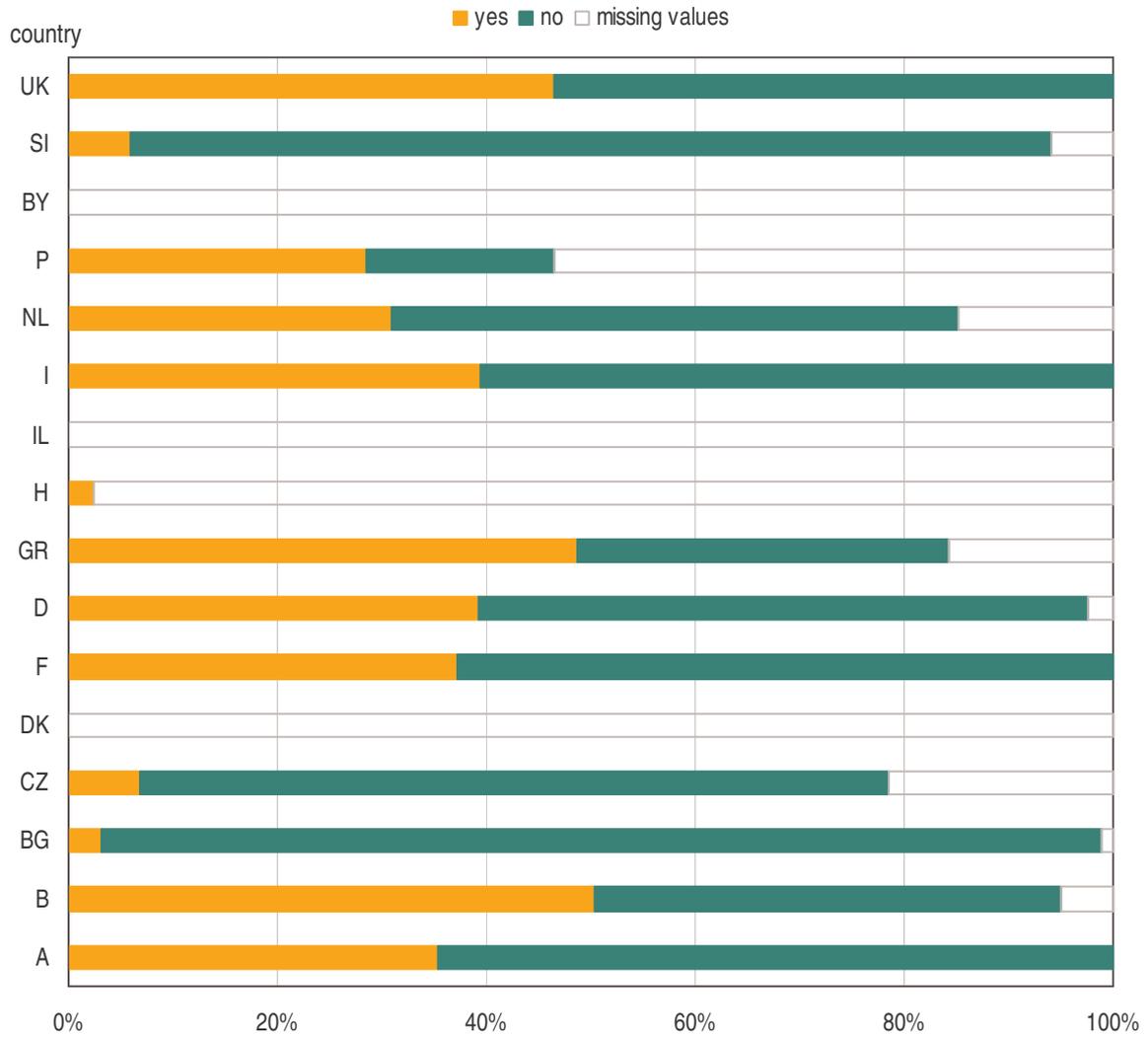


Figure 16 Oxygen therapy during 2007

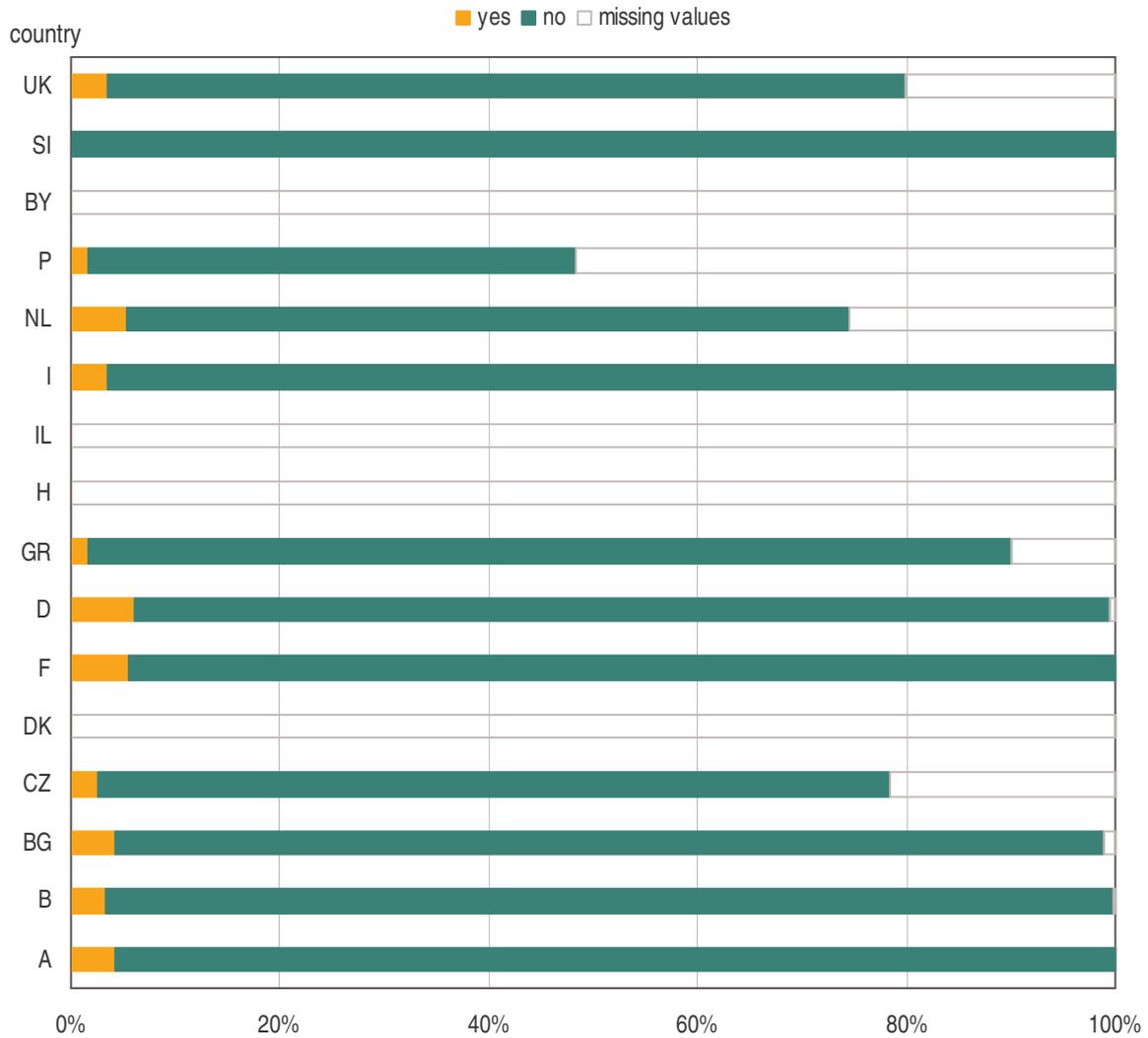


Figure 17 Use of rhDNase during 2007

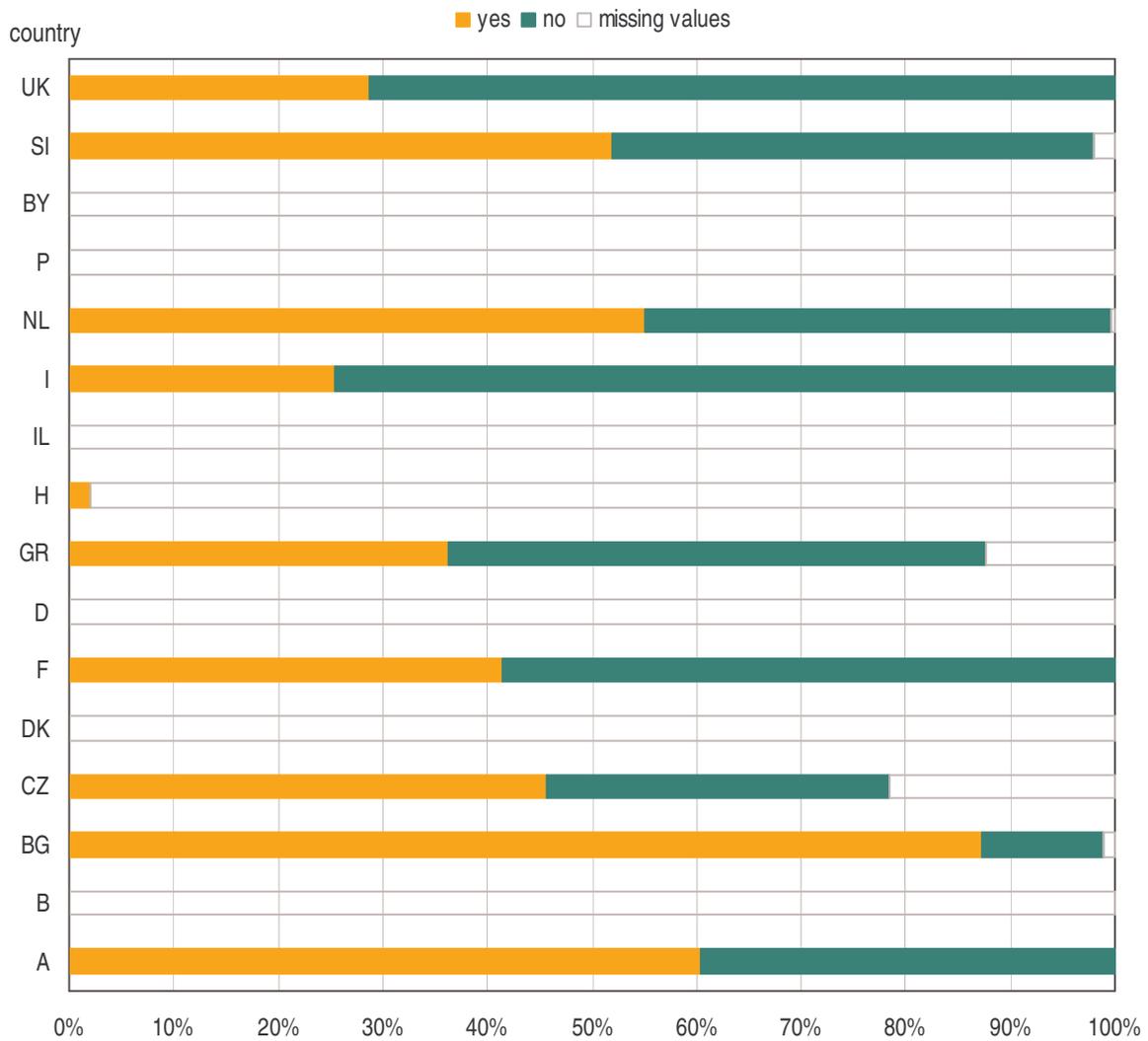
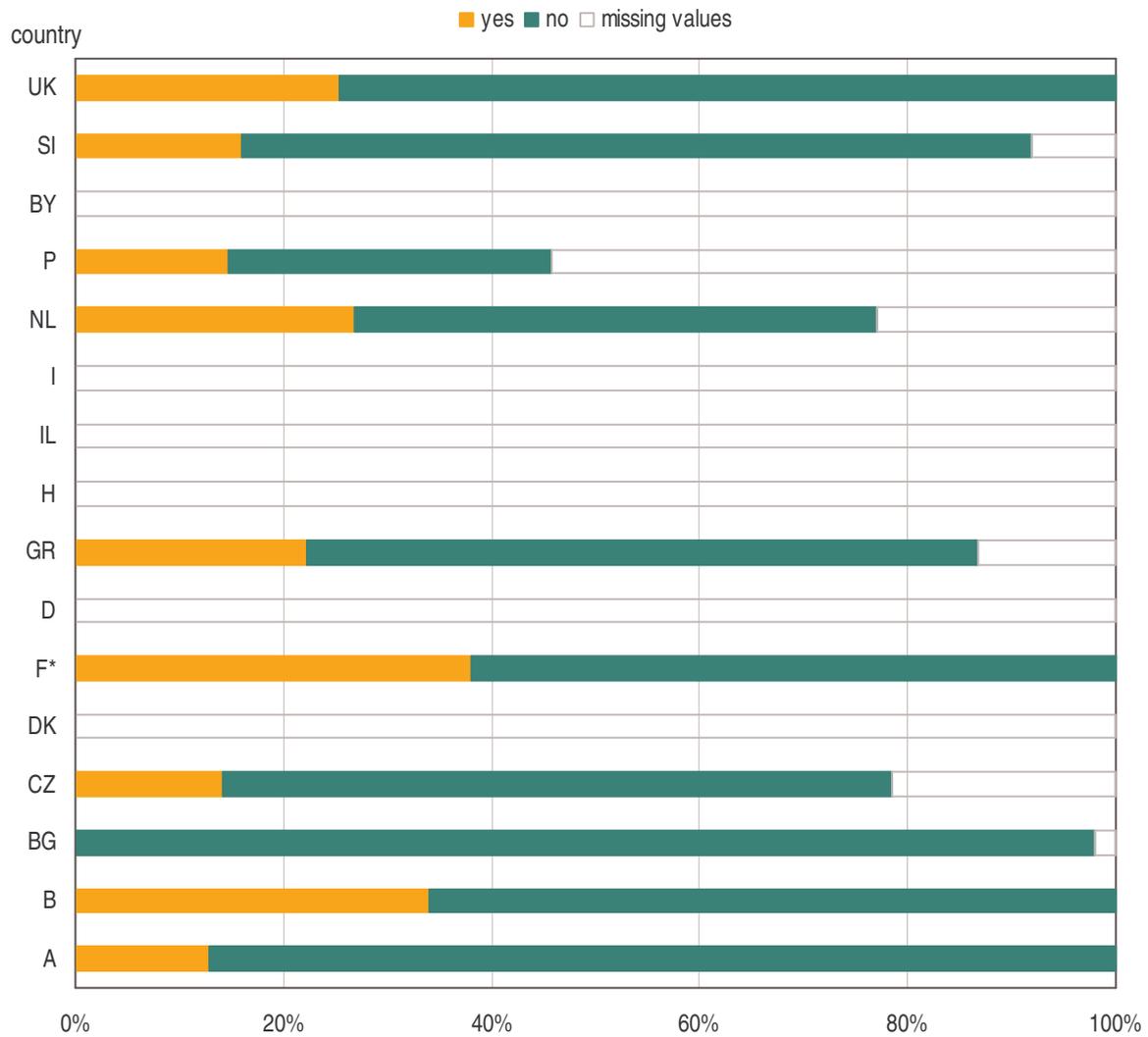
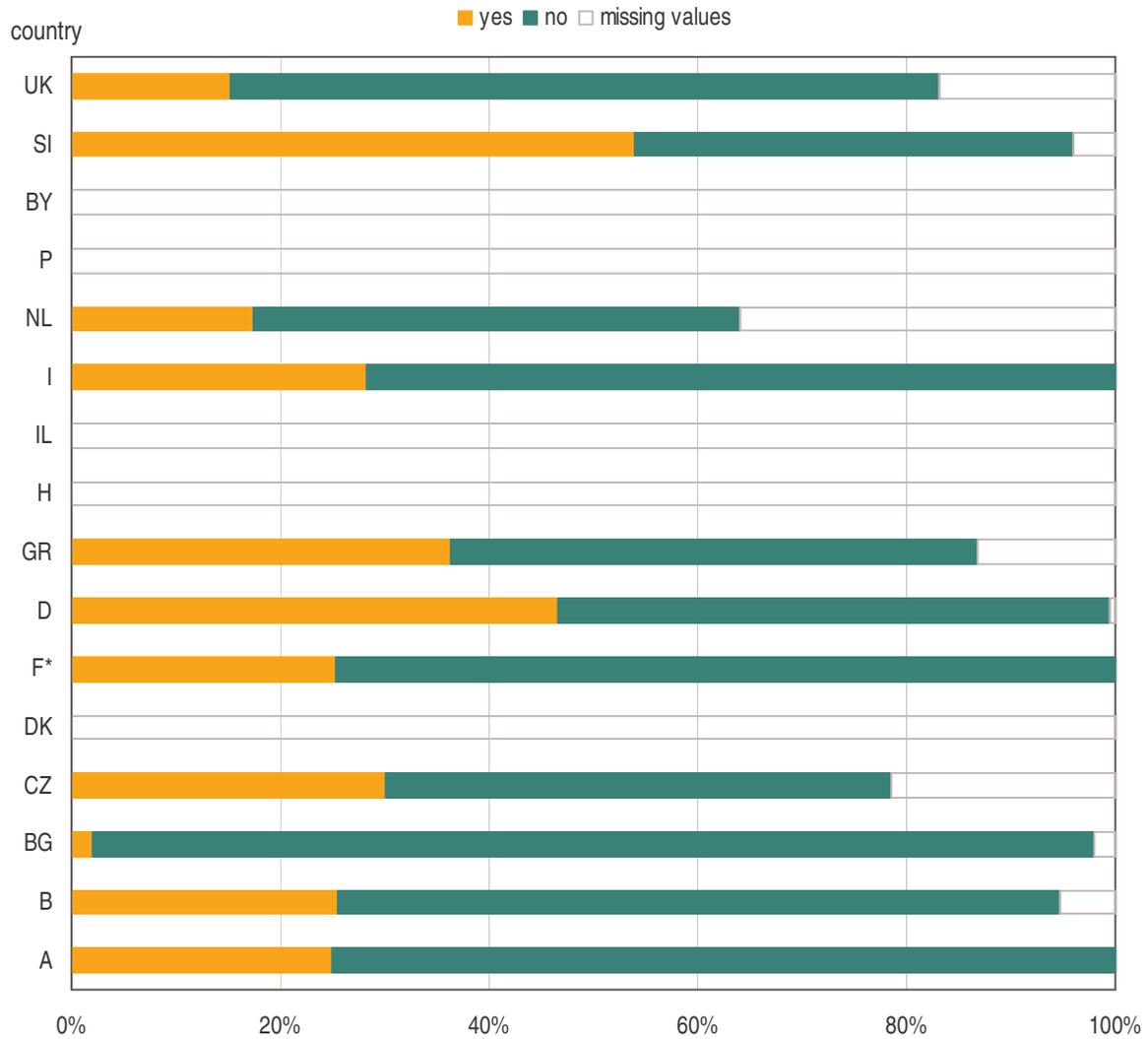


Figure 18 Use of continuous (>3 months) macrolides during 2007



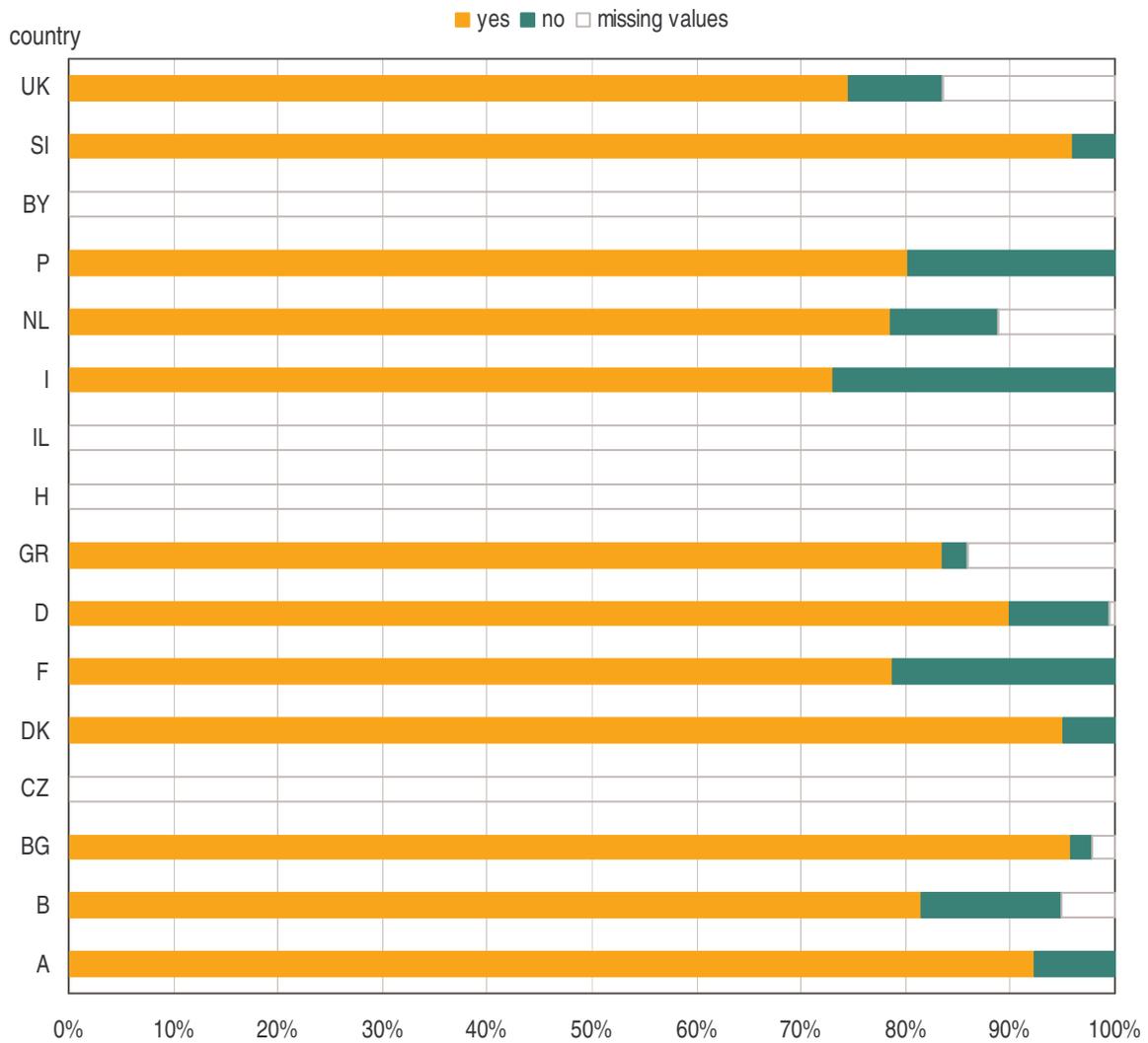
* Use of continuous (>3 months) azithromycin during 2007.

Figure 19 Use of ursodeoxycholic acid during 2007



* Use of continuous (>3 months) ursodeoxycholic acid during 2007.

Figure 20 Use of pancreatic enzymes



COMPLICATIONS

From Table 8 throughout Table 13, country breakdown is not shown due to small proportion of positive answers.

Table 8 Presence of ABPA during 2007

ABPA during 2007	N	%
no	12228	60.52
yes	786	3.89
missing values	7190	35.59

Table 9 Presence of diabetes (daily insulin treated) during 2007

Diabetes during 2007	N	%
no	16827	83.29
yes	2118	10.48
missing values	1259	6.23

Table 10 Presence of pneumothorax requiring chest drain during 2007

Pneumothorax during 2007	N	%
no	17122	84.75
yes	125	0.62
missing values	2957	14.64

Table 11 Presence of liver disease during 2007

Liver disease during 2007	N	%
no	6862	33.96
cirrhosis with hypertension/hypersplenism	234	1.16
cirrhosis without hypertension	22	0.11
liver disease without cirrhosis	507	2.51
cirrhosis, hypertension unknown	82	0.41
missing values	12497	61.85

For France information was available only for cirrhosis/portal hypertension.

Table 12 Presence of hemoptysis (major over 250 ml) during 2007

Hemoptysis during 2007	N	%
no	16399	81.17
yes	369	1.83
missing values	3436	17.01

Table 13 Occurrence of malignancy over the life of patient

Malignancy during life	N	%
never	11348	56.17
ever	65	0.32
missing values	8791	43.51

Pancreatic status should be assessed according to the following criteria, but, due to high frequencies of missing values, it was not possible to assess it.

Pancreatic insufficiency

Fecal elastase <200 µg/g (twice) and Fecal fat high (twice)

Pancreatic sufficiency

Fecal elastase ≥200 µg/g (twice) and Fecal fat normal (twice)

TRANSPLANTS

Table 14.1 Lung transplantation: frequencies (%)

country	transplantation performed during life		
	missing information	never	ever
A	-	115 (99.14)	1 (0.86)
B	-	958 (91.06)	94 (8.94)
BG	-	95 (100.00)	-
CZ	502 (100.00)	-	-
DK	-	400 (89.49)	47 (10.52)
F	-	4870 (94.62)	277 (5.38)
D	23 (0.46)	4923 (97.70)	93 (1.85)
GR	13 (10.74)	108 (89.26)	-
H	-	553 (96.68)	19 (3.32)
IL	507 (100.00)	-	-
I	-	738 (95.35)	36 (4.65)
NL	1006 (90.39)	91 (8.18)	16 (1.43)
P	-	113 (97.41)	3 (2.58)
BY	145 (100.00)	-	-
SI	-	50 (100.00)	-
UK	-	4396 (99.73)	12 (0.27)
<i>total</i>	<i>2196 (10.87)</i>	<i>17410 (86.17)</i>	<i>598 (2.96)</i>

Table 14.2 Year of lung transplantation: frequencies (%)

country	transplantation performed		
	before this year	during this year	during an unknown year
A	1 (0.86)	-	-
B	78 (7.41)	16 (1.52)	-
BG	-	-	-
CZ	-	-	-
DK	45 (10.07)	2 (0.45)	-
F	214 (4.16)	63 (1.22)	-
D	78 (1.55)	13 (0.26)	2 (0.04)
GR	-	-	-
H	19 (3.32)	-	-
IL	-	-	-
I	28 (3.62)	8 (1.03)	-
NL	7 (0.63)	5 (0.45)	4 (0.36)
P	2 (1.72)	1 (0.86)	-
BY	-	-	-
SI	-	-	-
UK	-	-	12 (0.27)
<i>total</i>	<i>472 (2.34)</i>	<i>108 (0.53)</i>	<i>18 (0.09)</i>

Table 15 Liver transplantation: frequencies (%)

country	transplantation performed during life		
	missing information	never	ever
A	-	111 (95.69)	5 (4.31)
B	-	1045 (99.33)	7 (0.67)
BG	-	95 (100.00)	-
CZ	502 (100.00)	-	-
DK	-	444 (99.33)	3 (0.67)
F	-	5124 (99.55)	23 (0.45)
D	23 (0.46)	5002 (99.27)	14 (0.28)
GR	15 (12.40)	106 (87.60)	-
H	572 (100.00)	-	-
IL	507 (100.00)	-	-
I	-	773 (99.87)	1 (0.13)
NL	1077 (96.77)	34 (3.05)	2 (0.18)
P	-	115 (99.14)	1 (0.86)
BY	145 (100.00)	-	-
SI	-	50 (100.00)	-
UK	-	4404 (99.91)	4 (0.09)
<i>total</i>	<i>2841 (14.06)</i>	<i>17303 (85.64)</i>	<i>60 (0.30)</i>

All liver transplantations were performed before 2007, except 2 transplantations performed in Germany and 6 performed in France in 2007, and 4 transplantations performed in United Kingdom in unknown years.