2008-2009

ECFS Patient Registry

Annual Data Report

European Cystic Fibrosis Society
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Denmark

ECFS Patient Registry

Annual Data Report

2008-2009 data

Table of contents

Preface **3**

To the cystic fibrosis patients **5**

List of centres and national registries that provided the data **6**

Authors **8**

Introduction **9**

The European Cystic Fibrosis Society Patient Registry (ECFSPR) *9*

General considerations *9*

Abbreviations and terms *10*

Summary of data report **12**

Data report **13**

1. Demographics *13*

2. Diagnosis *22*

3. Genetics *29*

4. Lung function *36*

5. Microbiology *45*

6. Nutrition *53*

7. Complications and therapy *75*

8. Transplantation *91*

9. Mortality *93*

Publications **95**

Contacts and information **95**

Partners and sponsors **95**

Appendix 1: technical notes **96**

Appendix 2: list of variables, inclusion criteria and definitions for the ECFSPR **97**

Preface

This report from the European Cystic Fibrosis Society Patient Registry (ECFSPR) contains epidemiological description of data from national CF registries and individual CF centres throughout Europe and neighbouring countries. It is the fifth official report, and includes some significant improvements and additions, as described below.

The ECFSPR has been through a major make-over since the latest report on 2007 data that was published in 2010.

The collection of data has been made more structured and has been fully computerised: data are directly sent by the users in an encrypted form to the central database. This process has taken some time and considerable effort from all parties involved: national registries, individual centres and their national coordinators, the ECFSPR help-desk and the statisticians team.

With this valuable and highly appreciated contribution from all parties, it is with great pleasure that we present this report with demographic and clinical data of almost 18,000 CF patients seen in 2009 and living in 20 countries – by far the greatest collection of European countries presenting clinical data in CF so far.

The data for the ECFSPR are collected through ECFRecord, software developed for the ECFSPR, and are sent to a central database either through the uploading and transmission of data files - where a national registry already exists - or through the manual data-entry feature. The national registries contribute the majority of patient data in the ECFSPR, but individual centres and new countries are joining at a fast rate. Compared to the first reports where 100% of the data came from national registries, the individual centres now contribute more than 10%, and this will increase even more in 2010. The list of contributing countries and individual centres can be found on page 6.

The national registries already publish their data in national annual reports, but carrying out the same statistical analyses on the different countries' data and presenting the results in the same format allows a comparison that is not possible simply by comparing the individual reports. Some difficulties exist even in this kind of comparison and the methods we have used to tackle these are described in Appendix 1.

The individual centres that contribute to the ECFSPR also get the benefit of a "country manager" option. If the participating centres of a country agree to appoint a country manager who can access anonimised data of those centres, a national CF registry in that country is thus created. Additionally, the individual centres, for the first time this year, will receive a centre report giving an epidemiological description of the centre data, including comparison with other centres within the same country and with other countries.

Another novelty this year is that we have aimed to make the report "patient friendly". The data in the report are presented in tables and graphs as usual, but this year we have added more information on how to read the graphs and tables and how to interpret the results. The ECFSPR

Annual Report uses data on CF patients, and we would like them to be able to understand and make use of the report contents as well.

In addition to being the basis for this annual report, the ECFSPR data are used for research and other purposes for the benefit of CF patients. These include epidemiological research, identification of patients eligible for clinical trials, and data needed for pharmaceutical companies in order to apply for approval of new treatments. To handle the data requests with the maximum consideration we have developed a Standard Operating Procedure, and all requests for data need to be approved by both the ECFSPR Scientific Committee and the Steering Group. If the requests come from the industry they will be reviewed by the Clinical Trial Network too. All governing bodies include patient representatives, and any applications must fulfil the data protection regulations concerning patient anonymity. We are very anxious to bring the data to good use for the current and future benefit of CF patients.

I would like to take this opportunity to thank the national registries and the individual centre representatives for their willingness to participate in the project, sometimes working under a tight schedule to meet our deadlines. Thanks also for the input and valuable comments from the members of the Steering Group and the Executive Committee; it is a privilege to work with such dedicated people.

Thanks also to the staff at the Help-Desk, Patrizia Iansa and Alice Fox for trying to sort out software issues in 21 countries with even more hospital IT systems, and in various languages – a challenging task. Huge thanks to the statisticians, Laura Viviani and Anna Zolin for their meticulous and professional treatment of the data. Finally, a great thanks to Jacqui van Rens, the ECFSPR Executive Coordinator, who has been coordinating everything, from data collection and meeting arrangements to handling of data requests, to everybody's satisfaction.

But most of all, I would like to thank the CF patients all over Europe for their willingness to participate in this project. The cooperation of the patients is essential for the success of the Patient Registry, both by giving us their permission to use their data, but also by encouraging their doctors to participate.

June 2012

Hanne Vebert Olesen, MD, PhD
ECFSPR Executive Director

To the cystic fibrosis patients

This report is about you and how cystic fibrosis (CF) affects patients all over Europe. It is based on the data collected by individual CF centres and the National CF registries which take part in the European Cystic Fibrosis Society Patient Registry (ECFSPR). Unlike the former ECFSPR reports, where tables and graphs were created mainly with doctors, researchers and health care professionals in mind, this year, we decided to create a more patient-friendly report, so as to be sure that all the CF patients will be able to read and understand the contents of the ECFS Patient Registry report more easily. That's why we have added more background notes which explain how we collect data from various sources, and which kind of data transformations we had to perform before analysing. We have made the explanations to the graphs and tables more informative and added instructions on how to read the various graphs. We have also included an *abbreviations and terms* section with some further explanations of statistical and medical terms.

We hope that you will find this report interesting and easy to understand. You are always welcome to contact us if there is something that is unclear, or if you have ideas on how to do it better next year. You can contact us by email: ecfs-pr@uzleuven.be. For discussions about the results in your country we encourage you to contact your own centre. You can find more information about the ECFSPR on the patient-dedicated pages of our website, at this link: http://www.ecfs.eu/projects/ecfs-patient-registry/information-about-ecfspr-cf-patients.

List of centres and national registries that provided the data

Country	Centre/National registry name	Contact person
Austria	6 individual centres: *CF Centre, Paediatrics and Adolescent Medicine, Medical University of Vienna* *Dept. of Thoracic Surgery, Medical University of Vienna* *CF Centre, Paediatrics and Adolescent Medicine, Teaching Hospital, Steyr* *CF Centre, Paediatrics and Adolescent Medicin, Klinikum Wels-Grieskirchen* CF Centre, University Hospital for Children and Adolescents, Innsbruck *CF Centre, Landes-Frauen- und Kinderklin, Linz*	Thomas Frischer Thomas Frischer Peter Jaksch, Stefanie Veith Josef Emhofer Elisabeth Steiner Helmut Ellemunter Klaus Schmitt, Maria Bauer
Belgium	Belgisch Mucoviscidose Register - Registre Belge de la Mucoviscidose	Herwig Jansen Muriel Thomas
Czech Republic	Cystic Fibrosis Registry of the Czech Republic	Pavel Drevinek Milan Macek
Denmark	Cystic Fibrosis Registry Denmark	Hanne V. Olesen Tania Pressler
France	Registre Francais de la Mucoviscidose	Sophie Ravilly Lydie Lemonnier
Germany	Qualitätssicherung Mukoviszidose	Martin Stern Marguerite Höner Paul Wenzlaff
Greece	1 individual centre: CF Centre of Aristotelian University of Thessaloniki	Elpis Hatziagorou John Tsanakas Elpis Hatziagorou Maria Fotoulaki John Kioumis
Hungary	Cystic Fibrosis Registry of Hungary	Rita Ujhelyi Geza Marsal
Ireland	Cystic Fibrosis Registry of Ireland	Godfrey Fletcher
Israel	National registry with 6 single centres reporting directly Hadassah Medical Centre, Jerusalem Schneider Children's Hospital, Petach Tiqva CF Centre,Carmel Medical Centre, Haifa Pediatric Pulmonology, Meyer Children's Hospital, Rambam Hospital, Haifa Safra Children's Hospital, Tel Hashomer Soroka Medical Centre, Be'er Sheva	Meir Mei-Zahav Eitan Kerem Eitan Kerem, Thea Pugatsch Meir Mei-Zahav Josef Rivlin, Michal Gur Lea Bentur, Galit Livnat Ori Efrati, Yael Soffer Aviram Micha
Italy	1 individual centre: Centro Fibrosi Cistica - Azienda Ospedaliero Universitaria di Verona - OCM	Baroukh M. Assael Patrizia Iansa Emily Pintani
Latvia	1 individual centre: *CF Centre, Children's Clinical University Hospital, Riga*	Karina Mahlina
The Netherlands	Dutch Cystic Fibrosis Registry	Vincent Gulmans
Portugal	2 individual centres: CF Centre, Hospital de Santa Maria, Lisbon *Hospital Dona Estefânia*	Celeste Barreto Celeste Barreto, Luisa Pereira Jose Cavaco

Country	Centre/National registry name	Contact person
Republic of Moldova	Cystic Fibrosis Registry of Moldova	Svetlana Sciuca
Serbia	1 individual centre: *National centre for Cystic Fibrosis, Mother and Child Health Institute of Serbia, "Dr. Vukan Cupic", Belgrade*	Predrag Minic Predrag Minic, Natasa Savic
Slovenia	2 individual centres: Pulmonology Dept, University Children's Hospital, Ljubljana Department of Pulmonary Diseases and Allergy, University Medical Centre, Ljubljana	Uros Krivec Uros Krivec, Jasna Rodman Barbara Salobir
Spain	8 individual centres: *CF Unit, Hospital de Sabadell. Corporació Parc Taulí, Barcelona* *CF Unit, CF Unit, Cruces University Hospital, Bizkaia* *CF Unit, Ramón y Cajal University Hospital, Madrid* *Pulmonology Dept, University Hospital de la Princesa, Madrid* *CF Unit, Hospital del Niño Jesús Madrid* *CF Unit, Hospital Universitaria Infantil La Paz, Madrid,* *Pediatric Pulmonology, Materno-Infantil, Carlos Haya University Hospital, Malaga* *Lung Transplant and Cystic Fibrosis Unit, Hospital Universitario La Fe, Valencia*	Carlos Vazquez-Cordero Montserrat Bosque Garcia Òscar Asensio, Miguel Garcia Carlos Vazquez Cordero Adelaida Lamas Ferreiro Rosa Maria Giron Moreno Jose R. Villa, Juan Jose Asensio Carmen Antelo, Maribel Barrio Francisco Javier Perez Frias, Estela Perez Ruiz Amparo Solé Jover, Mónica Cebrián Pinar
Sweden	4 individual centres: *West Swedish CF Centre and Sahlgrenska University Hospital, Gothenburg* *Pediatric Dept, Lund University Hospital, Lund* *Stockholm CF Centre, Karolinska University Hospital Huddinge, Stockholm* *Uppsala CF Centre, Uppsala University Hospital, Uppsala*	Anders Lindblad
Switzerland	5 individual centres: *CF Unit – Pediatric Department, Spitalnetz, Bern* *Dept of Ped and Dept of Internal Med, CF and Pulmonology Unit, Inselspital Berne* *CF and Pulmonology Unit, Pediatric Department, Vaudois Univ. Hospital Lausanne* *Dept of Pediatric Pulmonology, Ostsweitzer Kinderspital, St Gallen* *Kinderspital Zürich, Abt für Pneumologie; Zürich*	Martin Schöni Andreas Jung Carlo Mordasini Reta Fischer Martin Schöni Hafen Gaudenz Marie Hofer Jürg Barben Andreas Jung

List of individual centres and national registries contributing to the ECFSPR. New participants since last report of 2007 data are in *italic*. Some countries are new in the ECFSPR, other countries have increased the number of participating centres, some countries are back after a year or two of absence, and some centres and countries have been with us for several years. The contact persons in large print are the country representatives in the ECFSPR Steering Group, and for some national registries also the database manager (underlined).

Authors

For this report, the tables and graphs were written, commented and/or revised by:

Laura Viviani and **Anna Zolin**, statisticians, Dipartimento di Scienze Cliniche e di Comunità, Università degli Studi di Milano, Italy;
Jacqui van Rens, ECFSPR Executive Coordinator, Belgium;
Patrizia Iansa and **Alice Fox**, ECFSPR Help-Desk, Italy;
Angeliki Preftitsi, Greece and **Ulrike Pypops**, Belgium: CF Europe representatives in the ECFSPR;
Anil Mehta, United Kingdom; **Sophie Ravilly**, France; **Vincent Gulmans**, Netherlands: members of the ECFSPR Executive Committee;
Contributing country managers and national representatives (see names above);
Hanne Vebert Olesen, ECFSPR Executive Director, Denmark.

We would like to thank Maddalena Plebani and Anna Bossi for their help with the editing of tables and graphs and Jelle Gulmans for the help with the maps.

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Introduction

The European Cystic Fibrosis Society Patient Registry (ECFSPR)

The ECFSPR collects demographic and clinical data on cystic fibrosis patients from Europe and neighbouring countries. Data are collected using a common set of variables and definitions, and are then sent to the ECFSPR via one of these methods, both using ECFRecord, the ECFSPR software:

- National CF registries (or individual centres with local databases) extract data from their own database and import them into ECFRecord;
- Individual centres enter patient data directly into ECFRecord using the manual data entry module.

Collection of data locally must be approved by local data protection authorities and must adhere to EU data protection legislation. Data are anonymous in the central database, and year and month of birth and random centre numbers are used as identifiers. Use of data for scientific purposes is only possible after application and approval by the Scientific Committee as well as the country representatives in the Steering Group.

For more information, please visit our website http://www.ecfs.eu/projects/ecfs-patient-registry/intro.

General considerations

For the national registries, some of the definitions and data coding do not fully correspond to the ECFSPR ones, either because some pieces of information are not collected by the national registries or they are collected in a different way. When the national registries upload their data, they are also asked to state in a document whether their variables definitions meet the ECFSPR definitions. If the definitions present major discrepancies, those variables are omitted from the annual report, or in the case of minor discrepancies, a footnote is added to the graphs and tables explaining the difference. For example, the ECFSPR collects the information on presence of chronic *Pseudomonas aeruginosa* (Ps. A.) according to the modified Leeds criteria and/or elevated Pseudomonas antibodies (see Appendix 2). If one national registry collects such information as "at least one positive Ps. A. culture this year", this information would be too different from the definition of **chronic** Ps. A. of the ECFSPR and we would set this variable to "missing" for that country. If one country defines chronic Ps. A. as "presence of more than four positive cultures in 6 months", this variable would be included in the annual report because the definition is much closer to the ECFSPR definition, however a footnote will be added to the relevant tables and graphs.

You will find some differences in the findings between the national registries' reports and this report. This is because some variables are recoded or computed in different ways. For example, for lung function values, like FEV1, the raw data, 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 to be able to compare lung function between patients

and countries. We used common reference populations (one for children and one for adults) for all data when calculating the values in percent of predicted from the raw data. Slightly different values can be found 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.

If a country does not collect a certain variable (or if it is completely different from our definitions as described above), we omitted that country from the relevant graphs. The same happens for countries where the information is missing for more than 10% of the patients. All data will, however, be available in the tables. The number of missing values is important for the interpretation of the results, since it is impossible to know if a patient with missing value of e.g. a complication has this complication or not, making the given frequencies less accurate. For example, in a given country where 7% of the patients have liver disease, but where 20% of patients have unknown/missing information on liver disease, the true frequency of liver disease can be anything between 7 and 27%.

Abbreviations and terms

Country codes:

AT: Austria
BE: Belgium
CH: Switzerland
CZ: Czech Republic
DK: Denmark
DE: Germany
ES: Spain
FR: France
GR: Greece
HU: Hungary
IE: Ireland
IL: Israel
IT: Italy
LV: Latvia
MD: Republic of Moldova
NL: The Netherlands
PT: Portugal
RS: Serbia
SE: Sweden
SI: Slovenia

Medical abbreviations and terms:

FEV1: forced expiratory volume in one second (lung function parameter).
FEV1%: the FEV1 as a percentage of the average value for healthy people of the same age, height and sex.
BMI: body mass index (weight in kg/(height in m^2).
CFRD: CF related diabetes.
NaCl: sodium chloride – here: inhaled hypertonic saline.
rhDNase: ribosomal human DNase – marketed as Pulmozyme®.
Bronchodilator: medication that relaxes the muscles of the airways, used also for asthma.
ABPA: allergic broncho-pulmonary aspergillosis, a severe allergic reaction to the mould *Aspergillus.*
Meconium ileus: congenital obstruction of the gut with thick, sticky faeces.
Pneumothorax: collapsed lung, in CF usually because of severe lung damage.
Haemoptysis: coughing up blood. This happens frequently in small amounts in CF, so the complication we asked for here is major bleeding (more than 250 ml).
Pancreatic insufficiency: the absence of pancreatic enzymes in the gut leading to malnutrition if not treated (pancreatic sufficiency is therefore the presence of pancreatic enzymes in sufficient amounts).

Statistical abbreviations and terms:

N: the number of patients in a group.
N miss: number of missing values. It is the number of patients for whom the information was missing.
Min: minimum. It is the lowest value.
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.
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 are diagnosed before 1 month of age, and the other three quarters are diagnosed after 1 month of age.
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 3 years, the other quarter are diagnosed after 3 years.
Quartiles: The 25th Percentile, the median and the 75th percentile are collectively called quartiles, because they divide the set of measurements into quarters.
Z-score: it indicates how far (in other terms, how many standard deviations) a value is from the mean value of a reference population (see Appendix 1 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. 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 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.

Summary of data report

Outcome		Females	Males	Total
Patients registered this year	n	9,084	9,915	18,999
	(%)	(47.8)	(52.2)	
Age (years)	mean	18.3	18.8	18.6
	median	17.0	17.0	17.0
Patients over 18 years	%	46.8	49.1	48.0
Age at diagnosis	mean (years)	3.8	3.4	3.6
	median (months)	6.0	4.8	6.0
Patients with at least one F508del allele	%	82.8	83.2	83.0
Patients deceased during this year	n	94	76	170
	(%)	(1.0)	(0.8)	(0.9)
Age at death (years)	mean	24.2	29.9	26.7
	median	23.0	29.0	25.0
Patient living with lung transplant	n	409	395	804
	(%)	(4.6)	(4.0)	(4.3)
Patient living with liver transplant	n	41	52	93
	(%)	(0.5)	(0.5)	(0.5)

Note: Ireland contributed with data from 2008.

Data report

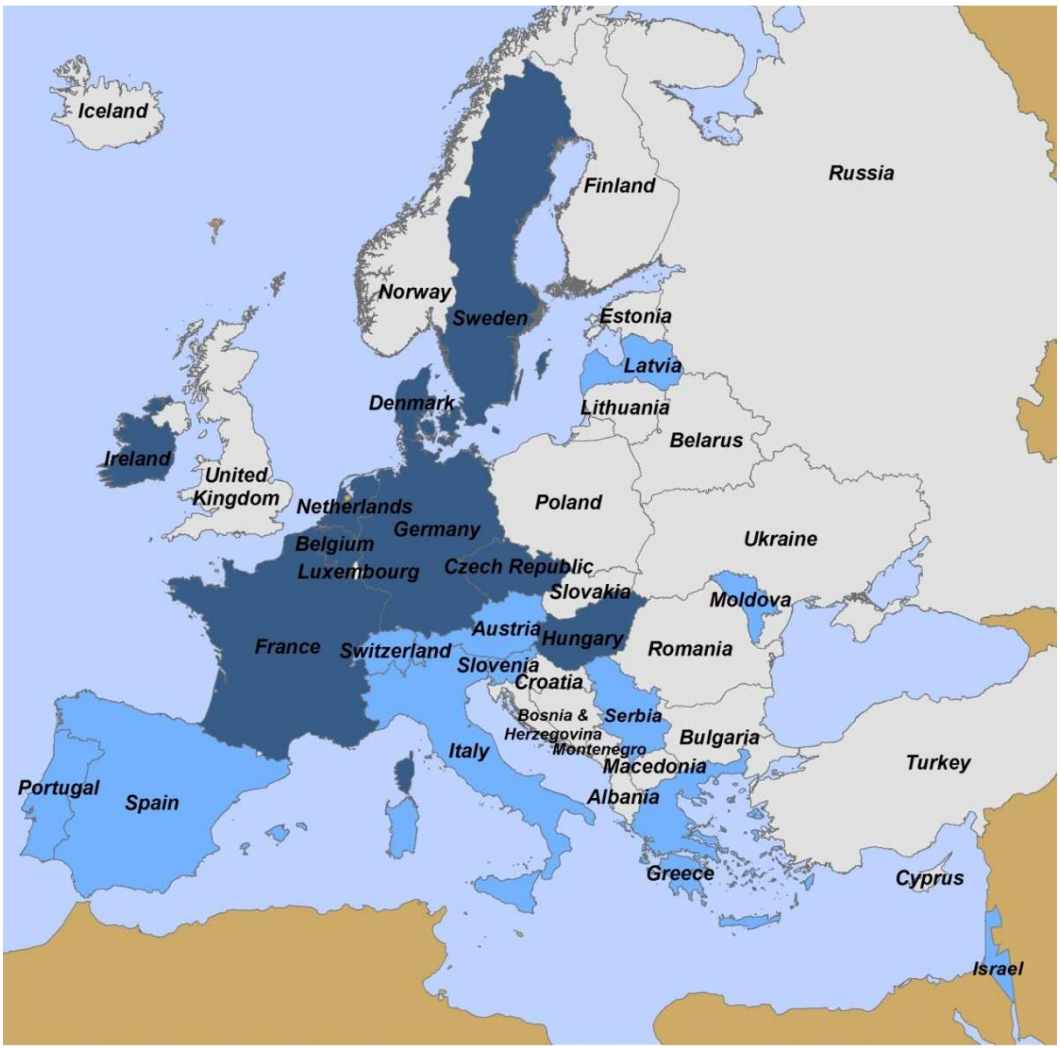
1. Demographics

This part of the report shows demographic data such as the number of patients living in the different countries, their sex, and their age.

For this report we asked the countries to give us data on CF patients in their care for two consecutive years: 2008 and 2009. We aimed at recording all the patients alive on 1st January 2008 as well as any new patients diagnosed during 2008 and 2009.

In table 1.1 we report the number of patients seen in these two years, but for the remaining report we refer only to the patients seen during year 2009, except for Ireland, for which we report patients seen in 2008.

Figure 1.1 Map of countries that contributed to the ECFSPR in year 2009.



Note: Ireland contributed with data from 2008.

Countries that sent the data to ECFSPR as national registries are in dark blue, countries that sent the data as individual centres are in light blue.

Table 1.1 Number of patients seen in year 2008 or in year 2009, by country.

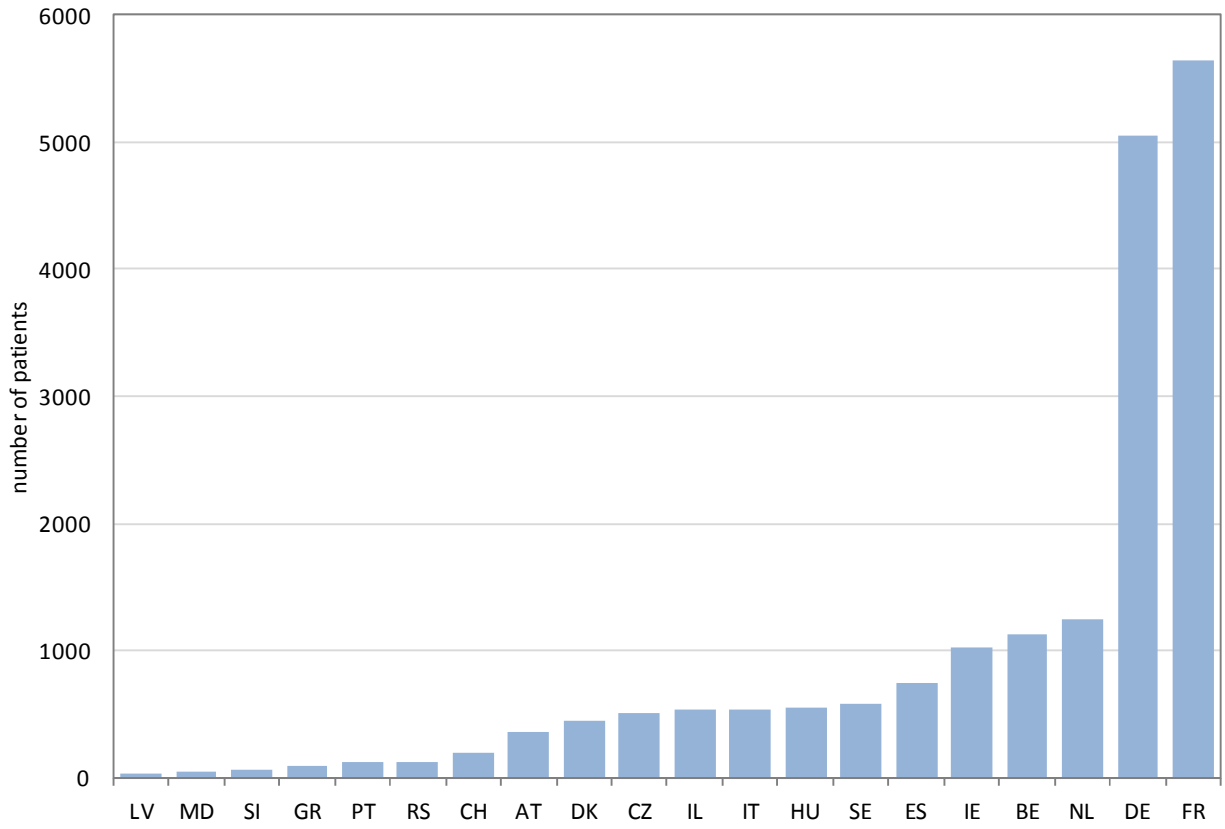
Country	2008	2009	Estimated coverage 2009
Austria	347	352	39%
Belgium*	1087	1129	>90%
Czech Republic*	490	507	100%
Denmark*	452	451	100%
France*	5366	5640	90%
Germany*	5533	5048	90%[1]
Greece	94	92	20%
Hungary*	547	555	90%
Ireland*	1021	-	90%
Israel**	516	533	90%
Italy	529	539	14%
Latvia	30	29	>90%
Republic of Moldova*	-	41	100%
The Netherlands*	1168	1249	97%
Portugal	61	117	42%
Serbia	118	122	>90%
Slovenia	57	66	75%[2]
Spain	582	740	30%[3]
Sweden*	367	578	85-90%[4]
Switzerland	173	190	24%
Total	18537	17978	

*Countries where a national CF registry is established.
** Although not officially a national registry, all centres in Israel participate in the ECFSPR, and it is considered a registry.
[1] Germany: in 2009, due to software updates, only 75% of patients already present in the registry were reported.
[2] Slovenia: coverage is 100% for children and 50% for adults.
[3] Spain: approximate estimate, since the total number of patients is not known
[4] Sweden: for 2008 only 3 out of 4 centres participated, hence the difference in patient numbers with 2009.

The column labelled "estimated coverage 2009" shows the estimated percentage of CF patients living in that country who are included in the national registries/national data collections. Note that one individual centre might include almost all patients for some countries (e.g. Latvia and Serbia).

In all subsequent tables and graphs, data refer to patients seen during 2009, except for Ireland, for which the data refer to patients seen during 2008. If the year 2009 is mentioned, it is implied that for Ireland this corresponds to 2008.

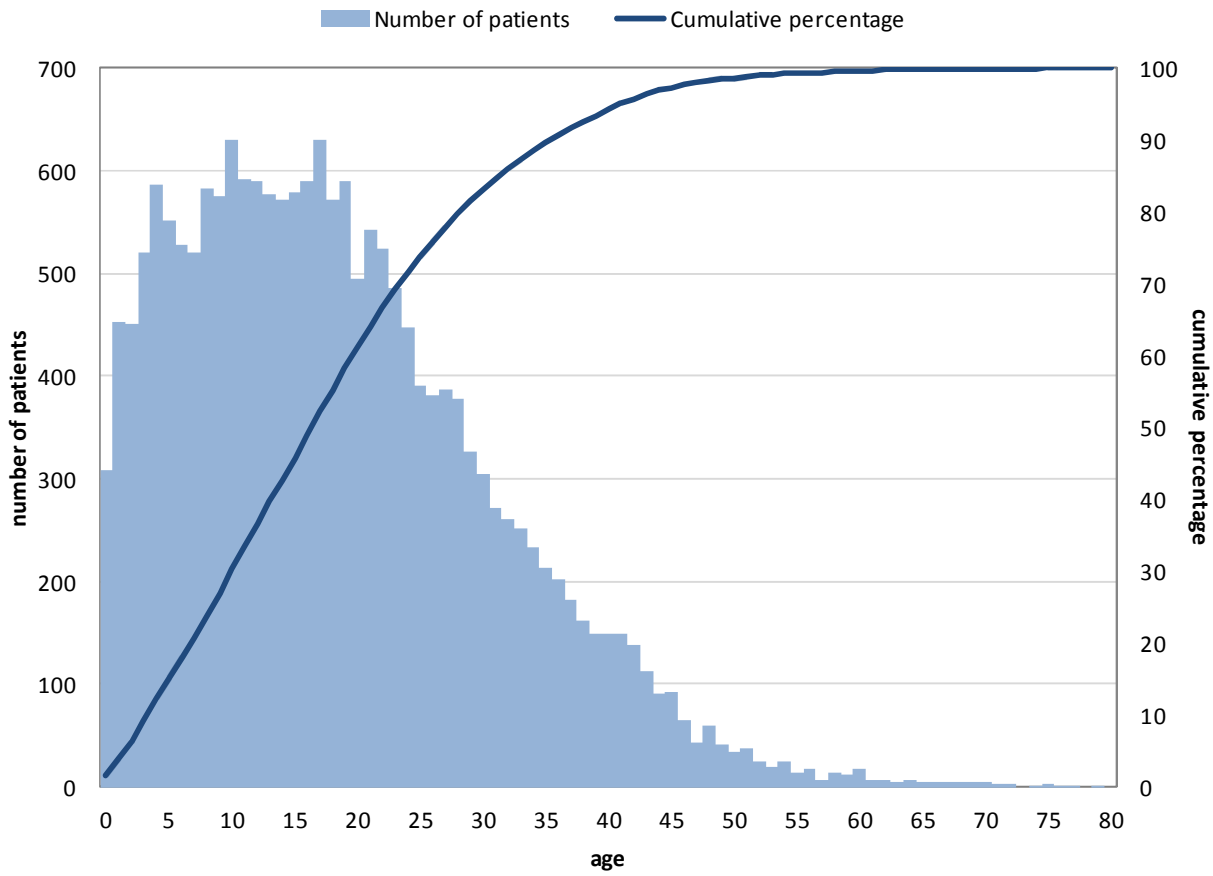
Figure 1.2 Number of patients in the ECFSPR in year 2009, by country.



Note: number of patients seen in year 2008 for Ireland.

Each vertical bar shows the number of patients living in that country and included in the ECFSPR in 2009. Please refer to table 1.1 for the coverage in each country. The two large registries, Germany and France account for 56% of the total.

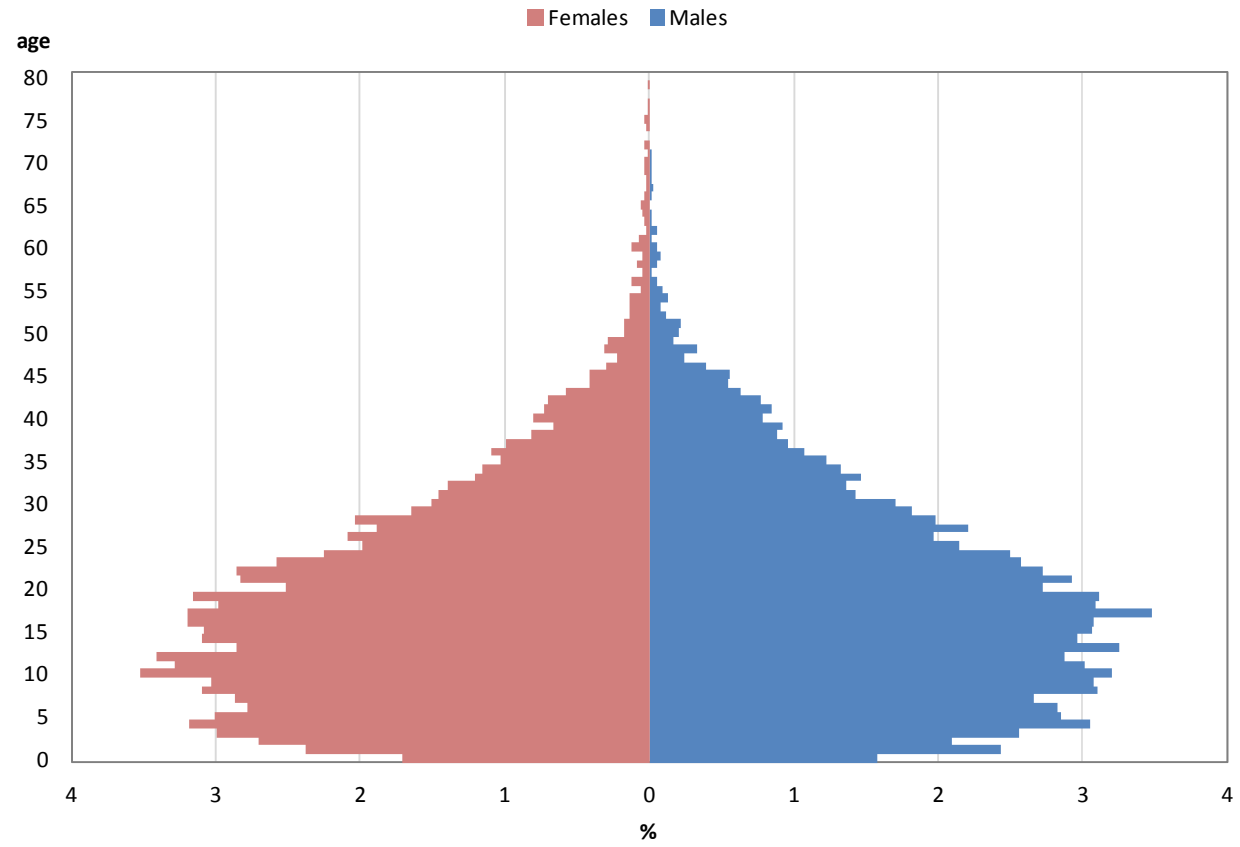
Figure 1.3 Age at follow up distribution. Patients alive on 31/12/2009.



Note: patients alive on 31/12/2008 for Ireland.

Each blue vertical bar represents the number of patients of that age alive in 2009. The cumulative percentage (blue line, right vertical axis) describes how many patients (in percent) are below a certain age (e.g. 50% of the patients are below 16 years).

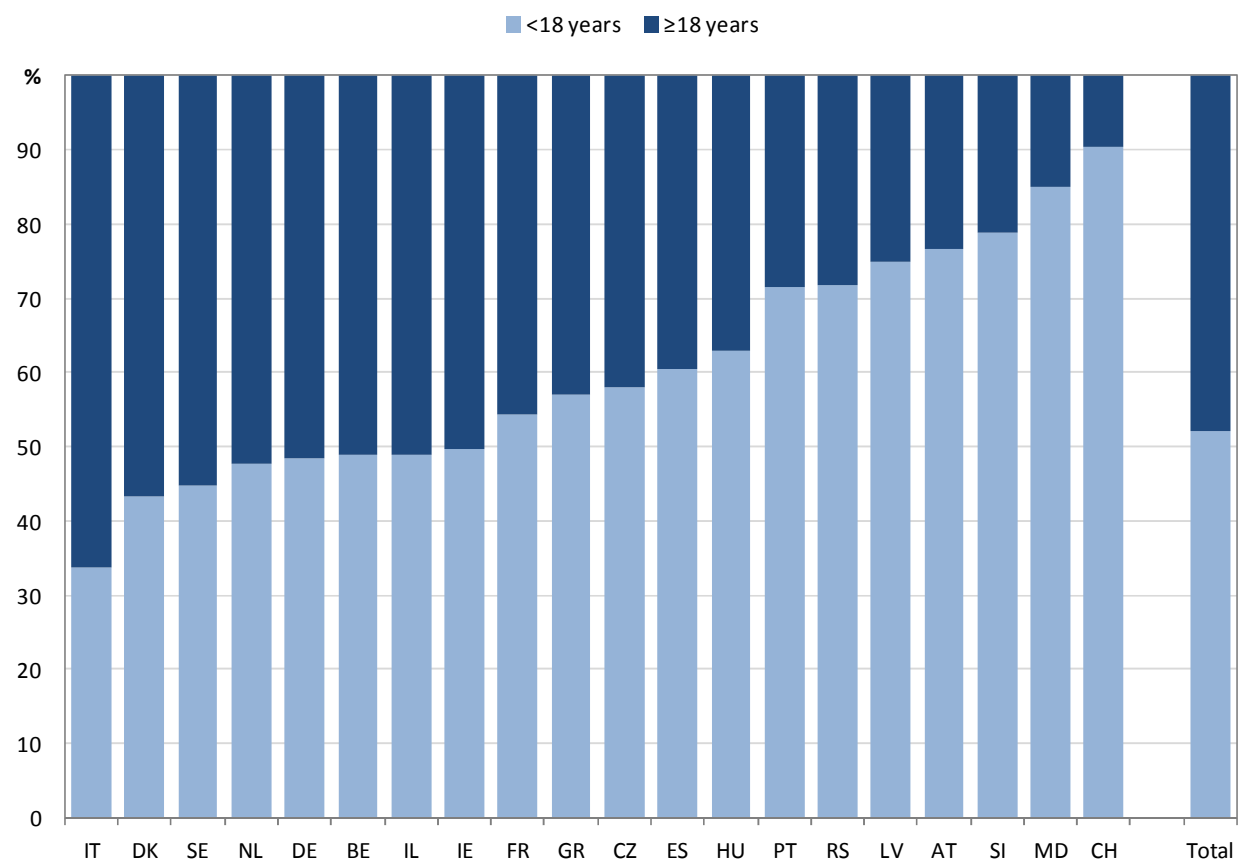
Figure 1.4 Age at follow up distribution by sex. Patients alive on 31/12/2009.



Note: patients alive on 31/12/2008 for Ireland.

The pyramid shows the percentage of patients in different ages as horizontal bars. The right side of the pyramid shows, among males, how many patients (in percent) have a certain age, and similarly for females on the left side (red). The lower number of patients at the bottom of the pyramid is due to the fact that some patients are not diagnosed yet (mean age at diagnosis is 3.6 years, see table 2.1).

Figure 1.5 Proportion of adults (≥18 years) and children (<18 years). Patients alive on 31/12/2009.



Note: patients alive on 31/12/2008 for Ireland.

This graph shows the percentage of patients in each country who are adults (dark blue) or children (light blue). The percentage of adult patients varies considerably between the different countries, but this is partly an effect of the way the patients are included: for some countries only a few individual centres sent the data to the ECFSPR, and the proportion of children and adults may reflect the proportion of paediatric and adult centres. Please refer to table 1.1 for coverage.

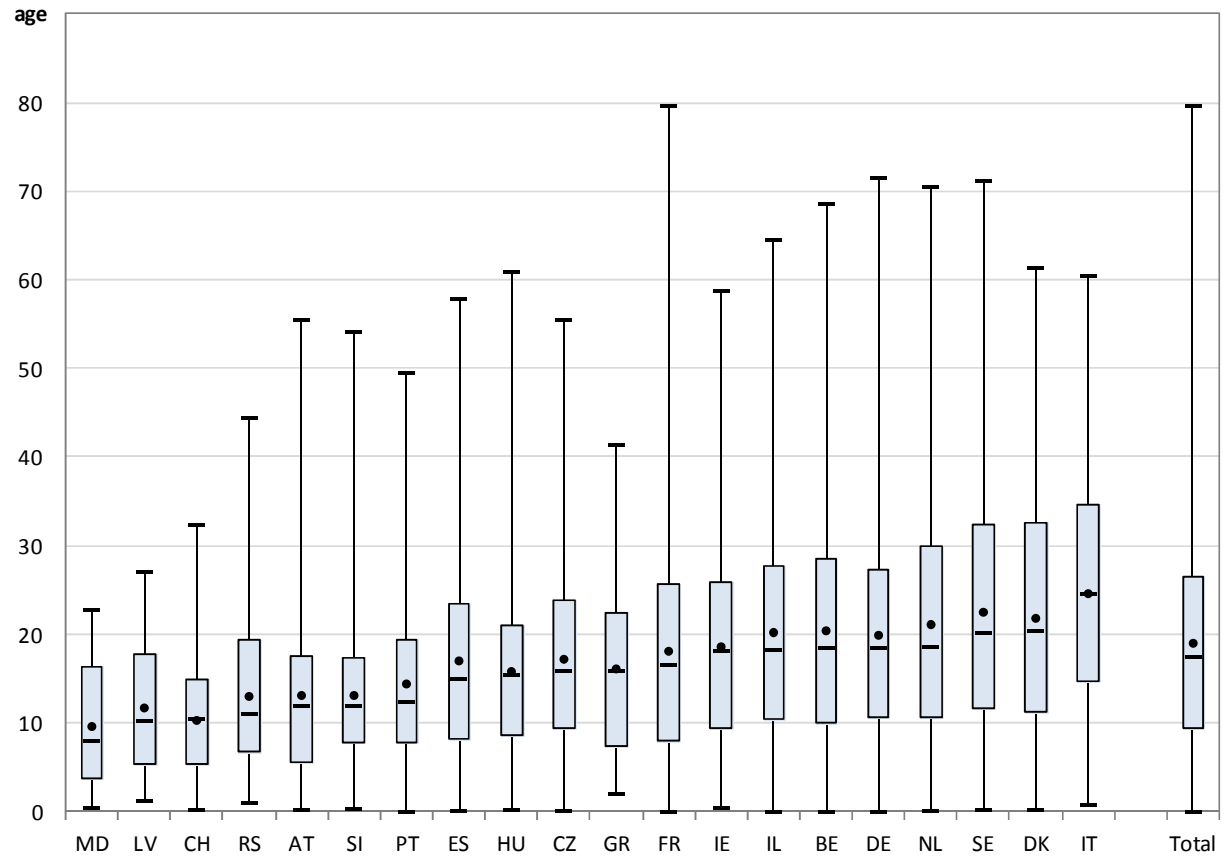
Table 1.2 Age at follow-up: descriptive statistics, by country and overall. Patients alive on 31/12/2009.

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)
Austria	349	13.1	0.2	5.5	11.9	17.6	55.5
Belgium	1119	20.4	0.0	10.1	18.5	28.5	68.5
Czech Rep	496	17.2	0.1	9.5	15.8	23.8	55.5
Denmark	442	21.8	0.2	11.2	20.4	32.5	61.3
France	5580	18.1	0.0	8.0	16.5	25.7	79.6
Germany	5025	19.9	0.0	10.7	18.5	27.4	71.5
Greece	91	16.1	2.0	7.5	15.9	22.5	41.4
Hungary	543	15.8	0.2	8.7	15.4	21.0	60.9
Ireland	1004	18.6	0.4	9.5	18.1	25.8	58.7
Israel	531	20.2	0.0	10.5	18.2	27.7	64.5
Italy	539	24.6	0.8	14.8	24.6	34.6	60.4
Latvia	28	11.7	1.2	5.3	10.2	17.7	27.0
Rep of Moldova	40	9.6	0.4	3.8	8.0	16.3	22.7
The Netherlands	1240	21.1	0.1	10.6	18.6	30.0	70.5
Portugal	116	14.4	0.0	7.8	12.4	19.3	49.5
Serbia	120	13.0	1.0	6.8	11.0	19.3	44.4
Slovenia	66	13.1	0.3	7.9	11.9	17.4	54.1
Spain	737	17.0	0.1	8.2	14.9	23.5	57.8
Sweden	573	22.5	0.2	11.6	20.2	32.3	71.1
Switzerland	190	10.3	0.2	5.4	10.5	14.9	32.3
Total	18829	19.0	0.0	9.4	17.4	26.5	79.6

Note: patients alive on 31/12/2008 for Ireland.

This table shows the descriptive statistics for age at follow-up of the patients by country and overall. Only patients who were alive on December 31st 2009 are included.

Figure 1.6 Age at follow-up: box-plot, by country and overall. Patients alive on 31/12/2009.



Note: patients alive on 31/12/2008 for Ireland.

This box-plot is a graphic representation of the age detailed in table 1.2. For each country 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. The following figure explains how to read the box for "Total".

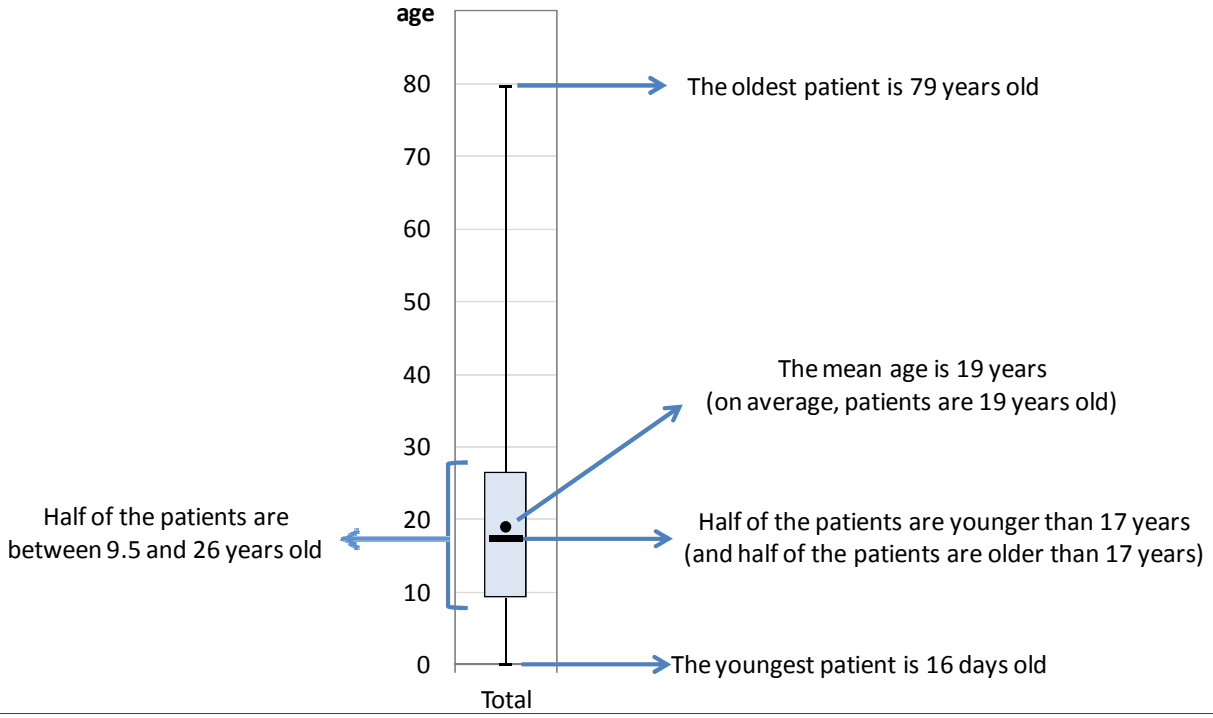
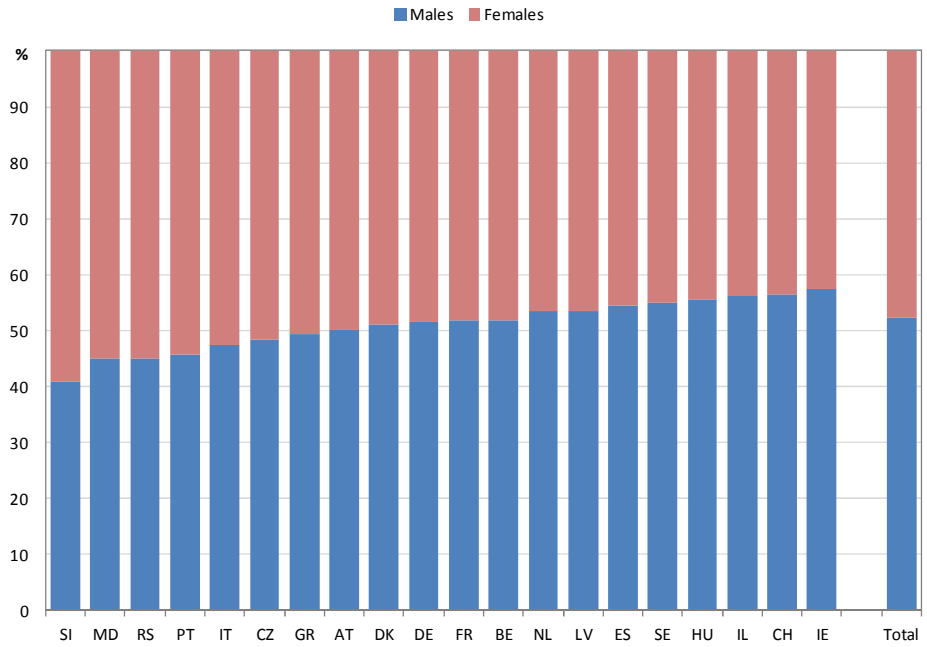


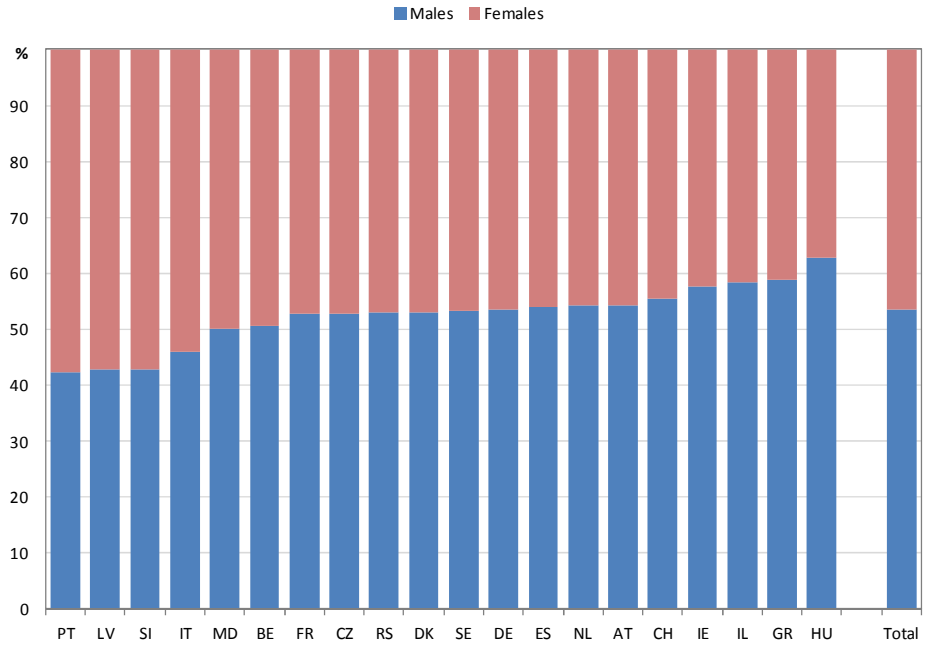
Figure 1.7 Sex distribution, by country and overall. Patients alive on 31/12/2009.



Note: patients alive on 31/12/2008 for Ireland.

Sex distribution of all patients. Overall (see "Total"), in the ECFSPR there are more male patients than female ones, which could reflect a higher mortality in the female CF patients. However, the proportion is not uniform across the different countries.

Figure 1.8 Sex distribution, by country and overall. Patients alive on 31/12/2009 and aged 18 years or more.



Note: patients alive on 31/12/2008 for Ireland.

Sex distribution for adult patients. The total proportion of females in the adult group is similar to the proportion of females in the whole population.

2. Diagnosis

This section summarises the information we have about diagnosis. We collect information on age at diagnosis, newborn screening, and meconium ileus (congenital intestinal obstruction).

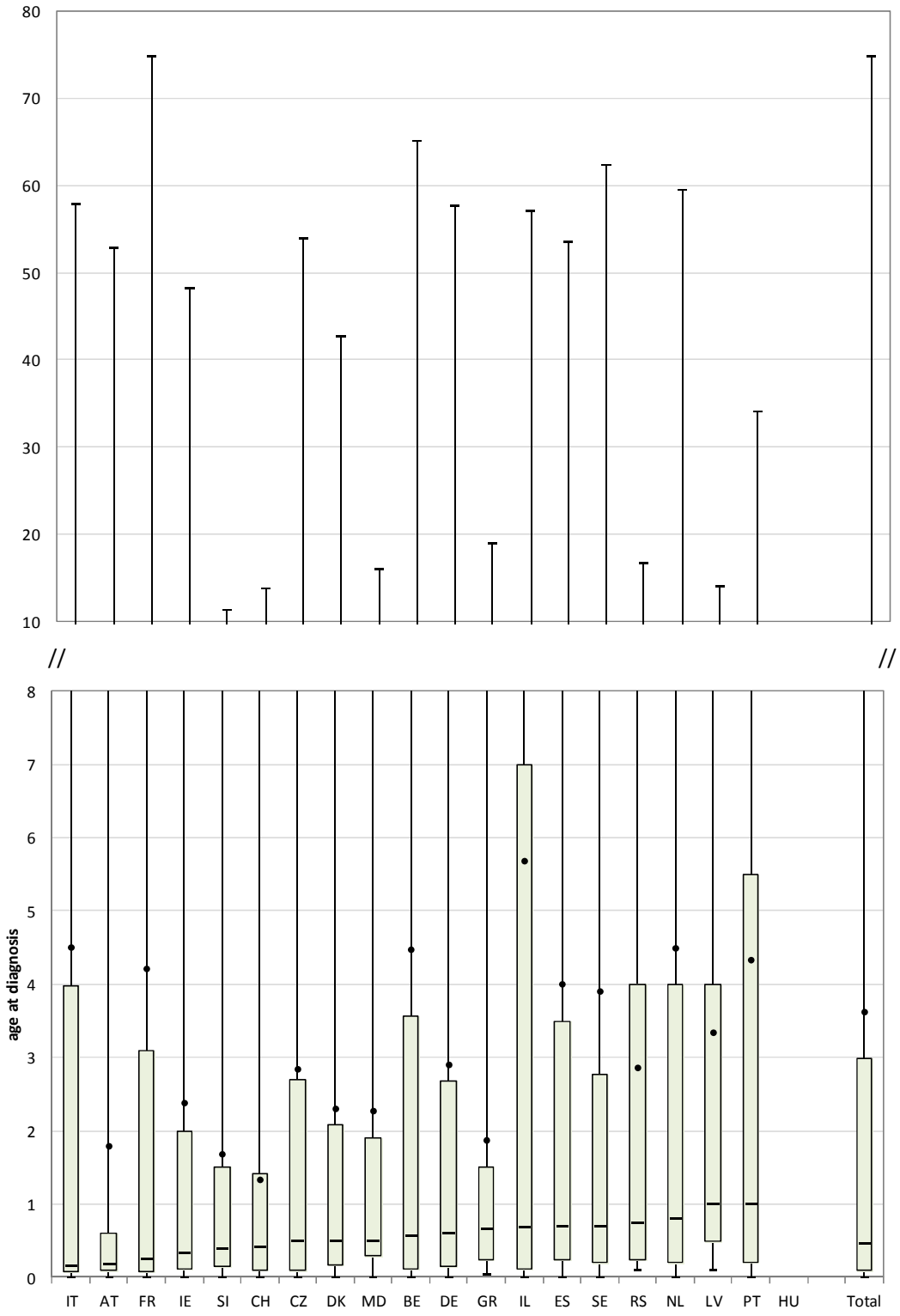
Table 2.1 Age at diagnosis: descriptive statistics, by country and overall. All patients seen in 2009.

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)
Austria	341	11	1.79	0.00	0.10	0.18	0.60	52.78
Belgium	1120	9	4.47	0.00	0.12	0.57	3.56	65.01
Czech Rep	507	0	2.84	0.00	0.10	0.50	2.70	53.90
Denmark	451	0	2.30	0.00	0.17	0.50	2.08	42.67
France	5363	277	4.21	0.00	0.08	0.25	3.09	74.75
Germany	4502	546	2.90	0.00	0.16	0.61	2.68	57.56
Greece	83	9	1.87	0.04	0.25	0.67	1.50	19.00
Hungary	0	555	-	-	-	-	-	-
Ireland	985	36	2.38	0.00	0.11	0.34	2.00	48.11
Israel	530	3	5.68	0.00	0.12	0.69	7.00	57.00
Italy	500	39	4.50	0.00	0.08	0.16	3.98	57.78
Latvia	29	0	3.34	0.10	0.50	1.00	4.00	14.00
Rep of Moldova	39	2	2.27	0.00	0.30	0.50	1.90	16.00
The Netherlands	911	338	4.49	0.00	0.20	0.80	4.00	59.40
Portugal	117	0	4.33	0.00	0.20	1.00	5.50	34.00
Serbia	116	6	2.86	0.10	0.25	0.75	4.00	16.70
Slovenia	65	1	1.68	0.00	0.15	0.40	1.50	11.30
Spain	737	3	4.00	0.00	0.25	0.70	3.50	53.50
Sweden	542	36	3.90	0.00	0.20	0.70	2.77	62.30
Switzerland	182	8	1.33	0.00	0.10	0.42	1.41	13.75
Total	17120	1879	3.62	0.00	0.10	0.46	2.98	74.75

Note: patients seen in 2008 for Ireland.

This table shows the descriptive statistics for age at diagnosis by country and overall. For prenatal diagnoses (children diagnosed before birth), the age at diagnosis has been set to 0.

Figure 2.1 Age at diagnosis: box-plot, by country and overall. All patients seen in 2009.



Note: patients seen in 2008 for Ireland.

This box-plot is a graphic representation of age at diagnosis detailed in table 2.1. For each country 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. Please note that the vertical axis is interrupted to emphasise the change of scale in the upper part of the graph. The figure on the next page explains how to read the box for "Total".

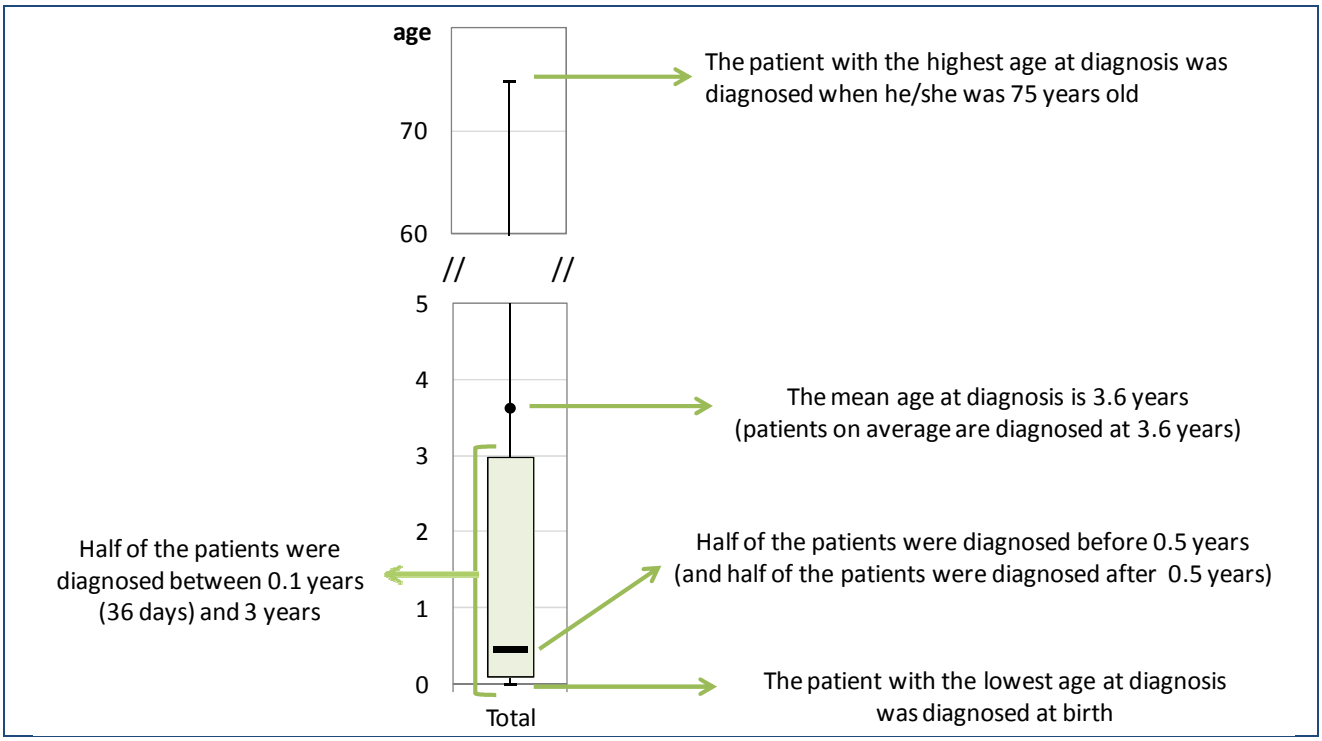
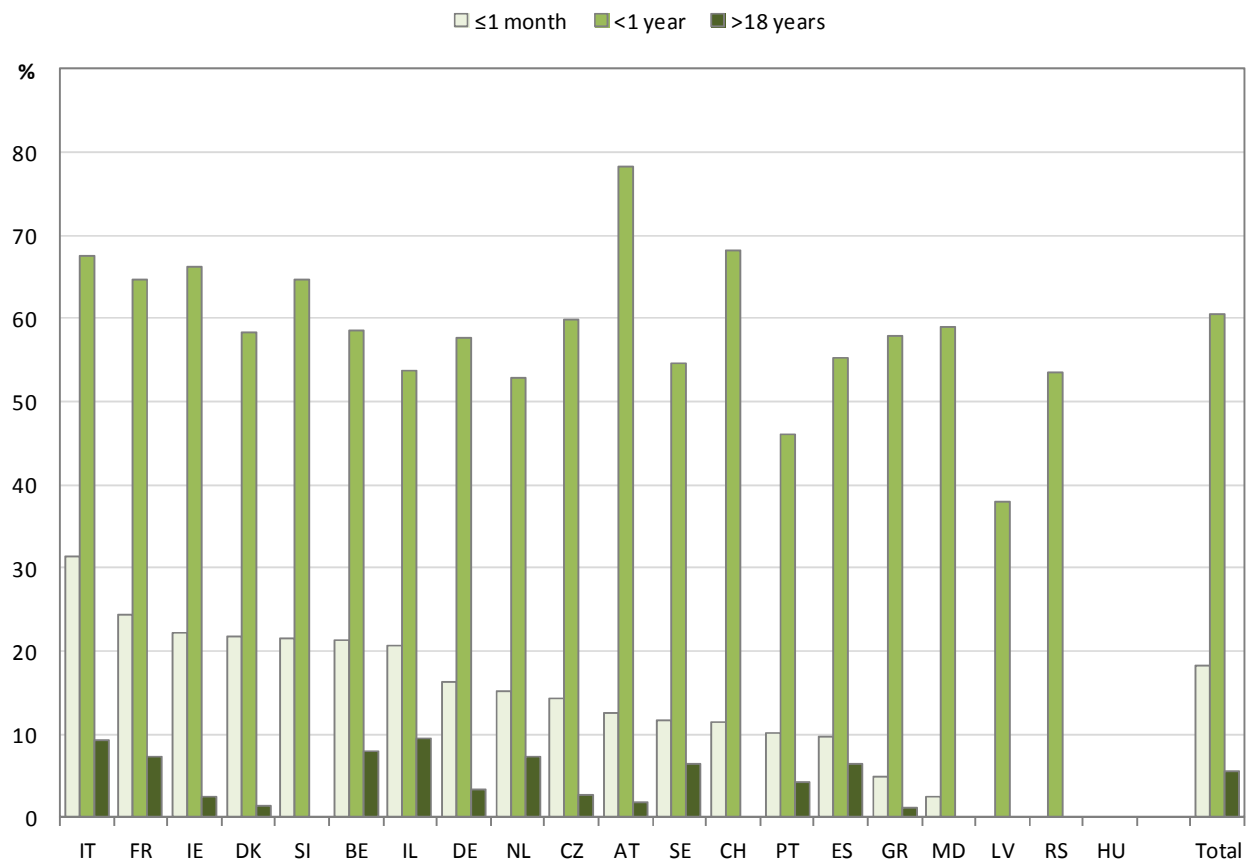

age
70
60
//
//
5
4
3
2
1
0
Total
The patient with the highest age at diagnosis was diagnosed when he/she was 75 years old
The mean age at diagnosis is 3.6 years (patients on average are diagnosed at 3.6 years)
Half of the patients were diagnosed before 0.5 years (and half of the patients were diagnosed after 0.5 years)
Half of the patients were diagnosed between 0.1 years (36 days) and 3 years
The patient with the lowest age at diagnosis was diagnosed at birth

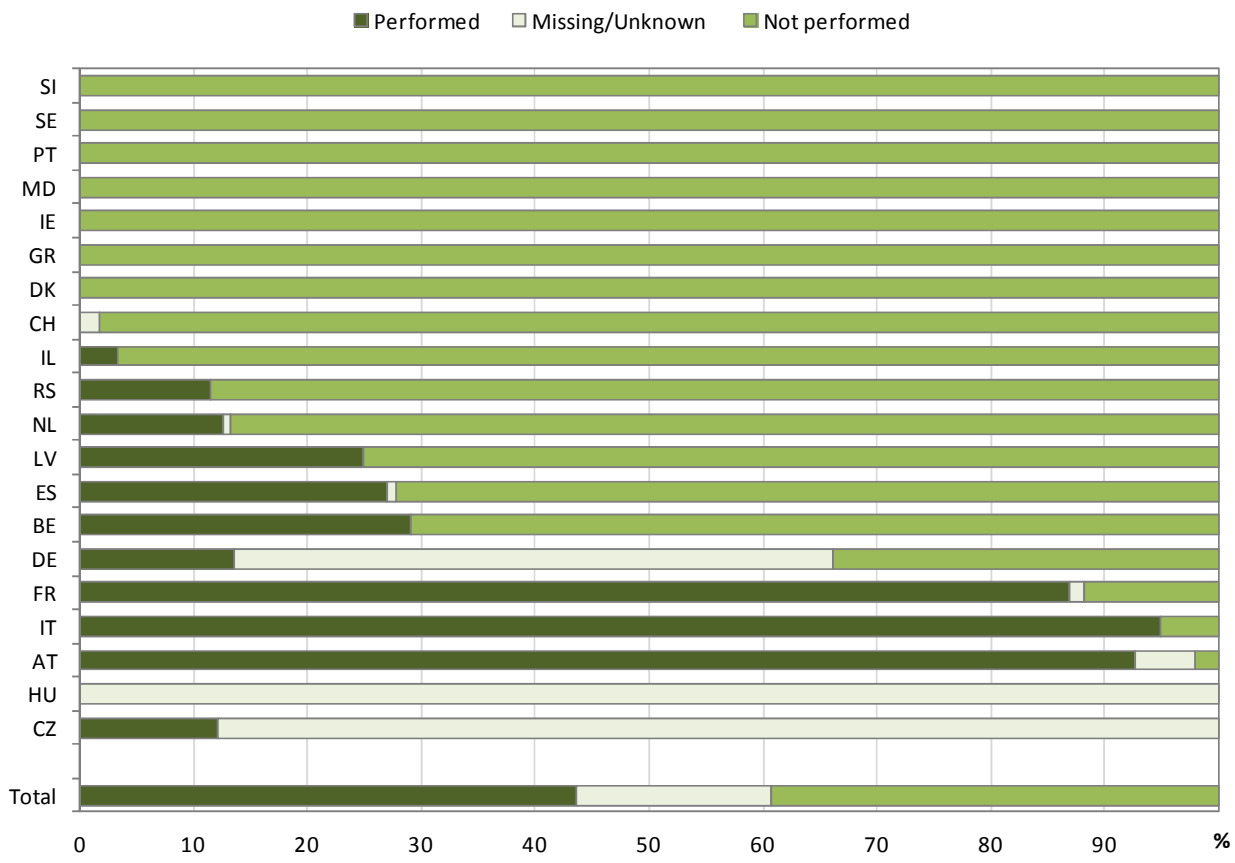
Figure 2.2 Proportion of patients diagnosed at age 1 month or younger, at 1 year or younger and at 18 years or older, by country and overall. All patients seen in 2009.



Note: patients seen in 2008 for Ireland.

This graphs shows age at diagnosis in subgroups. The vertical bars represent how many patients (in percent) were diagnosed within the first month of life (grey), within the first year of life (light green), and after 18 years of age (dark green). Note that the diagnoses performed within 1 month are also part of the diagnoses performed in the first year, and that the diagnoses performed between 1 year and 18 years are not shown in the graph, therefore the bars do not 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 2009.

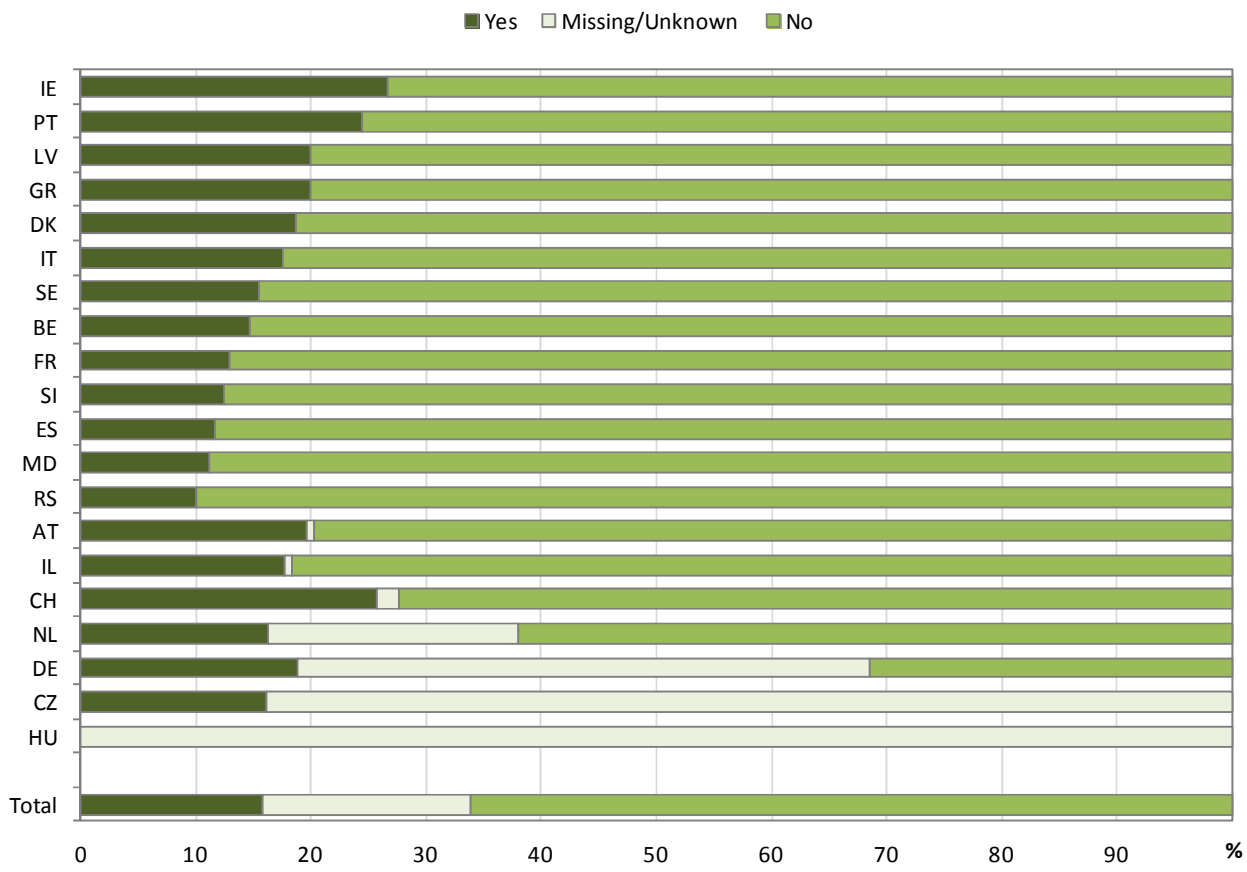


Note: patients 5 years old or younger seen in 2008 for Ireland.
Note:

Belgium: no national screening. Only positive answers are reported when they are given as one of the signs that lead to diagnosis in CF.
France: newborn screening is recorded only if it is part of the diagnosis.

This graph shows the percentage of patients 5 years old or younger in 2009 who had newborn screening performed (see country specific notes above). Dark green horizontal bars represent newborn screening "performed", light green ones "not done". This graph shows that in some countries there is no newborn screening and that in others almost all the CF patients underwent newborn screening during the five years previous to 2009. In total, at least 45% of all children 5 years old or younger registered in the ECFSPR in 2009, underwent newborn screening, but of course this estimate reflects the fact that not all the countries perform newborn screening.

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



Note: patients aged 10 years or younger seen in 2008 for Ireland.

Figure 2.5 Patients with meconium ileus, by country and overall. Patients aged 11 years or older.

Note: patients aged 11 years or older seen in 2008 for Ireland.

These two graphs show the prevalence of meconium ileus (operated or not) at birth in two age groups: 0 to 10 years (fig 2.4) and 11 years or older (fig 2.5). Overall, the proportion of child patients (≤10 years) with meconium ileus is higher than in the adults (>10 years). This difference is not due to an increase in the prevalence of meconium ileus in the younger generations but could be due to the fact that some older patients with meconium ileus have died, and are therefore not present in the current data collection (referring to only patients seen in 2009). The graphs also show that the frequency of reported meconium ileus varies between countries.

3. Genetics

This section describes the mutations in the cystic fibrosis transmembrane regulator (CFTR) gene. CF patients must have two CFTR mutations, one on each of their chromosomes, to get the disease.

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 identical to a known mutation, were renamed. We use the original mutation name (legacy name) in this report, since more than 90% of the mutations in the database use this nomenclature.

If DNA analysis to look for CFTR mutations was never performed, we asked the countries to report “Not done” in the genotype field. If the patient had undergone DNA analysis, but only one or no mutations were found, we asked the countries to write “Unknown” for the un-identified mutations. Please note that there are differences in the DNA testing between countries, with some countries using standard kits that tests only a limited number of common mutations (e.g. 28), and other countries performing DNA analyses of the whole gene until the mutation is identified.

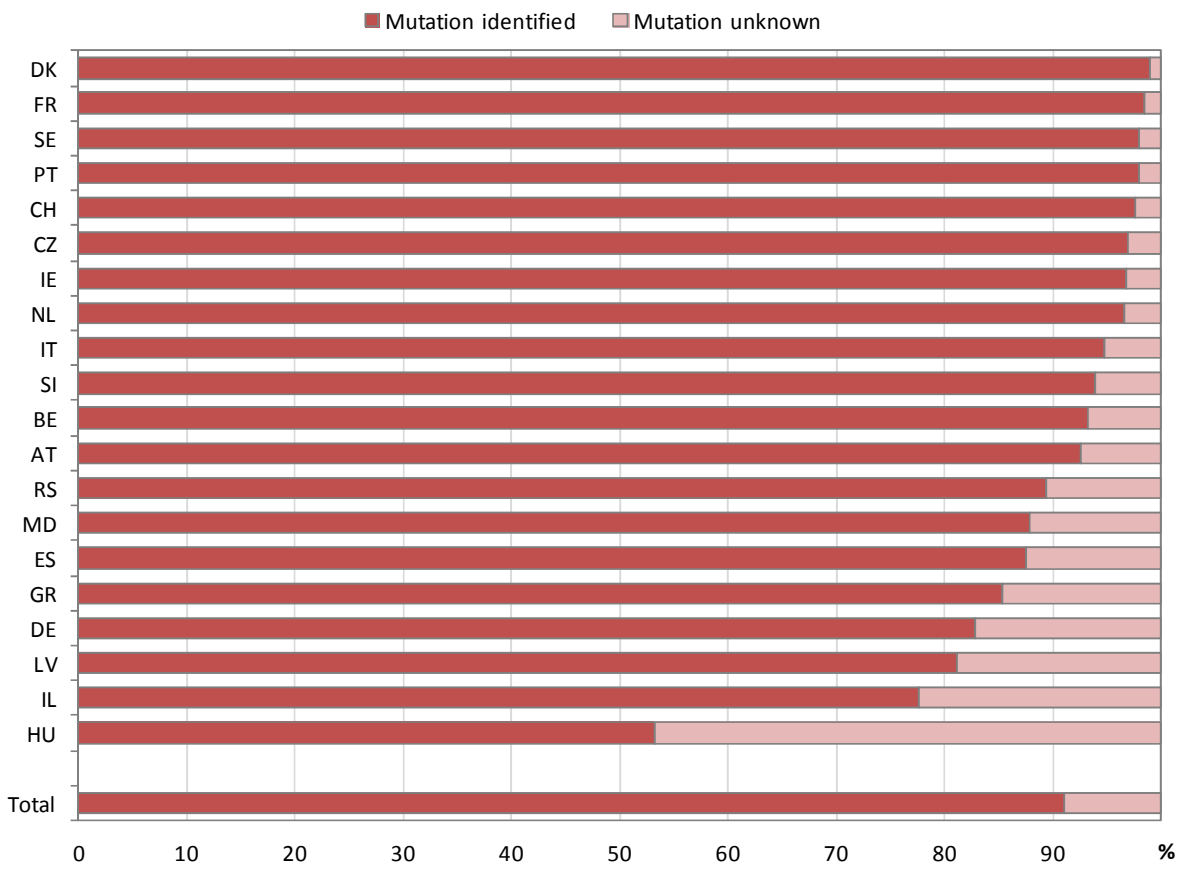
Table 3.1 Proportion of patients with DNA analysis and the result of this, by country and overall. All patients seen in 2009.

Country	N	Genotyping			Among genotyping done	
		missing information	not done	done	two mutations identified	at least one mutation unknown
Austria	352	0 (0%)	0 (0%)	352 (100%)	312 (88.6%)	40 (11.4%)
Belgium	1129	0 (0%)	22 (2.0%)	1107 (98.0%)	987 (89.2%)	120 (10.8%)
Czech Republic	507	0 (0%)	0 (0%)	507 (100%)	483 (95.3%)	24 (4.7%)
Denmark	451	0 (0%)	0 (0%)	451 (100%)	443 (98.2%)	8 (1.8%)
France	5640	167 (3.0%)	0 (0%)	5473 (97.0%)	5292 (96.7%)	181 (3.3%)
Germany	5048	0 (0%)	514 (10.2%)	4534 (89.8%)	3397 (74.9%)	1137 (25.1%)
Greece	92	3 (3.3%)	0 (0%)	89 (96.7%)	67 (75.3%)	22 (24.7%)
Hungary	555	0 (0%)	0 (0%)	555 (100%)	241 (43.4%)	314 (56.6%)
Ireland	1021	0 (0%)	40 (3.9%)	981 (96.1%)	920 (93.8%)	61 (6.2%)
Israel	533	0 (0%)	3 (0.6%)	530 (99.4%)	372 (70.2%)	158 (29.8%)
Italy	539	0 (0%)	20 (3.7%)	519 (96.3%)	469 (90.4%)	50 (9.6%)
Latvia	29	0 (0%)	0 (0%)	29 (100%)	18 (62.1%)	11 (37.9%)
Rep of Moldova	41	0 (0%)	0 (0%)	41 (100%)	33 (80.5%)	8 (19.5%)
The Netherlands	1249	0 (0%)	70 (5.6%)	1179 (94.4%)	1112 (94.3%)	67 (5.7%)
Portugal	117	0 (0%)	2 (1.7%)	115 (98.3%)	110 (95.6%)	5 (4.4%)
Serbia	122	0 (0%)	18 (14.8%)	104 (85.2%)	84 (80.8%)	20 (19.2%)
Slovenia	66	0 (0%)	0 (0%)	66 (100%)	59 (89.4%)	7 (10.6%)
Spain	740	1 (0.1%)	0 (0%)	739 (99.9%)	575 (77.8%)	164 (22.2%)
Sweden	578	0 (0%)	0 (0%)	578 (100%)	559 (96.7%)	19 (3.3%)
Switzerland	190	1 (0.5%)	0 (0%)	189 (99.5%)	181 (95.8%)	8 (4.2%)
Total	18999	172 (0.9%)	689 (3.6%)	18138 (95.5%)	15714 (86.6%)	2424 (13.4%)

Note: patients seen in 2008 for Ireland.

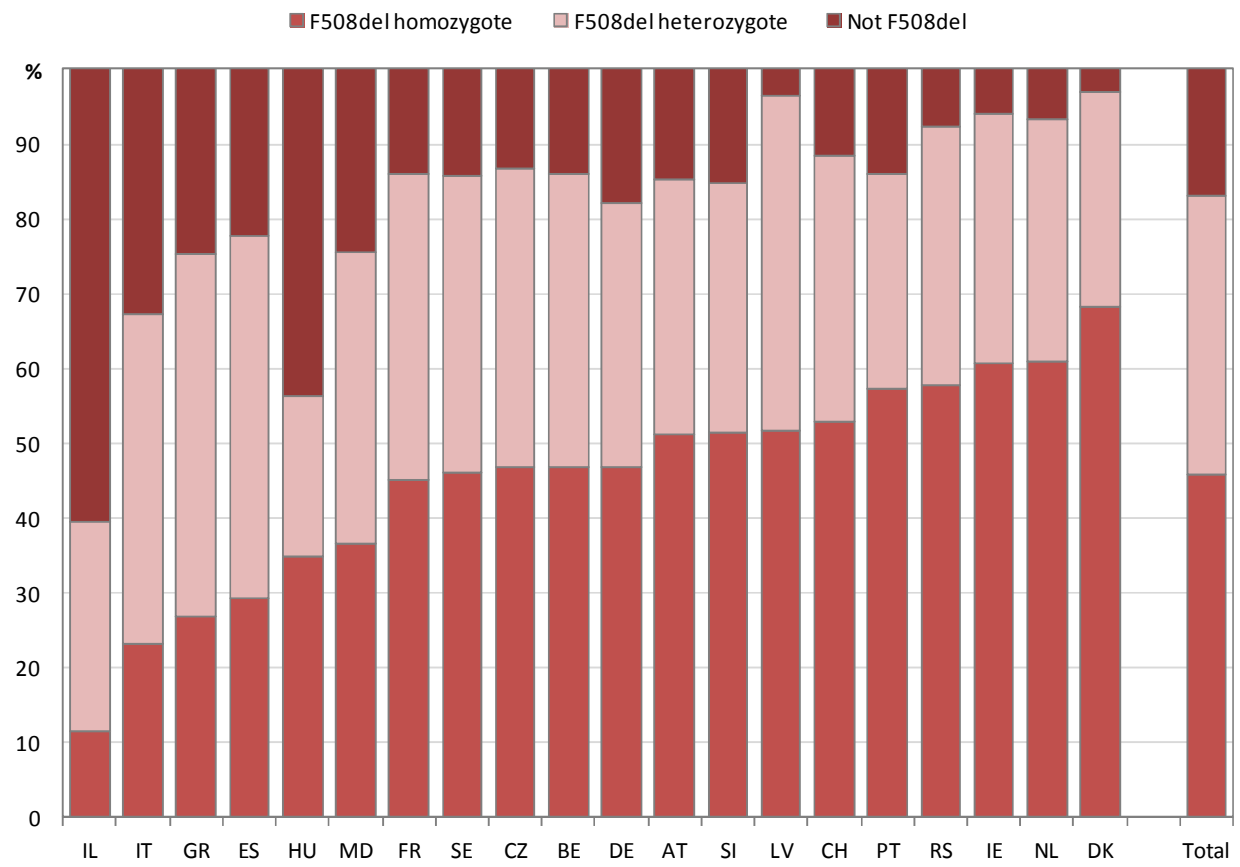
This table shows how many patients underwent DNA analysis to identify the CFTR mutations (column “genotyping done”) and, for those patients, how many patients had both mutations identified (column “two mutations identified”) and for how many one or both mutations remained unidentified (column “ at least 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 (unknown, 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, to some extent due to the availability of DNA testing. Overall, 9.8% of mutations remain unidentified after DNA analysis, leaving 15.5% 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 2009.



Note: patients seen in 2008 for Ireland.

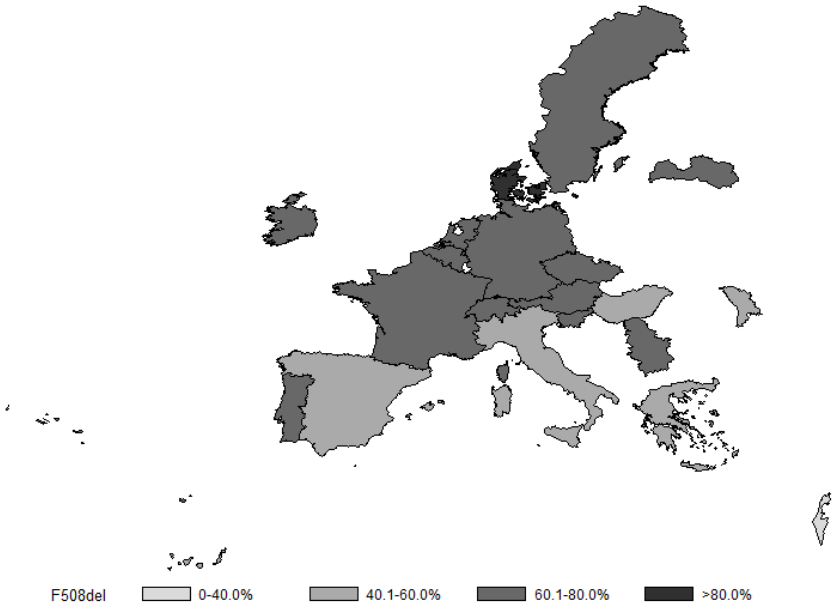
F508del is the most common CFTR mutation in the world, accounting for about 70% of all mutations in Caucasians. Patients carrying two F508del mutations are often described as the "typical CF patient", but other combinations of mutations may cause the same degree of disease. We have grouped the genotypes in F508del homozygous patients (carrying two F508del mutations), F508del heterozygous patients (carrying one F508del mutation and another mutation, different from F508del), and patients without F508del mutations. Only patients who had genotyping done 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 12 most common mutations in the ECFSPR database.

Mutation name	Number of alleles	Percentage among tested	Country with highest frequency
F508del	23386	64.5	Denmark (82.6%)
G542X	890	2.5	Greece (6.7%)
N1303K	687	1.9	Italy (4.2%)
W1282X	429	1.2	Israel (22.5%)
G551D	410	1.1	Ireland (7.6%)
R553X	371	1.0	Switzerland (2.1%)
1717-1G->A	345	1.0	Italy (3.7%)
R117H	267	0.7	Ireland (2.3%)
2789+5G->A	266	0.7	Republic of Moldova (4.9%)
3849+10KbC->T	255	0.7	Israel (3.0%)
R1162X	250	0.7	Italy (7.7%)
2183AA->G	197	0.5	Italy (5.2%)

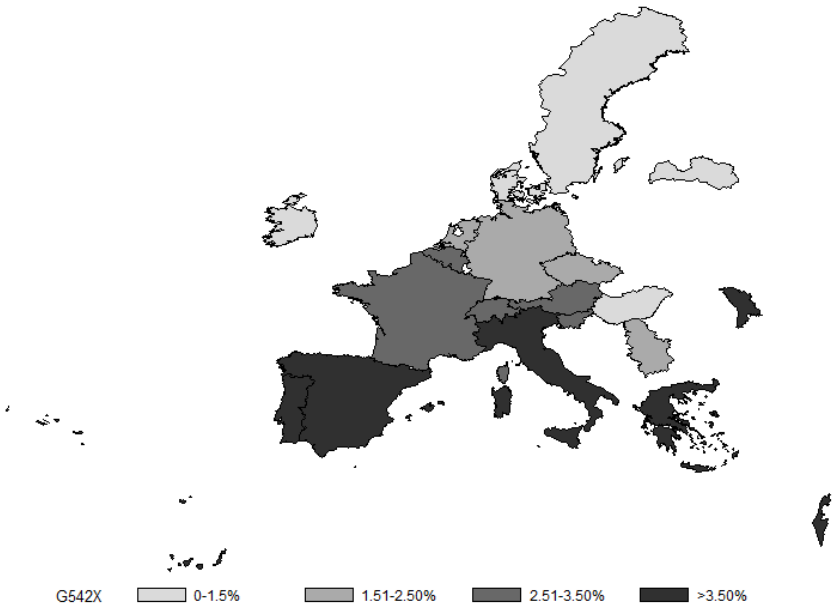
This table lists the 12 most common mutations found in the ECFSPR database. The last column reports in which country this particular mutation is most frequent. F508del is by far the most frequent mutation. Additionally, since F508del is included in all genetic screening tests, this is also the mutation with the highest detection rate.

Figure 3.3 Geographical distribution of mutation F508del.



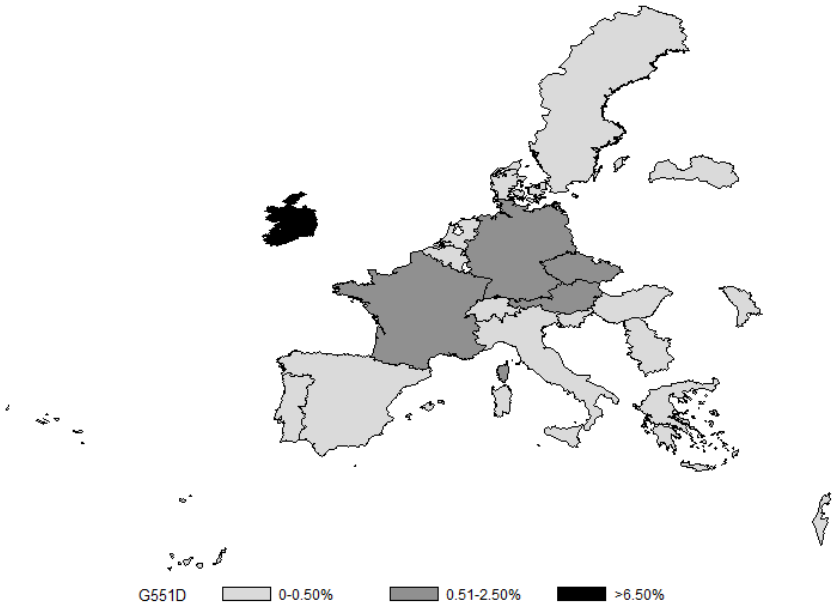
Although this mutation is the most common in all countries, the frequency still varies from 25.5% in Israel to 82.6% in Denmark.

Figure 3.4 Geographical distribution of mutation G542X.



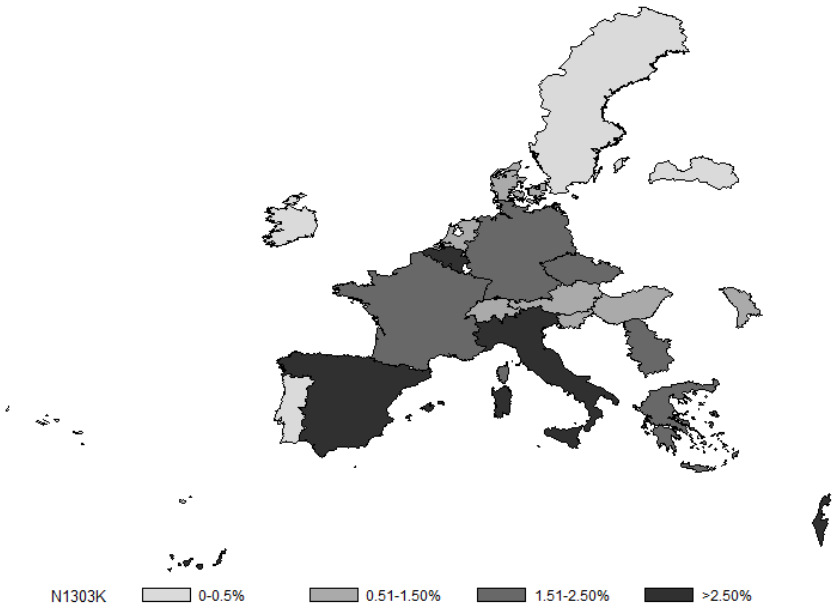
This mutation is most frequent in southern Europe, with the highest frequency in Greece (6.7%), whereas it is very rarely found in Scandinavia (0.7% in Denmark and Sweden).

Figure 3.5 Geographical distribution of mutation G551D.



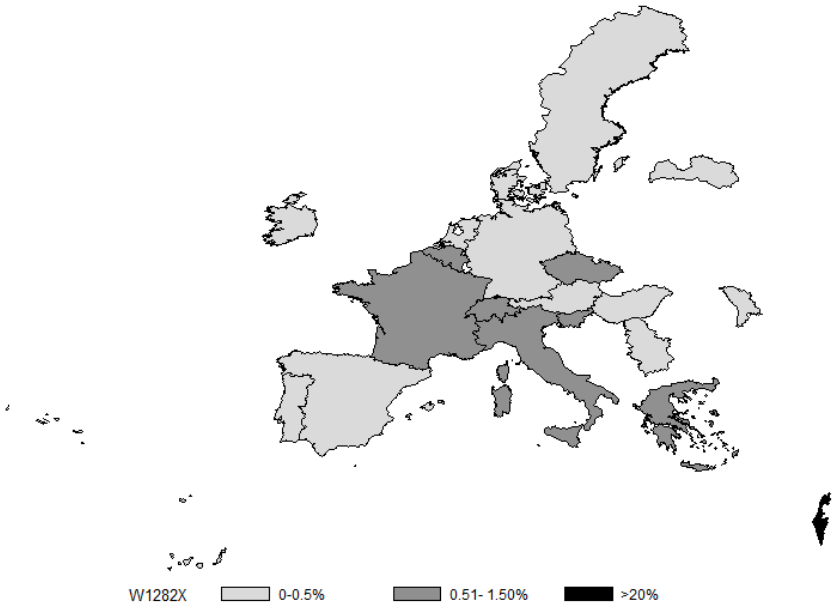
This mutation is most frequent in Ireland (7.6%), whereas it is very rare in Scandinavia and in Southern Europe (less than 0.5%).

Figure 3.6 Geographical distribution of mutation N1303K.



This mutation is most frequent in Italy (4.2%) and other countries in Southern Europe, but rare in Northern Europe.

Figure 3.7 Geographical distribution of mutation W1282X.



This mutation is by far most frequent in Israel (22.5%), being of Middle-Eastern origin, with a very high frequency in Ashkenazi Jews. The distribution across Europe is fairly uniform.

4. Lung function

The most important complication in cystic fibrosis today is lung disease, and respiratory insufficiency is by far the most common cause of death. The most frequently used prognostic factor for lung disease is forced expiratory volume in first second (FEV1), measured by the lung function test spirometry.

FEV1 is measured in litres but it is normally expressed as a percentage of the expected value (FEV1%). The expected value is computed from healthy individuals of the same sex, height and age, what is called the reference population. For this report we used the reference populations and the equations described by Wang et al. for children and Hankinson et al. for adults (see Appendix 1 for full reference). An FEV1% of 100 means that the lung function measure is equal to the mean lung function measure of people of the same age, sex and height of the reference population.

Spirometry requires a certain amount of coordination, and can generally not be performed until about six years of age. We have therefore only computed FEV1% values for children aged 6 years or older.

We asked the countries to report to the ECFSPR the best FEV1 recorded throughout the year (according to the FEV1% computed at the CF centres). A few national registries did not record the best value, but other FEV1 values, so we have added a footnote to the tables and graphs describing which FEV1 was reported from those countries. Research has shown that when comparing groups of patients, the difference between the best FEV1% and a random value from the same year can be up to 4.3% points[1]. This finding should be taken into consideration when comparing the results.

We excluded patients who have had lung transplant from the analyses on FEV1, since their lung function does not reflect the severity of their disease.

[1] Wanyama et al, JCF 2010; 9,S1:428

Table 4.1 FEV1% of predicted: descriptive statistics, by country. Patients aged 6-17 years who have never had a lung transplant.

Country	N	N Miss	Mean (average FEV1%)	Min	25th pctl (25% of patients have FEV1% below this value)	Median (50% of patients have FEV1% below this value)	75th pctl (75% of patients have FEV1% below this value)	Max
Austria	170	5	92.3	27.0	81.5	94.6	106.8	129.4
Belgium	387	10	94.6	31.9	84.5	97.3	106.5	143.4
Czech Rep	162	29	86.5	24.5	76.1	89.1	100.0	124.9
Denmark	134	2	100.4	35.1	90.2	101.8	111.7	143.0
France[1]	1653	154	84.8	17.0	71.6	87.2	100.6	148.4
Germany[2]	1673	86	84.1	15.9	71.4	86.8	99.7	140.9
Greece	34	0	92.9	25.3	76.0	98.1	110.9	149.0
Hungary	-	-	-	-	-	-	-	-
Ireland	254	62	85.8	24.7	73.9	92.9	99.1	139.6
Israel	197	2	90.7	28.4	81.1	93.5	105.0	136.9
Italy	126	18	97.6	45.9	86.8	98.7	108.7	132.6
Latvia	12	2	91.9	51.7	79.6	97.0	101.9	126.9
Rep of Moldova	11	0	68.3	49.0	56.8	69.1	77.1	86.0
The Netherlands	437	8	90.7	19.8	80.7	91.8	103.8	142.9
Portugal	44	8	86.0	26.8	72.5	92.3	103.2	120.8
Serbia	61	0	82.1	21.9	63.4	82.4	105.5	129.6
Slovenia	39	0	85.5	33.0	73.8	88.9	102.1	112.6
Spain	308	4	89.6	20.0	78.7	92.4	103.7	135.4
Sweden[3]	174	4	90.4	32.7	79.3	93.0	102.3	137.7
Switzerland	112	0	92.8	35.9	82.7	95.6	105.2	127.1

[1] France: reports the last FEV1 of the year.
[2] Germany: reports the FEV1 value closest to the patient's birthday (without exacerbation).
[3] Sweden: reports FEV1 collected at the time of the annual review.

This table shows some descriptive statistics for FEV1 in children, expressed as % of predicted. Note that transplanted patients and children below 6 years of age have been excluded from the analyses.

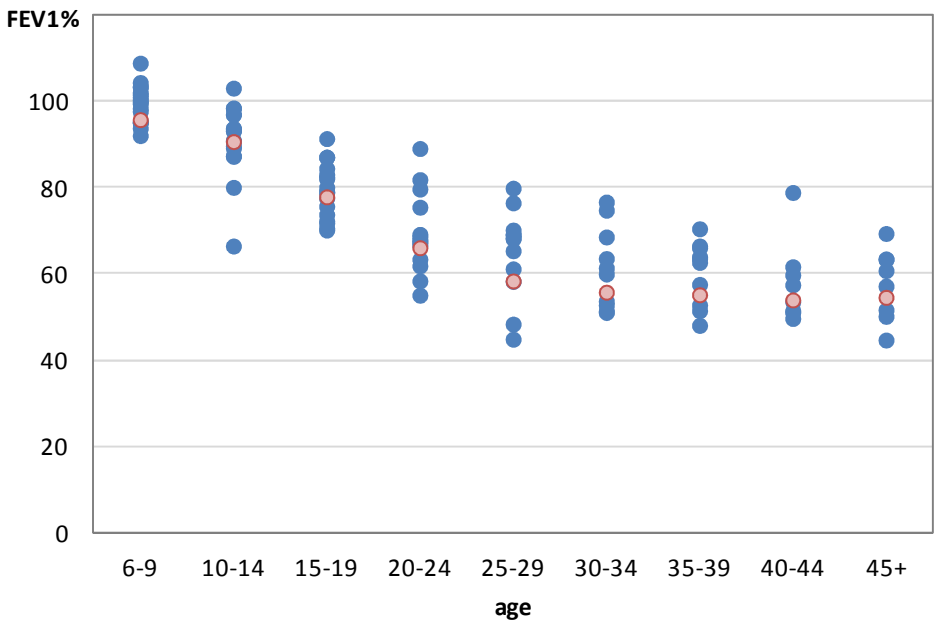
Table 4.2 FEV1% of predicted: descriptive statistics, by country. Patients aged 18 years or older who have never had a lung transplant.

Country	N	N Miss	Mean (average FEV1%)	Min	25th pctl (25% of patients have FEV1% below this value)	Median (50% of patients have FEV1% below this value)	75th pctl (75% of patients have FEV1% below this value	Max
Austria	68	2	73.0	18.5	52.5	73.7	92.8	118.7
Belgium	433	9	69.4	15.4	52.1	69.8	85.3	144.0
Czech Republic	20	53	67.4	40.5	51.0	71.1	80.7	100.5
Denmark	193	2	75.1	17.4	57.3	78.2	92.4	126.2
France[1]	1962	84	57.8	13.3	37.3	55.4	76.6	129.6
Germany[2]	1862	127	60.1	12.2	40.1	58.6	78.3	127.8
Greece	30	0	53.3	26.0	41.3	50.4	67.8	95.3
Hungary	-	-	-	-	-	-	-	-
Ireland	243	83	62.3	18.1	42.8	61.6	79.5	120.1
Israel	226	9	67.0	19.2	49.2	68.1	83.0	116.7
Italy	221	95	68.4	16.6	50.0	67.9	87.5	116.6
Latvia	6	0	33.3	21.7	25.7	34.9	39.2	43.2
Rep of Moldova	3	0	86.6	82.3	82.3	86.9	90.6	90.6
The Netherlands	575	13	62.0	14.0	42.4	60.4	81.5	127.0
Portugal	30	0	59.0	18.3	46.1	57.6	77.7	106.2
Serbia	33	0	56.9	17.3	36.4	56.5	71.7	105.1
Slovenia	7	0	64.5	40.6	41.7	72.7	78.2	84.0
Spain	251	0	65.8	21.4	47.5	64.7	82.6	114.9
Sweden[3]	230	34	72.6	17.0	53.7	74.1	91.0	132.9
Switzerland	15	0	69.0	31.0	47.4	62.0	96.2	113.2

[1] France: reports the last FEV1 of the year.
[2] Germany: reports the FEV1 value closest to the patient's birthday (without exacerbation).
[3] Sweden: reports FEV1 collected at the time of the annual review.

This table shows some descriptive statistics for FEV1 in adults, expressed as % of predicted. Note that transplanted patients have been excluded from the analyses.

Figure 4.1 Median FEV1% of predicted by age group and by country. Patients aged 6 years or older who have never had a lung transplant.



Note: we excluded from the analyses those age groups where the number of patients was <10.
Note: not all the countries reported the best FEV1 value of the year (see tables 4.1 and 4.2).

This graph shows the median FEV1% (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 is that the FEV% slowly decreases until the age of 30-34, 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.

Table 4.3 FEV1% of predicted: descriptive statistics by age group (patients aged 6 years or older who have never had a lung transplant.

Age at FEV1 measurement	N	N Miss	Mean	Min	25th pctl	Median	75th pctl	Max
6-9	1900	166	93.7	22.7	83.8	95.8	105.9	149.0
10-14	2557	146	88.1	17.0	76.5	90.7	102.4	142.9
15-19	2405	141	75.6	13.6	59.3	77.9	92.9	139.6
20-24	1851	138	65.1	12.2	45.1	66.1	85.0	127.2
25-29	1350	106	59.4	12.3	39.9	58.4	77.4	144.0
30-34	846	86	58.2	12.2	39.1	55.8	74.4	127.2
35-39	626	57	57.9	13.8	37.3	55.2	75.8	129.6
40-44	441	36	57.7	14.1	38.5	54.0	73.9	117.7
45+	420	29	57.2	16.1	37.1	54.6	73.1	128.9

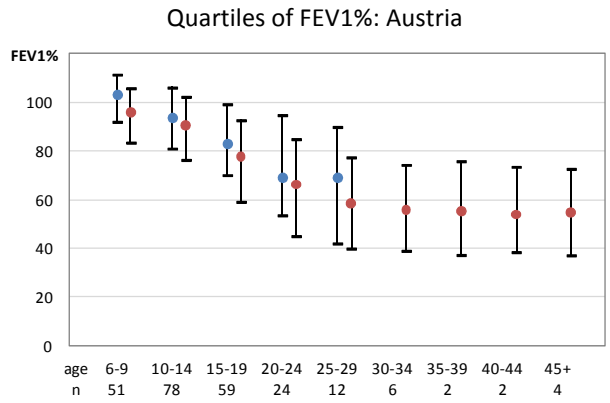
Note: not all the countries reported the best FEV1 value of the year (see tables 4.1 and 4.2).

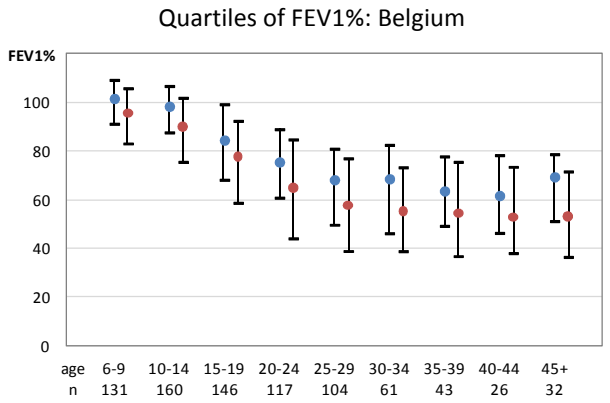
This table shows FEV1% by age group for the total data set. The median values reported in this table are shown as red dots in fig 4.1.

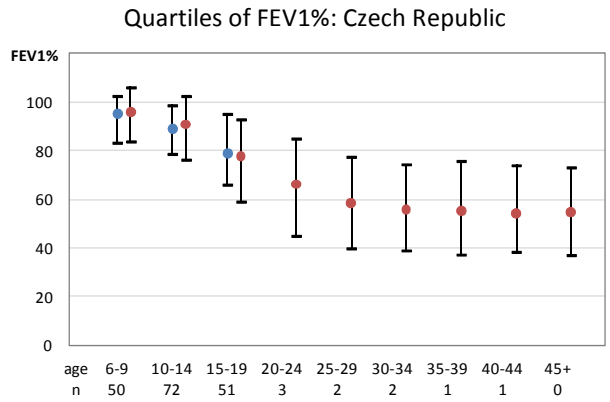
Figure 4.2 Quartiles of FEV1% of predicted by age group and by country. Patients aged 6 years or older and who have never had a lung transplant.

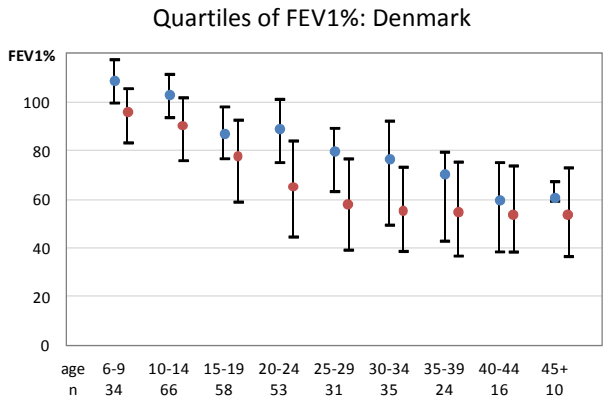
The figures below show the FEV1% in different age groups, separately for each country. The dot shows the median, and the whiskers show the 25th and 75th percentiles (the median, the 25th percentile and the 75th percentile are collectively named "quartiles"). In blue are the quartiles for the country, 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 underneath the horizontal axis). We therefore excluded Latvia and the Republic of Moldova from the graphs because none of the age groups had more than 10 patients.

Note: not all the countries reported the best FEV1 value of the year:
France reported the last FEV1 of the year,
Germany reported the FEV1 value closest to the patient's birthday (without exacerbation),
Sweden reported FEV1 collected at the time of the annual review.



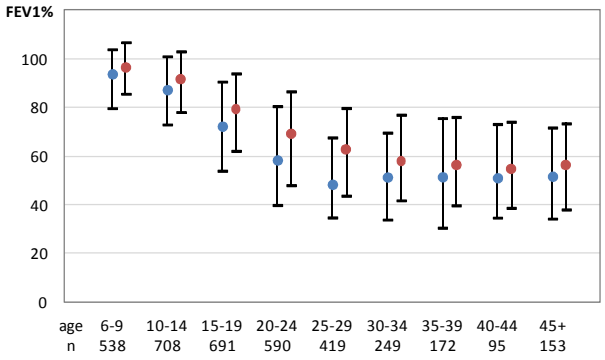




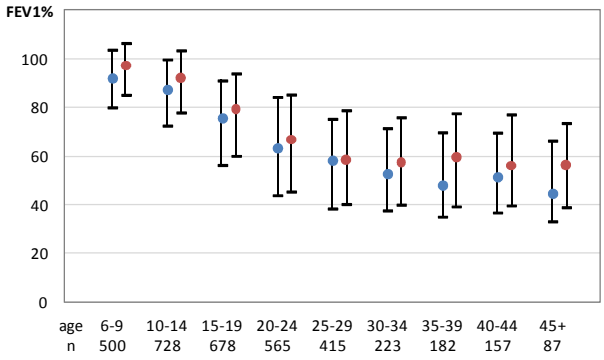


[figure 4.2 continued]

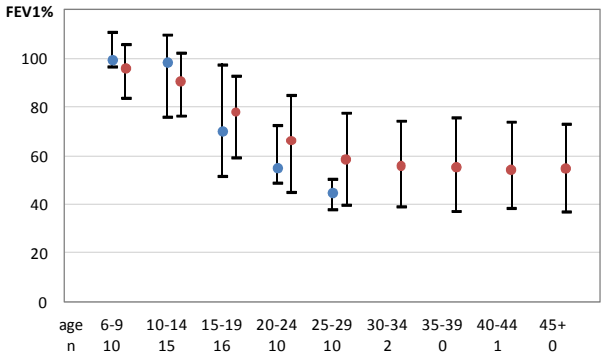
Quartiles of FEV1%: France[1]



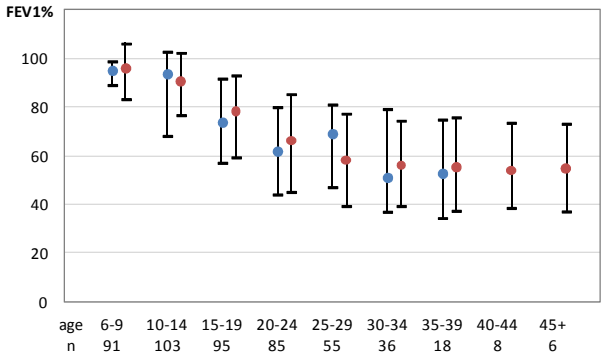
Quartiles of FEV1%: Germany[2]



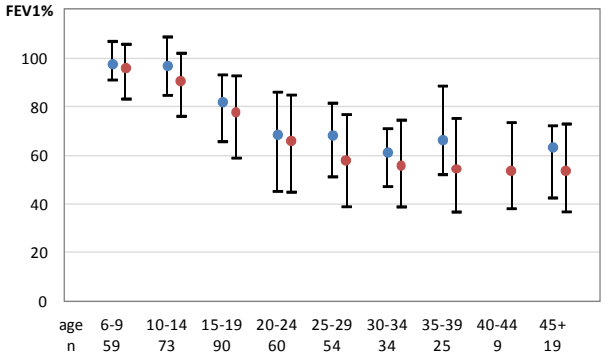
Quartiles of FEV1%: Greece



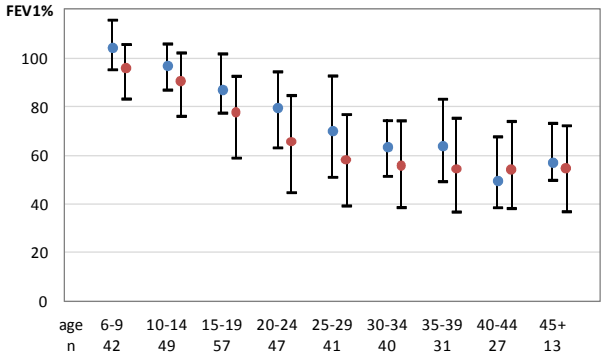
Quartiles of FEV1%: Ireland



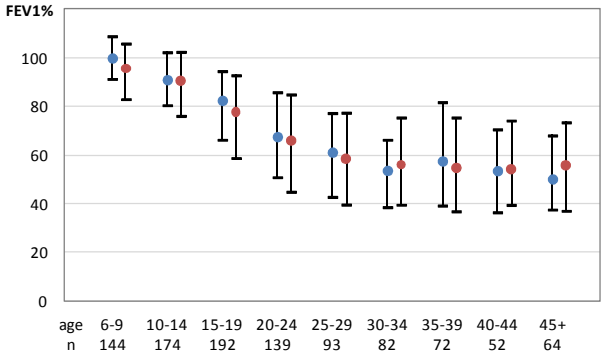
Quartiles of FEV1%: Israel



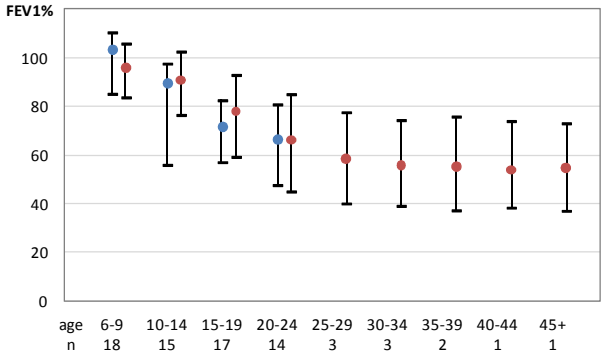
Quartiles of FEV1%: Italy



Quartiles of FEV1%: The Netherlands



Quartiles of FEV1%: Portugal

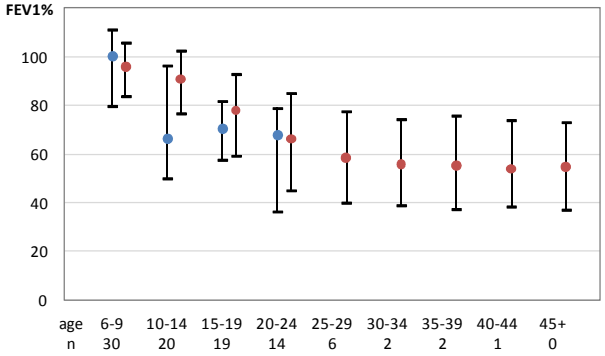


[1] France: reports the last FEV1 of the year.

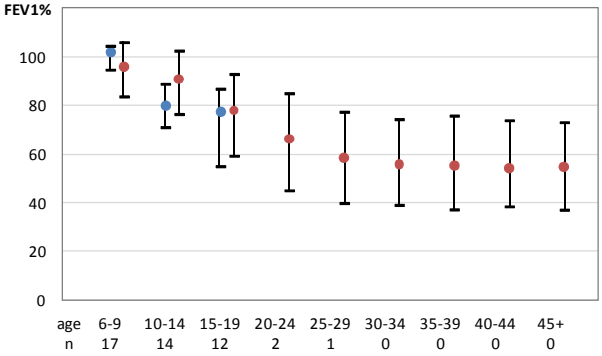
[2] Germany: reports the FEV1 value closest to the patient's birthday (without exacerbation).

[figure 4.2 continued]

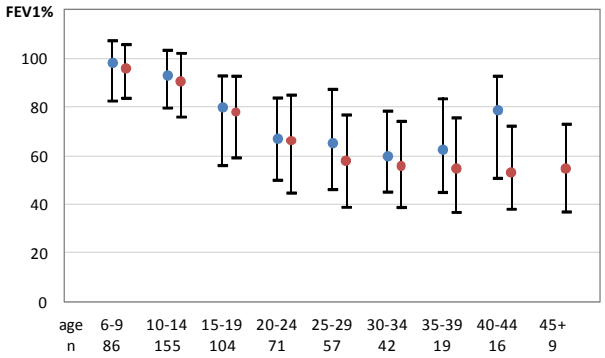
Quartiles of FEV1%: Serbia



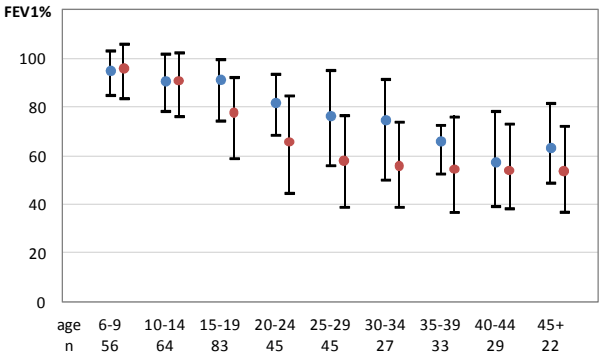
Quartiles of FEV1%: Slovenia



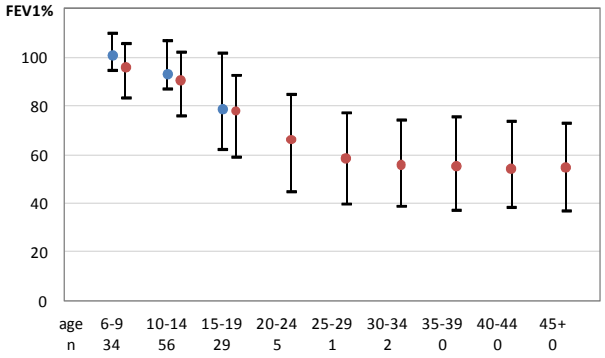
Quartiles of FEV1%: Spain



Quartiles of FEV1%: Sweden[3]

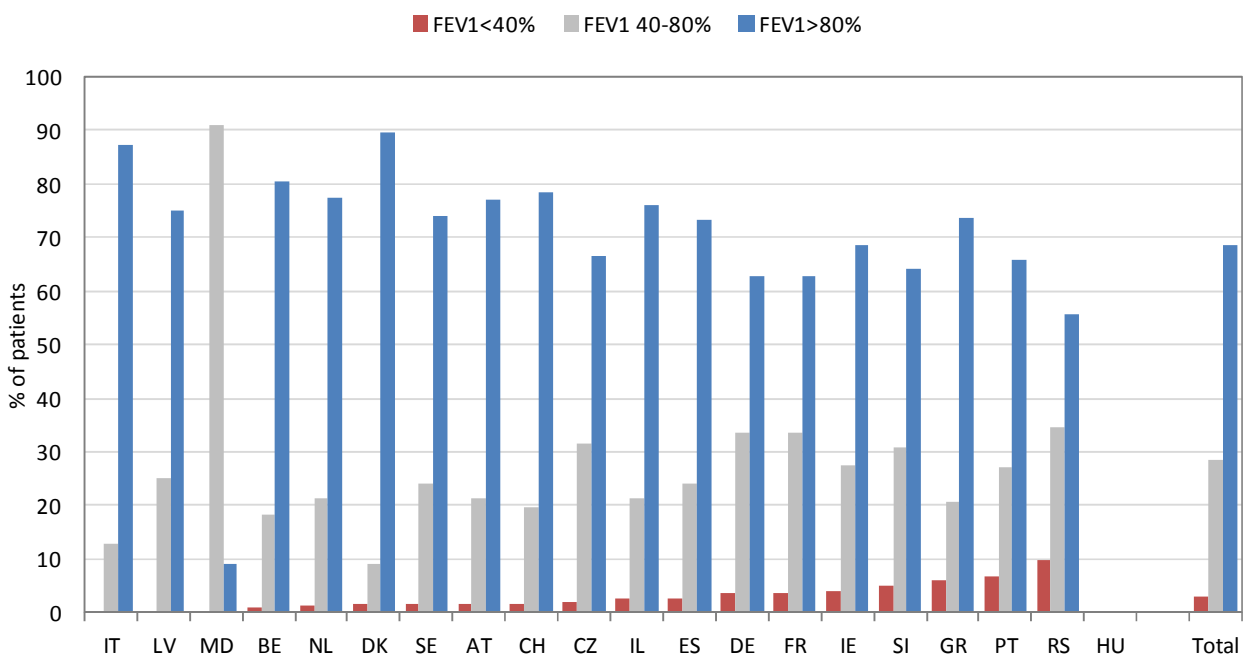


Quartiles of FEV1%: Switzerland



[3] Sweden: reports FEV1 collected at the time of the annual review.

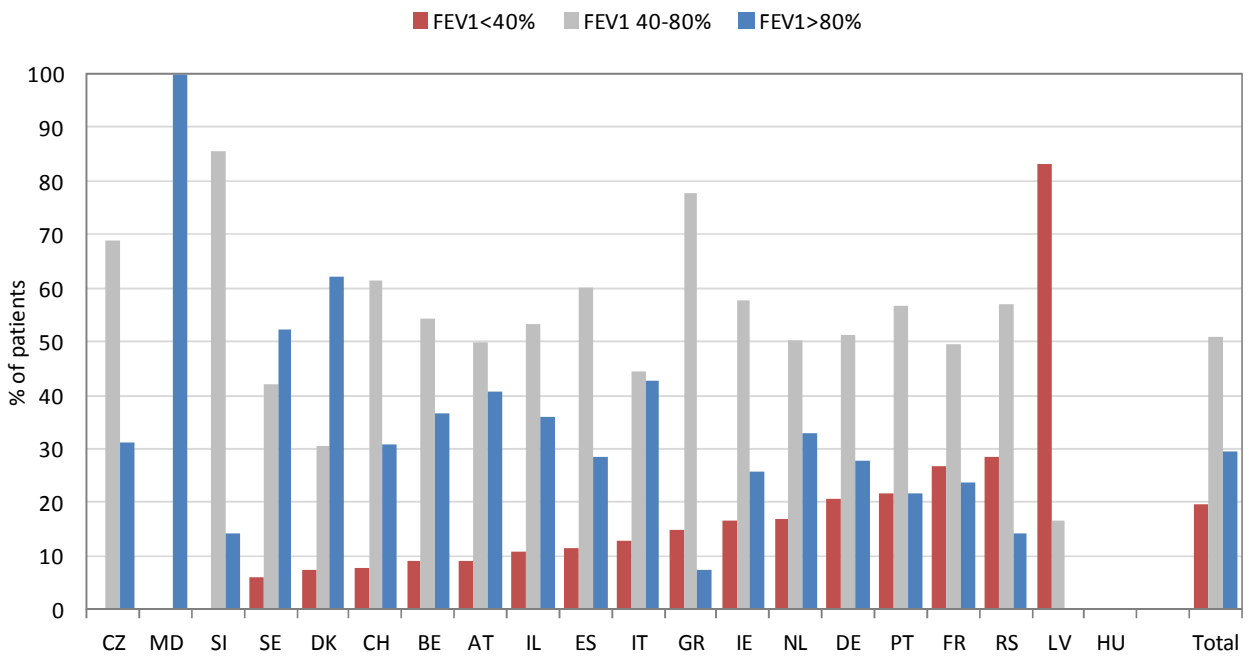
Figure 4.3 FEV1% of predicted according to severity group and age group, by country and overall. Patients aged 6-17 years who have never had a lung transplant.



Note: not all the countries reported the best FEV1 value of the year:
France reported the last FEV1 of the year,
Germany reported the FEV1 value closest to the patient's birthday (without exacerbation),
Sweden reported FEV1 collected at the time of the annual review.

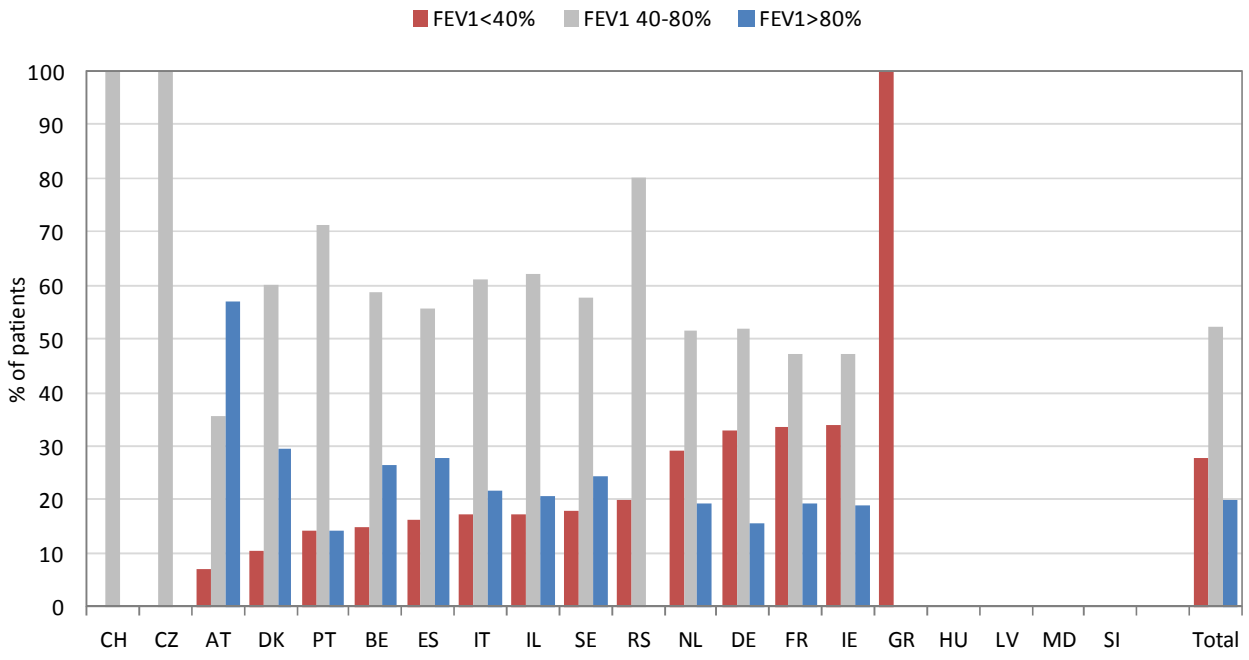
Figures 4.3, 4.4 and 4.5 show the FEV1% by severity group by country and overall. Patients with an FEV1% higher than 80% are generally considered to have mild lung disease, patients with FEV1% between 80 and 40% moderate lung disease and patients with FEV1 <40% severe lung disease. However, since a 10 year old child with a lung function of 50% has considerably worse lung disease than a 50 year old patient with the same FEV1%, and the age distribution is not the same in all countries, we have chosen to show children (fig 4.3) and adults (fig 4.4 and 4.5) separately.

Figure 4.4 FEV1% of predicted according to severity group and age group, by country and overall. Patients aged 18-29 years who have never had a lung transplant.



Note: not all the countries reported the best FEV1 value of the year:
France reported the last FEV1 of the year,
Germany reported the FEV1 value closest to the patient's birthday (without exacerbation),
Sweden reported FEV1 collected at the time of the annual review.

Figure 4.5 FEV1% of predicted according to severity group and age group, by country and overall. Patients aged 30 years or older who have never had a lung transplant.



Note: not all the countries reported the best FEV1 value of the year:
France reported the last FEV1 of the year,
Germany reported the FEV1 value closest to the patient's birthday (without exacerbation),
Sweden reported FEV1 collected at the time of the annual review.

5. Microbiology

Cystic fibrosis patients suffer from recurrent, sometimes chronic, lung infections, and some of these have been associated with poorer prognosis. We collect data on three chronic infections – *Pseudomonas aeruginosa*, *Burkholderia species* and *Staphyloccocus aureus* – as well as the occurrence of non-tuberculous mycobacteria (NTM) and *Stenotrophomonas maltophilia*. In the microbiology category discrepancies in definitions between the ECFSPR and the national registries exist. The ECFSPR definition of chronic infection (see Appendix 2) is:

> 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
>
> a. modified Leeds criteria, chronic infection: >50% of the sputum samples positive, collected during the last 12 months. At least 4 sputum samples during that period;
> b. and/or significantly raised bacteria-specific antibodies according to local laboratories).

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

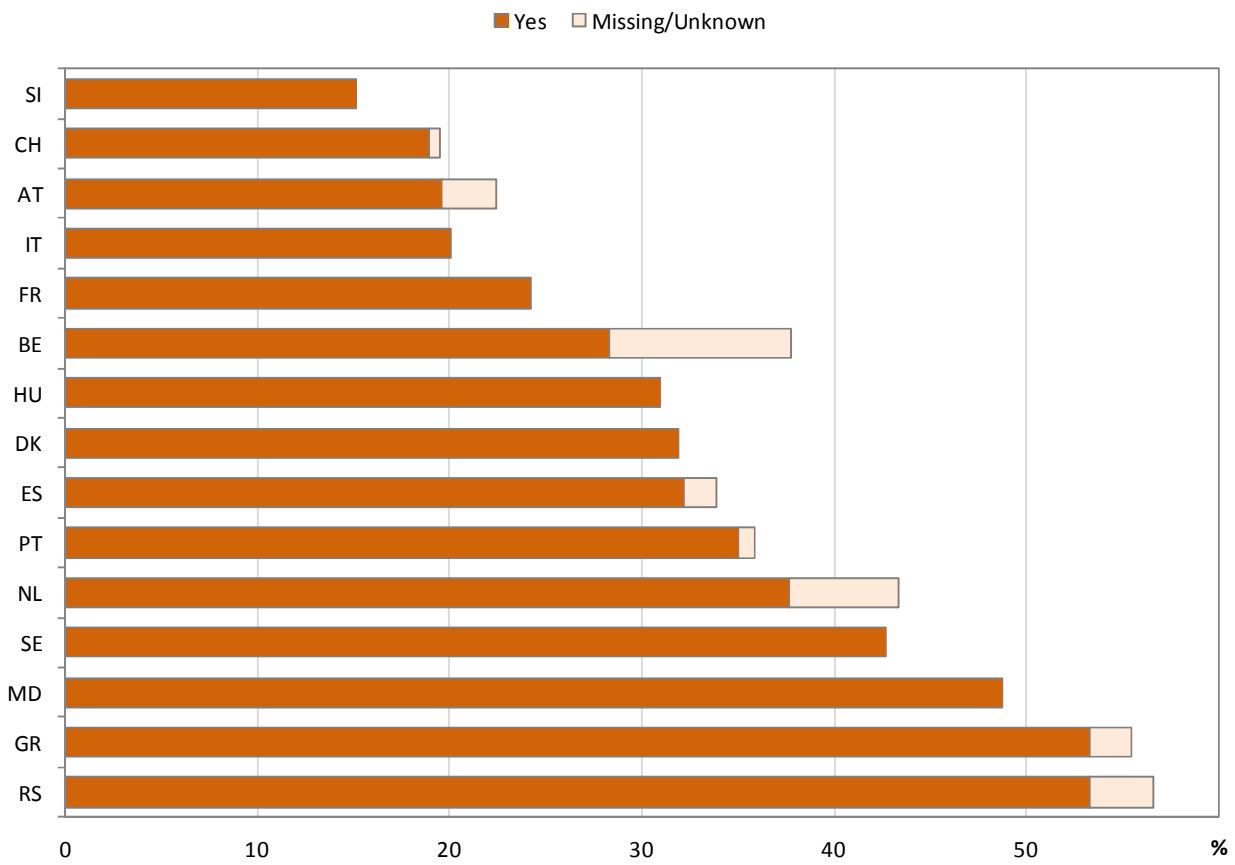
Table 5.1 Prevalence of chronic bacterial infection in all patients seen in 2009, by country.

Country	Chronic *Pseudomonas aeruginosa* number (%)			Chronic *Burkholderia species* number (%)			Chronic *Staphylococcus aureus* number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	10 (2.8)	273 (77.6)	69 (19.6)	9 (2.6)	332 (94.3)	11 (3.1)	13 (3.7)	187 (53.1)	152 (43.2)
Belgium	106 (9.4)	703 (62.3)	320 (28.3)	112 (9.9)	1000 (88.6)	17 (1.5)	1129 (100)	-	-
Czech Republic	461 (90.9)	32 (6.3)	14 (2.8)	461 (90.9)	40 (7.9)	6 (1.2)	461 (90.9)	15 (3.0)	31 (6.1)
Denmark	0 (0)	307 (68.1)	144 (31.9)	0 (0)	424 (94.0)	27 (6.0)	451 (100)	-	-
France	0 (0)	4275 (75.8)	1365 (24.2)	0 (0)	5566 (98.7)	74 (1.3)	5640 (100)	-	-
Germany	5048 (100)	-	-	5048 (100)	-	-	5048 (100)	-	-
Greece	2 (2.2)	41 (44.5)	49 (53.3)	2 (2.2)	89 (96.7)	1 (1.1)	2 (2.2)	66 (71.7)	24 (26.1)
Hungary	0 (0)	383 (69.0)	172 (31.0)	0 (0)	546 (98.4)	9 (1.6)	555 (100)	-	-
Ireland	209 (20.5)	475 (46.5)	337 (33.0)	209 (20.5)	802 (78.5)	10 (1.0)	209 (20.5)	546 (53.5)	266 (26.0)
Israel	54 (10.1)	252 (47.3)	227 (42.6)	52 (9.7)	479 (89.9)	2 (0.4)	57 (10.7)	323 (60.6)	153 (28.7)
Italy	0 (0)	431 (80.0)	108 (20.0)	0 (0)	532 (98.7)	7 (1.3)	0 (0)	473 (87.8)	66 (12.2)
Latvia	13 (44.8)	3 (10.4)	13 (44.8)	20 (69.0)	6 (20.7)	3 (10.3)	17 (58.6)	1 (3.5)	11 (37.9)
Rep of Moldova	0 (0)	21 (51.2)	20 (48.8)	41 (100)	-	-	0 (0)	17 (41.5)	24 (58.5)
The Netherlands	71 (5.7)	708 (56.7)	470 (37.6)	65 (5.2)	1157 (92.6)	27 (2.2)	68 (5.4)	735 (58.9)	446 (35.7)
Portugal	1 (0.9)	75 (64.1)	41 (35.0)	0 (0)	107 (91.5)	10 (8.5)	0 (0)	72 (61.5)	45 (38.5)
Serbia	4 (3.3)	53 (43.4)	65 (53.3)	5 (4.1)	103 (84.4)	14 (11.5)	5 (4.1)	53 (43.4)	64 (52.5)
Slovenia	0 (0)	56 (84.8)	10 (15.2)	0 (0)	66(100)	0 (0)	0 (0)	33 (50.0)	33 (50.0)
Spain	13 (1.7)	489 (66.1)	238 (32.2)	14 (1.9)	700 (94.6)	26 (3.5)	13 (1.8)	420 (56.7)	307 (41.5)
Sweden	0 (0)	331 (57.3)	247 (42.7)	0 (0)	563 (97.4)	15 (2.6)	197 (34.1)	218 (37.7)	163 (28.2)
Switzerland	1 (0.5)	153 (80.5)	36 (19.0)	1 (0.5)	189 (99.5)	0 (0)	0 (0)	83 (43.7)	107 (56.3)

Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.

This table shows, separately by country, the frequencies of chronic *Pseudomonas aeruginosa*, chronic *Burkholderia species* and chronic *Staphylococcus aureus*. The number of missing values is also included. The identification rate of *Burkholderia species* especially may also be influenced by differences in culture techniques.

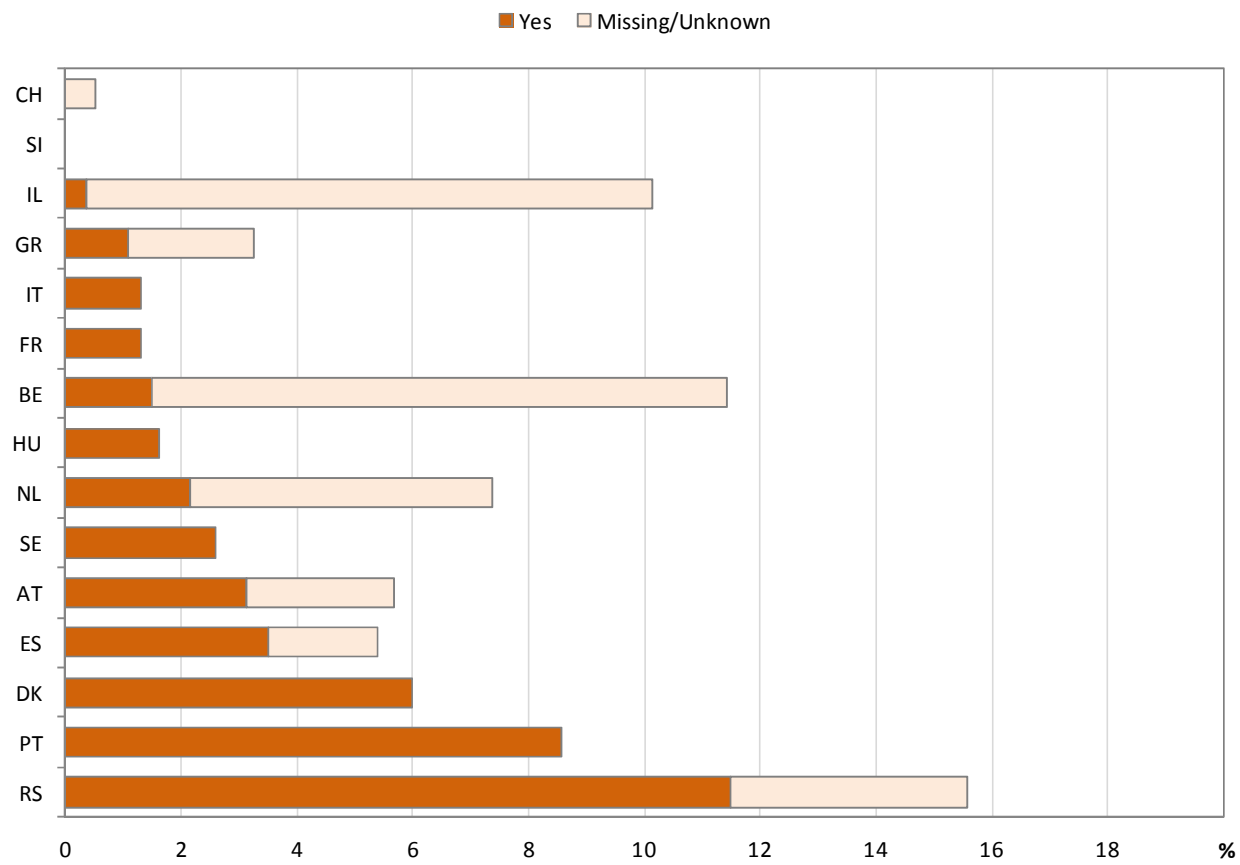
Figure 5.1 Prevalence of chronic Pseudomonas aeruginosa infection in all patients seen in 2009, by country.



Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.
Note: we excluded from the graph the countries for which the information on *Pseudomonas Aeruginosa* was missing for more than 10% of the patients.

The horizontal bars describe the percentage of patients with chronic *Pseudomonas Aeruginosa* infection (in dark orange) and the percentage of patients where information on *Pseudomonas aeruginosa* infection was missing (in light orange). This is a frequent infection, but prevalence varies considerably between countries.

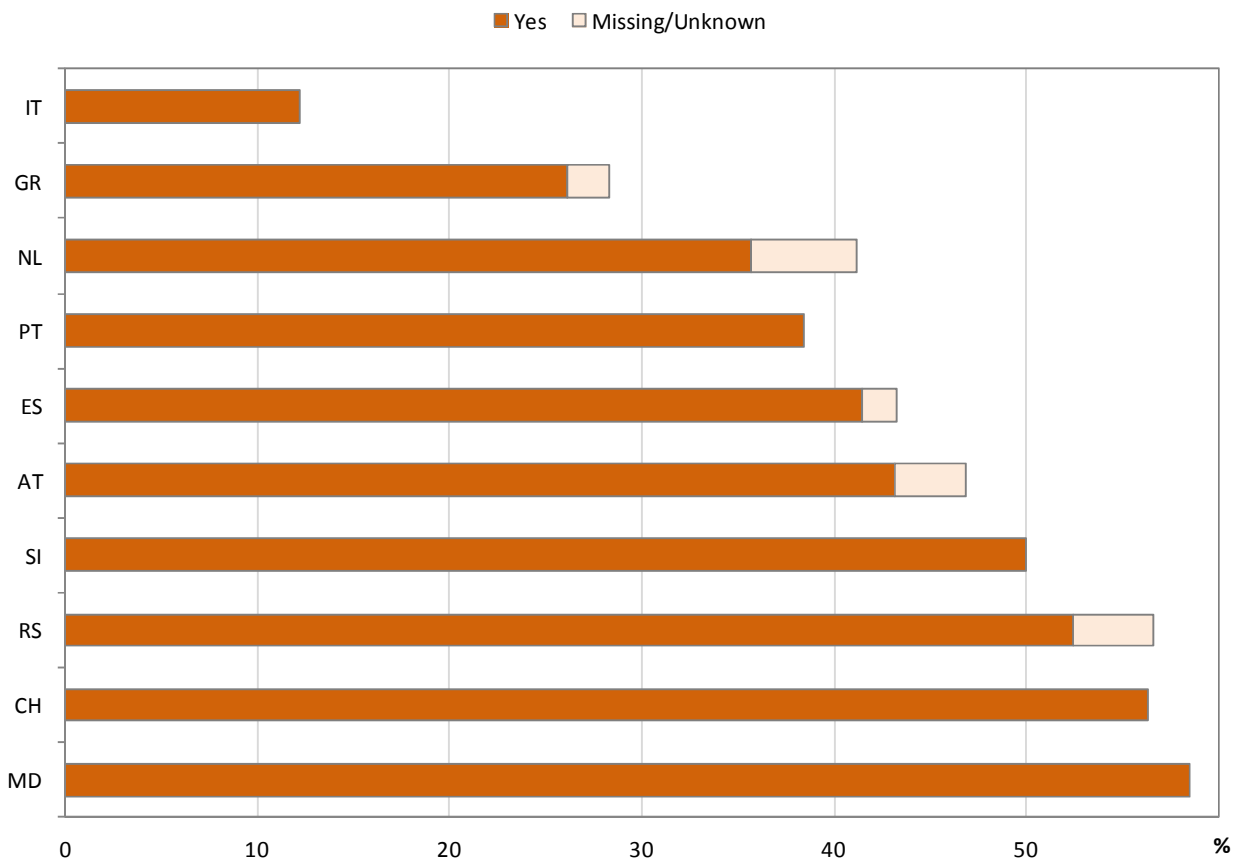
Figure 5.2 Prevalence of chronic Burkholderia species infection in all patients seen in 2009, by country.



Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.
Note: we excluded from the graph the countries for which the information on *Burkholderia species* was missing for more than 10% of the patients.

The horizontal bars describe the percentage of patients with chronic *Burkholderia* infection (in dark orange) and the percentage of patients where information on *Burkholderia* infection was missing (in light orange). This infection is much less frequent than *Pseudomonas aeruginosa* (note the different scale on the horizontal axis), but there is still some variation.

Figure 5.3 Prevalence of chronic Staphylococcus aureus infection in all patients seen in 2009, by country.



Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.
Note: we excluded from the graph the countries for which the information on *Staphylococcus aureus* was missing for more than 10% of the patients.

The horizontal bars describe the percentage of patients with chronic *Staphylococcus aureus* infection (in dark orange) and the percentage of patients where information on *Staphylococcus aureus* was missing (in light orange). This infection is as frequent as chronic *Pseudomonas aeruginosa* infection and with the same degree of variation between the countries.

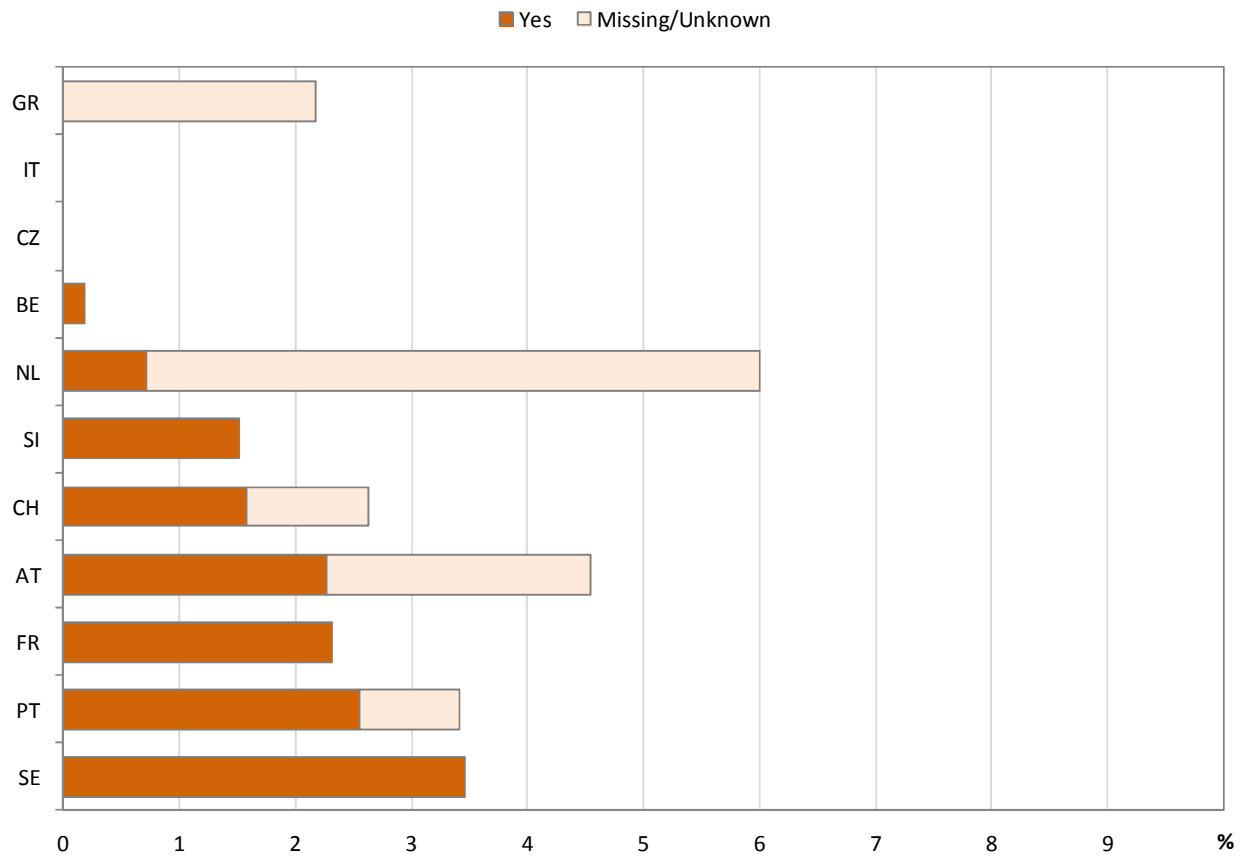
Table 5.2 Prevalence of non-tuberculous mycobacteria and Stenotrophomonas maltophilia infection in all patients seen in 2009, by country.

Country	Non-tuberculous mycobacteria (NTM) infection this year number (%)			*Stenotrophomonas maltophilia* infection this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	8 (2.3)	336 (95.4)	8 (2.3)	8 (2.3)	303 (86.0)	41 (11.7)
Belgium	0 (0)	1127 (99.8)	2 (0.2)	0 (0)	1033 (91.5)	96 (8.5)
Czech Republic	0 (0)	507 (100)	0 (0)	461 (90.9)	35 (6.9)	11 (2.2)
Denmark	451 (100)	-	-	451 (100)	-	-
France	0 (0.00)	5509 (97.7)	131 (2.3)	0 (0)	5202 (92.2)	438 (7.8)
Germany	5048 (100)	-	-	5048 (100)	-	-
Greece	2 (2.2)	90 (97.8)	0 (0)	2 (2.2)	87 (94.6)	3 (3.3)
Hungary	555 (100)	-	-	555 (100)	-	-
Ireland	209 (20.5)	809 (79.2)	3 (0.3)	1021 (100)	-	-
Israel	63 (11.8)	432 (81.1)	38 (7.1)	63 (11.8)	454 (85.2)	16 (3.0)
Italy	0(0)	539 (100)	0 (0)	0(0)	491 (91.1)	48 (8.9)
Latvia	29 (100)	-	-	11 (37.9)	17 (58.6)	1 (3.5)
Rep of Moldova	41 (100)	-	-	41 (100)	-	-
The Netherlands	66 (5.3)	1174 (94.0)	9 (0.7)	65 (5.2)	1078 (86.3)	106 (8.5)
Portugal	1 (0.8)	113 (96.6)	3 (2.6)	0 (0)	107 (91.4)	10 (8.6)
Serbia	121 (99.2)	1 (0.8)	0 (0)	5 (4.1)	111 (91.0)	6 (4.9)
Slovenia	0 (0)	65 (98.5)	1 (1.5)	0 (0)	59 (89.4)	7 (10.6)
Spain	193 (26.1)	528 (71.3)	19 (2.6)	16 (2.2)	664 (89.7)	60 (8.1)
Sweden	0 (0)	558 (96.5)	20 (3.5)	0 (0)	555 (96.0)	23 (4.0)
Switzerland	2 (1.0)	185 (97.4)	3 (1.6)	0 (0)	158 (83.2)	32 (16.8)

Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.

This table shows the frequency of two other infections, non-tuberculous mycobacteria (NTM) and *Stenotrophomonas maltophilia.* Both these infections seem to be relatively rare, in line with the frequencies of *Burkholderia* infection. The identification rate of these bacteria may also be influenced by differences in culture techniques.

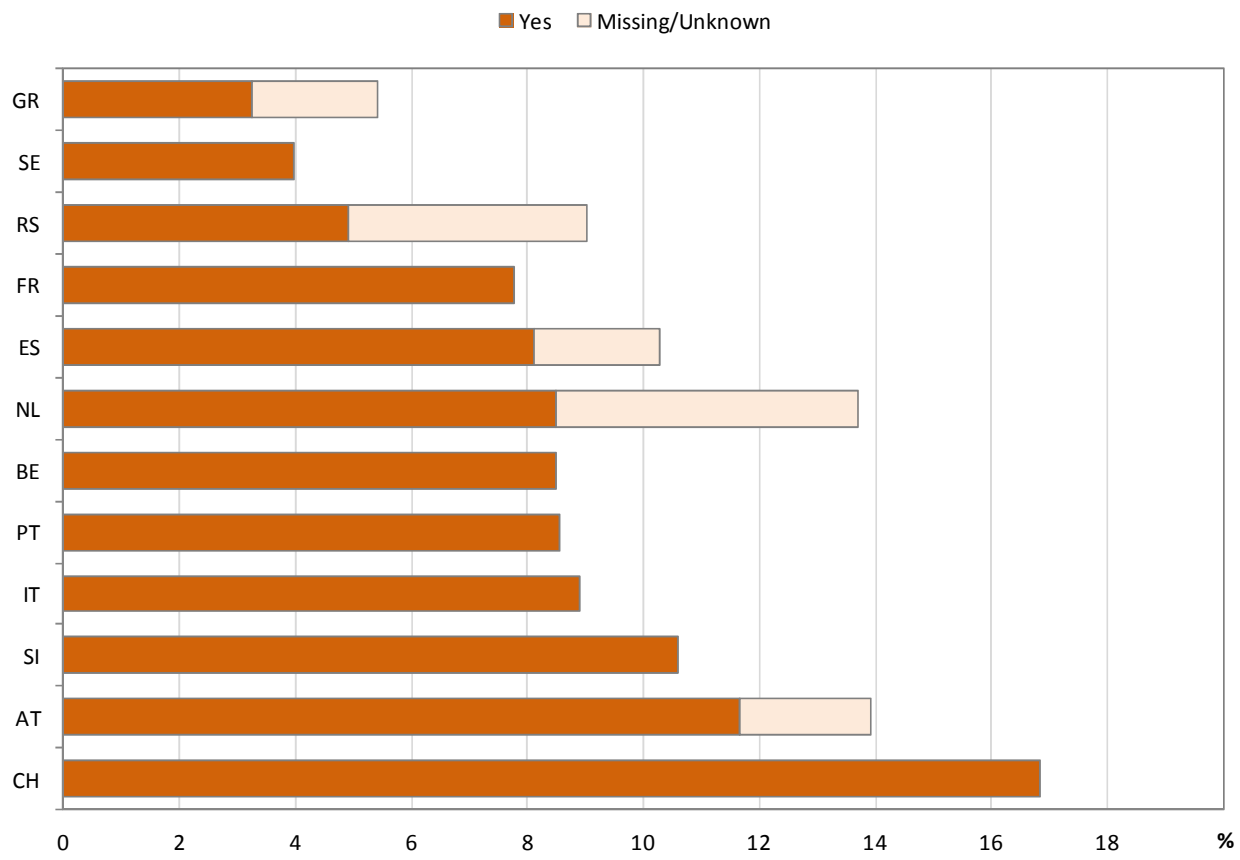
Figure 5.4 Prevalence of non-tuberculous mycobacteria in all patients seen in 2009, by country.



Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.
Note: we excluded from the graph the countries for which the information on non-tuberculous mycobacteria was missing for more than 10% of the patients.

The horizontal bars describe the percentage of patients with non-tuberculous mycobacteria infection (in dark orange) and the percentage of patients where information on non-tuberculous mycobacteria infection was missing (in light orange). Generally, infections from these bacteria are not very frequent in any country.

Figure 5.5 Prevalence of Stenotrophomonas maltophilia infection in all patients seen in 2009, by country.



Note: prevalence in 2008 for Ireland, computed on patients seen in 2008.
Note: we excluded from the graph the countries for which the information on *Stenotrophomonas maltophilia* was missing for more than 10% of the patients.

The horizontal bars describe the percentage of patients with *Stenotrophomonas maltophilia* infection (in dark orange) and the percentage of patients where information on *Stenotrophomonas maltophilia* was missing (light orange). The frequency varies considerably between countries.

6. Nutrition

Nutrition is another key aspect in cystic fibrosis. Pancreatic insufficiency, as seen in most patients, impairs the uptake of fat and protein from food, leading to malnutrition if not treated. Recurrent or chronic lung infections and sometimes respiratory insufficiency require extra energy intake, and poor nutrition may be a consequence. Control of nutrition is therefore important in CF and normal nutritional status is the goal. Since not all CF patients suffer from pancreatic insufficiency, we included data on pancreatic status in this chapter.

We collected weight and height measured at the time when the best FEV1 value was recorded, or last measurements of the year for patients that did not perform spirometry. From the raw measurements we calculated body mass index (BMI). A patient with low weight is not necessarily underweight if the height is also low, and BMI may better illustrate the nutritional status: BMI describes the weight/height relationship and is considered a good measure of nutritional status. A BMI of 18.5 kg/m^2 or less in adults is considered underweight by the WHO[2].

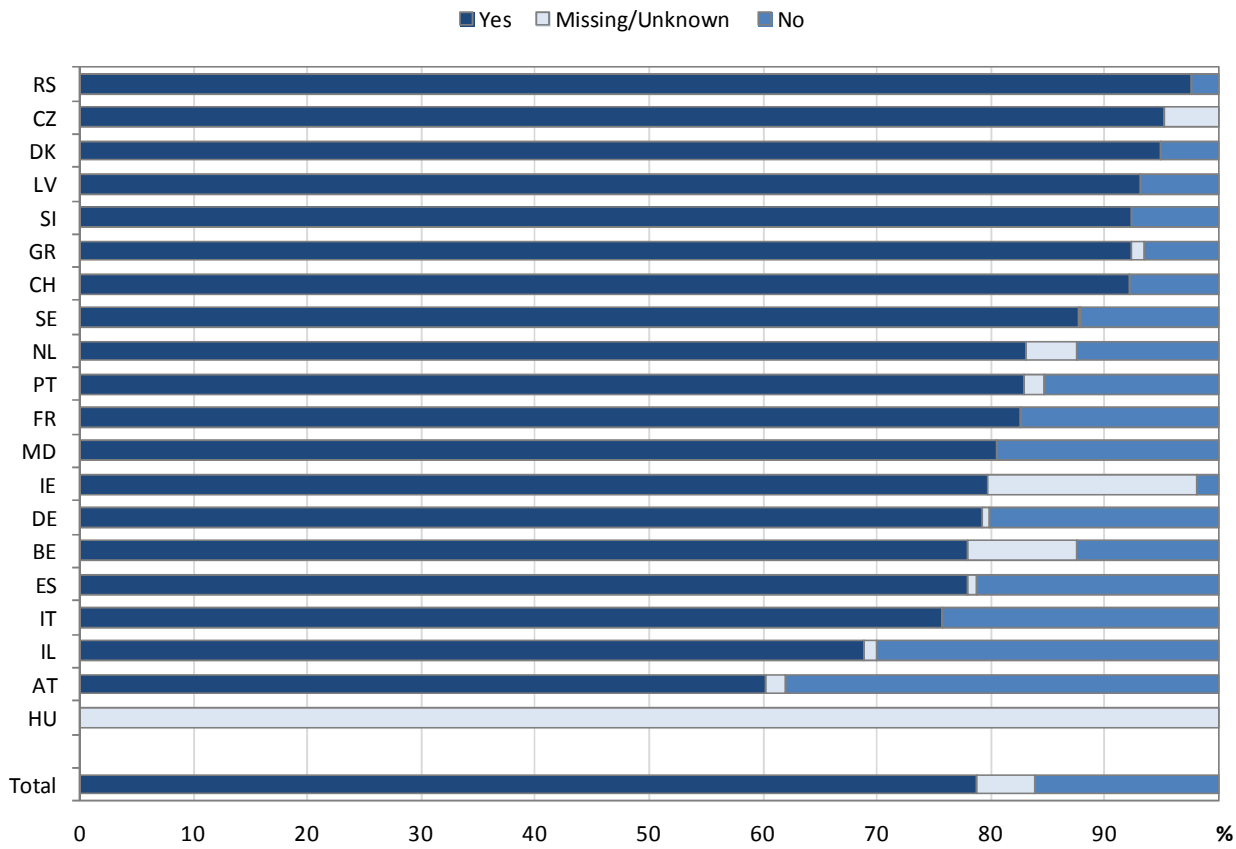
Weight, height and BMI were then expressed in terms of so-called z-scores by using a reference population of healthy individuals (in this case the US population: we used the reference values issued by the Centre for Disease Control, USA , see Appendix 1 for details).

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, 99.7% of all individuals have a z-score for weight between -3 and +3 (the same for height) and it is expected that the same happens for approximately 99.7% 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.

Pancreatic insufficiency is usually defined as absence of pancreatic enzymes in two stool samples (or too high levels of fat in stools). However, this information was rarely collected by the national registries, therefore we used the information on the use of pancreatic enzymes as an indicator of pancreatic insufficiency.

[2] http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

Figure 6.1 Use of pancreatic enzymes in 2009 for all patients, by country and overall.



Note: use of pancreatic enzymes in 2008 for Ireland, computed on patients seen in 2008.

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

Table 6.1 Number of patients for whom anthropometric measurements were available. All patients seen in 2009.

Country	Number of patients	Height		Weight	
		N	N miss	N	N miss
Austria	352	345	7	346	6
Belgium	1129	993	136	993	136
Czech Republic	507	271	236	274	233
Denmark	451	416	35	416	35
France	5640	5038	602	5050	590
Germany	5048	4685	363	4685	363
Greece	92	84	8	84	8
Hungary	555	0	555	0	555
Ireland	1021	702	319	712	309
Israel	533	507	26	507	26
Italy	539	538	1	538	1
Latvia	29	21	8	21	8
Republic of Moldova	41	15	26	15	26
The Netherlands	1249	1215	34	1207	42
Portugal	117	97	20	98	19
Serbia	122	119	3	120	2
Slovenia	66	66	0	66	0
Spain	740	708	32	708	32
Sweden	578	556	22	521	57
Switzerland	190	189	1	189	1

Note: number of patients seen in year 2008 for Ireland.

Table 6.2 Z-scores for height: descriptive statistics by country. Patients aged 17 years or younger.

Country	N	Mean	Min	25th pctl (25% of the patients are below this z-score for height)	Median (50% of the patients are below this z-score for height)	75th pctl (75% of the patients are below this z-score for height)	Max
Austria	273	-0.3	-3.4	-1.0	-0.2	0.5	2.7
Belgium	552	-0.3	-4.0	-0.9	-0.2	0.5	3.2
Czech Republic	243	-0.1	-2.8	-0.8	-0.1	0.6	3.6
Denmark	195	-0.1	-2.3	-0.7	-0.2	0.5	2.4
France	2738	-0.5	-4.8	-1.3	-0.5	0.2	6.9
Germany	2364	-0.3	-5.9	-1.1	-0.3	0.5	5.5
Greece	54	-0.3	-3.4	-1.2	-0.3	0.3	3.2
Hungary	-	-	-	-	-	-	-
Ireland	374	-0.6	-6.7	-1.2	-0.6	0.1	2.1
Israel	252	-0.7	-3.6	-1.4	-0.7	-0.1	1.9
Italy	189	-0.2	-3.4	-1.0	-0.3	0.6	3.1
Latvia	15	-0.6	-3.9	-1.5	-0.5	0.3	1.5
Rep of Moldova	12	-1.9	-5.1	-3.1	-2.0	-0.2	0.6
The Netherlands	607	0.2	-5.7	-0.5	0.2	0.9	4.9
Portugal	66	-0.7	-3.8	-1.3	-0.8	-0.1	1.6
Serbia	86	-0.5	-5.9	-1.2	-0.5	0.3	1.8
Slovenia	54	-0.4	-3.0	-1.0	-0.3	0.2	1.4
Spain	439	-0.5	-4.5	-1.2	-0.5	0.2	2.9
Sweden	259	-0.2	-3.0	-0.8	-0.1	0.5	2.8
Switzerland	173	-0.4	-3.8	-1.0	-0.4	0.4	2.7

Note: patients aged less than 18 years in 2008 for Ireland.

This table reports the median z-score for height (the value that separates the highest and lowest half of the patients), the mean z-score for height (the average) and other descriptive statistics for children (17 years or younger).

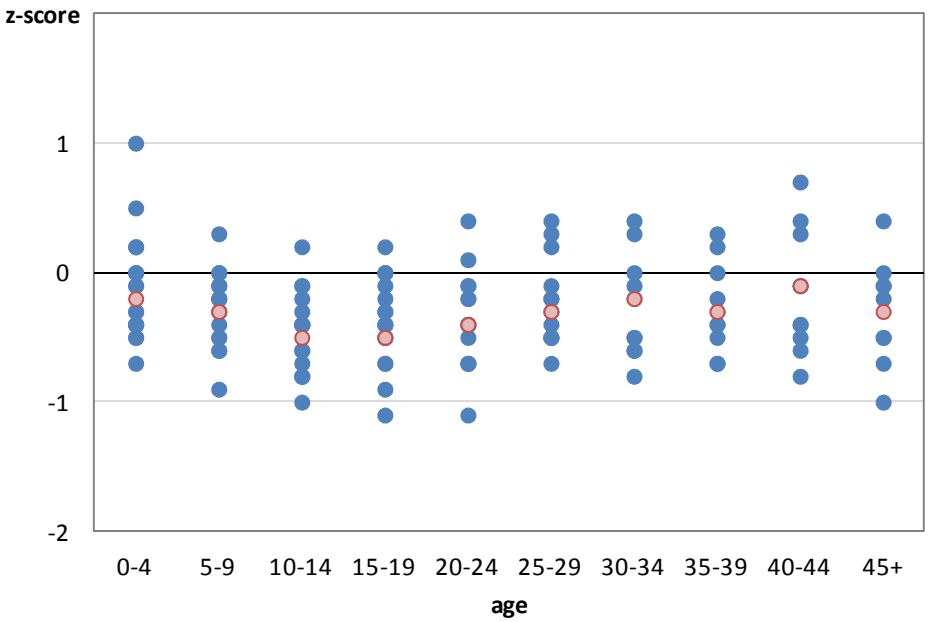
Table 6.3 Z-scores for height: descriptive statistics by country. Patients aged 18 years or older.

Country	N	Mean	Min	25th pctl (25% of the patients are below this z-score for height)	Median (50% of the patients are below this z-score for height)	75th pctl (75% of the patients are below this z-score for height)	Max
Austria	72	-0.2	-2.4	-0.7	-0.2	0.3	2.0
Belgium	441	-0.3	-3.4	-1.0	-0.3	0.4	2.4
Czech Republic	28	-0.0	-1.3	-0.7	-0.2	0.2	3.5
Denmark	221	0.0	-2.7	-0.7	0.0	0.7	3.2
France	2300	-0.6	-5.1	-1.2	-0.5	0.1	2.9
Germany	2321	-0.1	-4.0	-0.8	-0.1	0.6	3.8
Greece	30	-0.3	-2.1	-0.8	-0.3	0.2	2.1
Hungary	-	-	-	-	-	-	-
Ireland	328	-0.5	-3.7	-1.1	-0.5	0.3	2.0
Israel	255	-0.7	-4.7	-1.4	-0.7	0.1	2.6
Italy	349	-0.4	-3.4	-1.0	-0.5	0.2	2.6
Latvia	6	-0.1	-0.8	-0.5	-0.1	0.3	0.9
Rep of Moldova	3	0.9	0.0	0.0	0.9	1.8	1.8
The Netherlands	608	0.2	-3.8	-0.5	0.3	0.9	3.3
Portugal	31	-0.7	-2.9	-1.5	-0.7	-0.2	1.5
Serbia	33	-0.1	-2.3	-0.8	-0.2	0.4	2.0
Slovenia	12	0.1	-1.5	-0.6	0.2	0.4	2.3
Spain	269	-0.7	-4.0	-1.4	-0.7	-0.2	1.6
Sweden	297	0.2	-3.0	-0.5	0.3	0.9	3.3
Switzerland	16	-0.0	-1.7	-0.8	0.1	0.4	1.9

Note: patients aged 18 years or more in 2008 for Ireland.

This table reports the median z-score for height (the value that separates the highest and lowest half of the patients), the mean z-score for height (the average) and other descriptive statistics for adults (18 years or older).

Figure 6.2 Median z-scores for height by age group and by country. All patients seen in 2009.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the analyses those age groups where the number of patients was <10.

This graph shows the median z-scores for height by age group. Each country is represented by a dot (in blue) and the overall estimate is in red. The median z-scores for height tend to slowly decrease up to the teenage years and then rise again before levelling out. Since the z-scores are computed using healthy people as a reference, this pattern can be explained by the fact that CF patients reach the puberty growth spurt later than their peers but then catch up. The graph also shows that there is large variability between countries.

Table 6.4 Z-scores for height: descriptive statistics by age group. All patients seen in 2009.

Age at height measurement	N	Mean	Min	25th pctl	Median	75th pctl	Max
0-4	2034	-0.2	-5.9	-0.9	-0.2	0.6	6.9
5-9	2573	-0.3	-4.5	-1.0	-0.3	0.4	3.3
10-14	2694	-0.5	-6.7	-1.2	-0.5	0.3	3.2
15-19	2609	-0.5	-5.1	-1.1	-0.5	0.3	3.9
20-24	2111	-0.4	-4.7	-1.1	-0.4	0.3	3.8
25-29	1610	-0.3	-5.1	-1.0	-0.3	0.4	3.6
30-34	1087	-0.2	-3.4	-1.0	-0.2	0.4	3.3
35-39	799	-0.2	-3.7	-1.0	-0.3	0.4	2.6
40-44	555	-0.1	-3.3	-0.8	-0.1	0.6	2.7
45+	493	-0.2	-3.4	-1.0	-0.3	0.6	2.6

Note: patients seen in 2008 for Ireland.

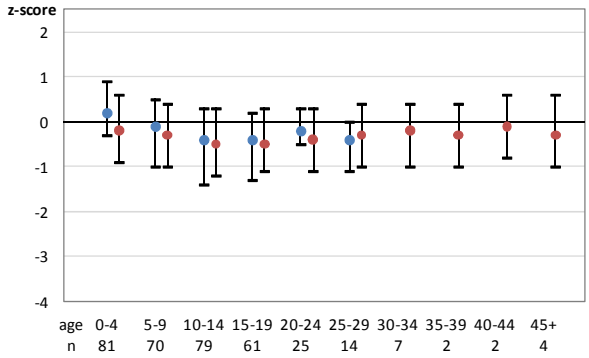
This table reports the median z-score for height and other descriptive statistics by age group for all the patients seen in 2009. The median values reported in this table are shown as red dots in fig 6.2.

Figure 6.3 Quartiles of z-scores for height by age group and by country. All patients seen in 2009.

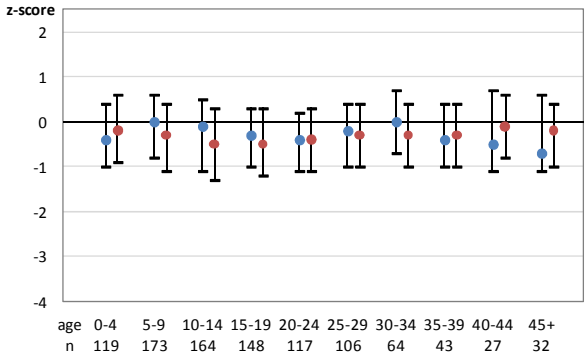
The figures below show the z-scores for height by country. The dot is the median and the whiskers show the 25th and 75th percentiles. In blue are the quartiles for the country, in red are the pooled quartiles computed on all other countries (i.e. excluding that country). We did not compute quartiles 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 Latvia and the Republic of Moldova from the graphs because none of the age groups had more than 10 patients.

Note: patients seen in 2008 for Ireland.

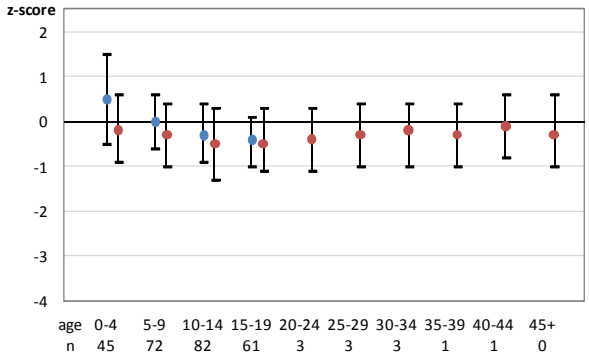
Quartiles of z-scores for height: Austria



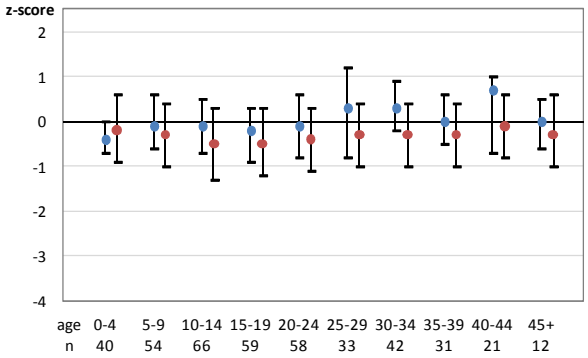
Quartiles of z-scores for height: Belgium



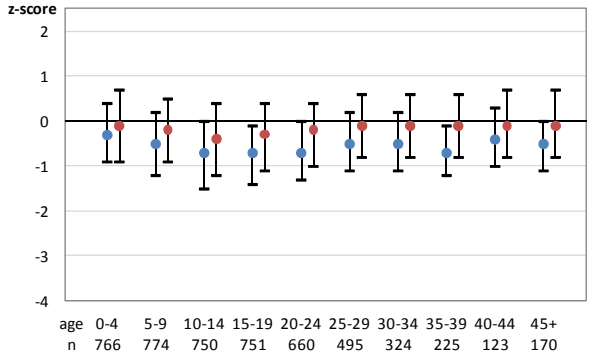
Quartiles of z-scores for height: Czech Republic



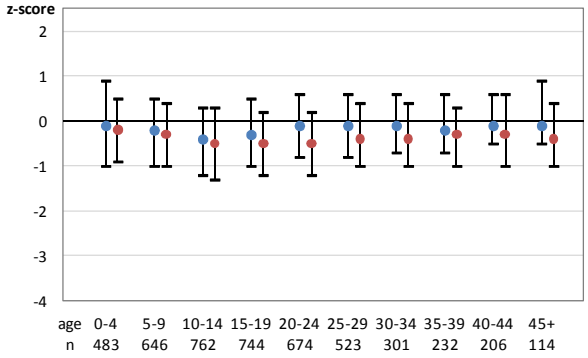
Quartiles of z-scores for height: Denmark



Quartiles of z-scores for height: France

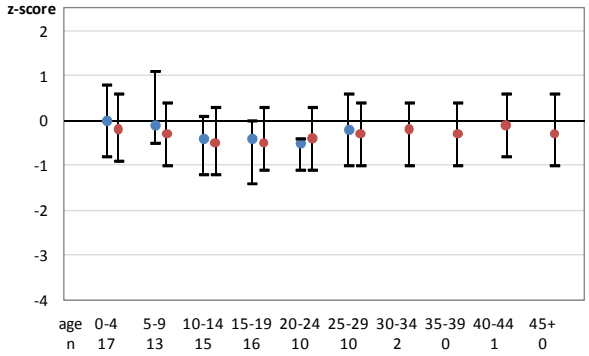


Quartiles of z-scores for height: Germany

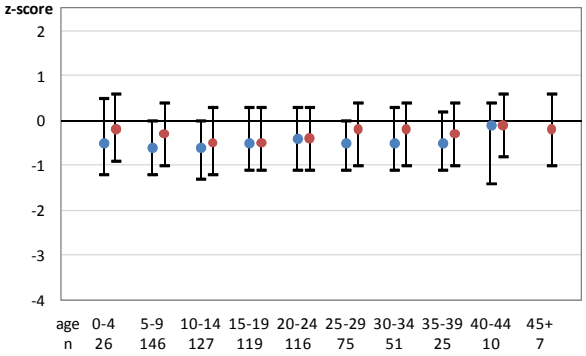


[figure 6.3 continued]

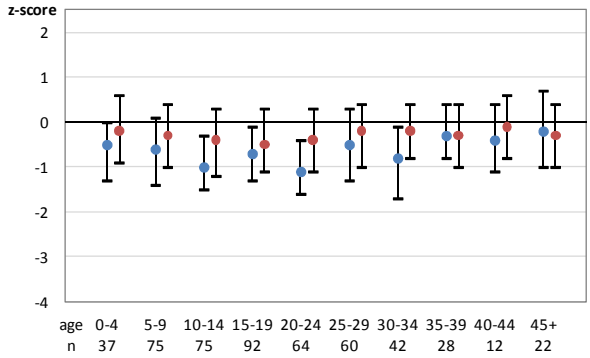
Quartiles of z-scores for height: Greece



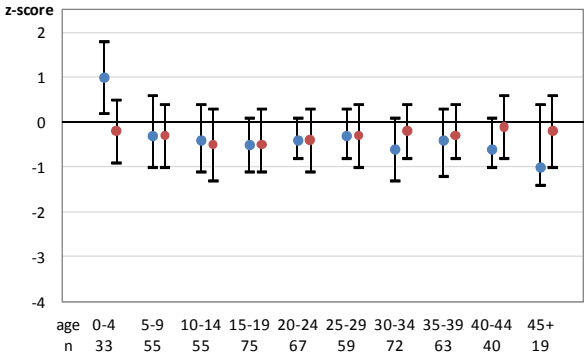
Quartiles of z-scores for height: Ireland



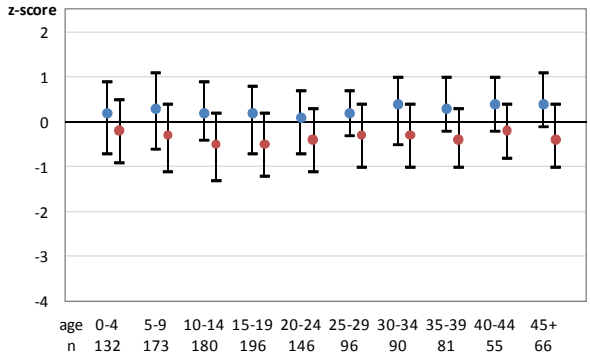
Quartiles of z-scores for height: Israel



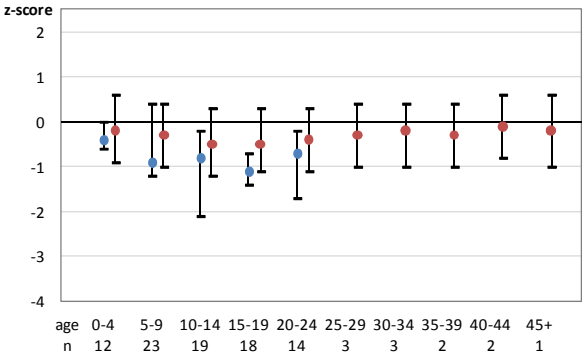
Quartiles of z-scores for height: Italy



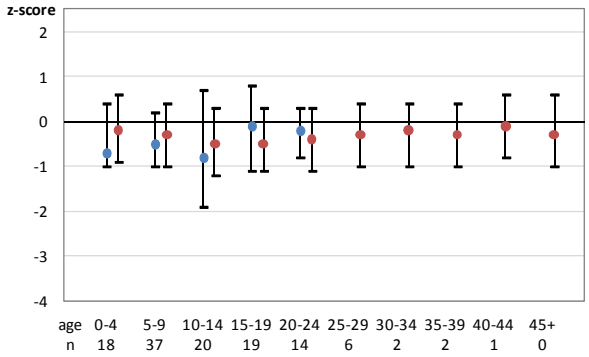
Quartiles of z-scores for height: The Netherlands



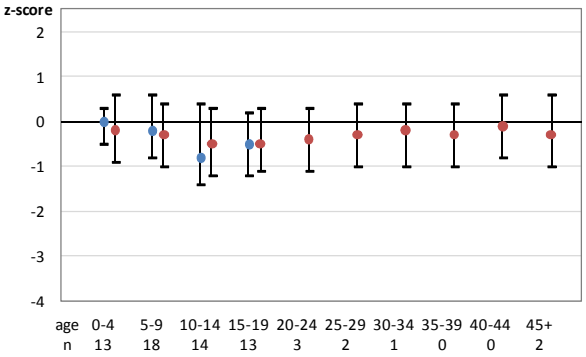
Quartiles of z-scores for height: Portugal



Quartiles of z-scores for height: Serbia

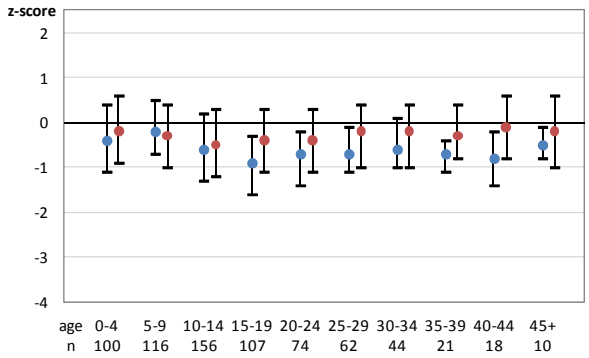


Quartiles of z-scores for height: Slovenia

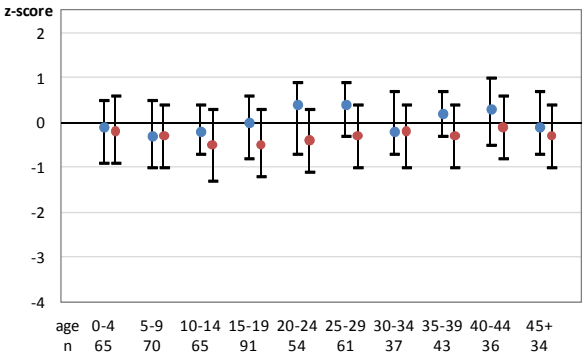


[figure 6.3 continued]

Quartiles of z-scores for height: Spain



Quartiles of z-scores for height: Sweden



Quartiles of z-scores for height: Switzerland

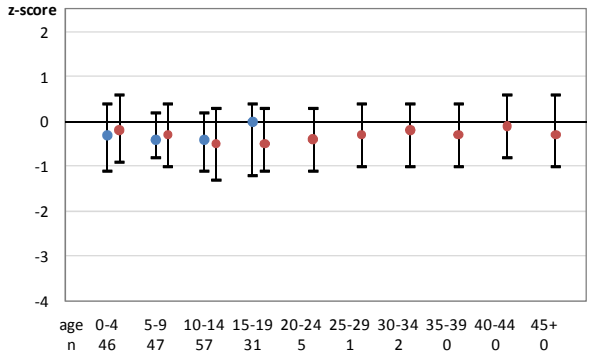


Table 6.5 Z-scores for weight: descriptive statistics by country. Patients aged 17 years or younger.

Country	N	Mean	Min	25th pctl (25% of the patients are below this z-score for weight)	Median (50% of the patients are below this z-score for weight)	75th pctl (75% of the patients are below this z-score for weight)	Max
Austria	274	-0.4	-5.0	-1.2	-0.3	0.4	2.1
Belgium[1]	553	-0.5	-4.9	-1.1	-0.4	0.3	2.1
Czech Republic	246	-0.4	-4.4	-1.1	-0.3	0.4	3.9
Denmark	195	-0.3	-2.9	-0.9	-0.3	0.2	1.9
France	2739	-0.7	-7.1	-1.4	-0.6	0.0	3.6
Germany	2364	-0.6	-7.0	-1.2	-0.5	0.2	9.3
Greece	54	-0.3	-3.1	-1.3	-0.4	0.8	4.3
Hungary	-	-	-	-	-	-	-
Ireland	371	-0.5	-5.8	-1.1	-0.4	0.3	2.4
Israel	252	-0.6	-3.2	-1.2	-0.5	0.1	1.8
Italy	189	-0.3	-3.3	-0.9	-0.2	0.5	2.3
Latvia	15	-1.3	-4.9	-1.9	-1.1	0.1	0.7
Rep of Moldova	12	-2.7	-5.7	-3.5	-2.8	-1.1	-0.2
The Netherlands	607	-0.1	-3.8	-0.7	0.0	0.6	5.9
Portugal	67	-0.7	-4.8	-1.3	-0.7	0.1	2.0
Serbia	87	-0.7	-5.7	-1.5	-0.5	0.4	2.4
Slovenia	54	-0.8	-5.4	-1.5	-0.6	0.1	1.6
Spain	439	-0.5	-5.3	-1.1	-0.4	0.3	3.2
Sweden	259	-0.2	-3.7	-0.8	-0.0	0.4	1.9
Switzerland	173	-0.6	-3.6	-1.3	-0.5	0.2	2.6

Note: patients seen in 2008 for Ireland.

[1]Belgium: last weight of the year for all patients.

This table reports the median z-score for weight (the value that separates the highest and lowest half of the patients), the mean z-score for weight (the average) and other descriptive statistics for children (17 years or younger).

Table 6.6 Z-scores for weight: descriptive statistics by country. Patients aged 18 years or older.

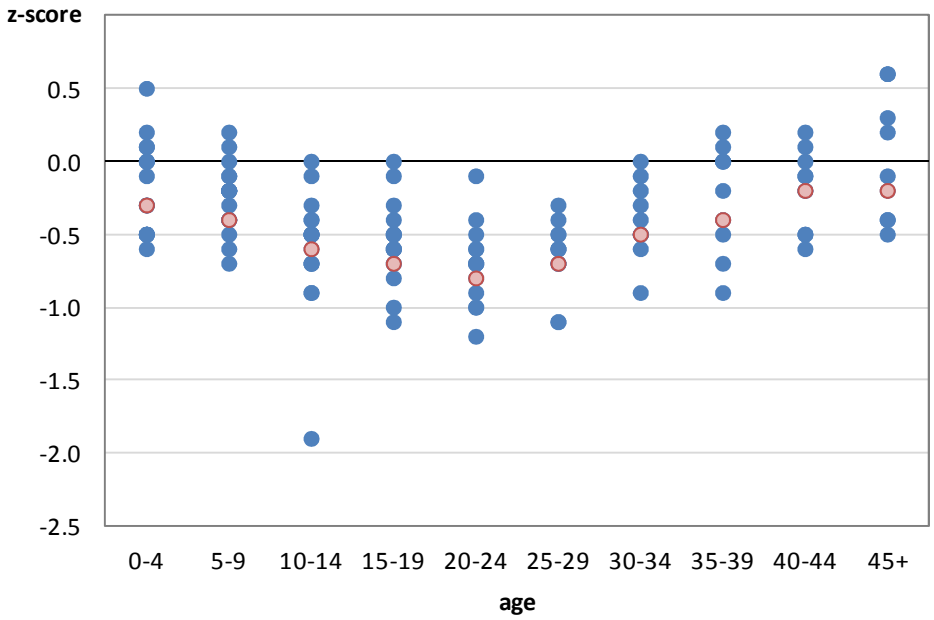
Country	N	Mean	Min	25th pctl (25% of the patients are below this z-score for weight)	Median (50% of the patients are below this z-score for weight)	75th pctl (75% of the patients are below this z-score for weight)	Max
Austria	72	-0.8	-3.8	-1.4	-0.7	0.1	1.7
Belgium[1]	440	-0.6	-6.1	-1.3	-0.6	0.2	2.6
Czech Republic	28	-0.6	-3.2	-1.1	-0.7	0.2	1.2
Denmark	221	-0.3	-3.9	-1.1	-0.3	0.5	2.6
France	2311	-1.0	-8.5	-1.7	-1.0	-0.2	3.1
Germany	2321	-0.6	-6.5	-1.3	-0.5	0.1	2.9
Greece	30	-0.8	-3.1	-1.6	-0.8	-0.1	0.9
Hungary	-	-	-	-	-	-	-
Ireland	341	-0.6	-4.1	-1.2	-0.5	0.2	2.8
Israel	255	-0.6	-4.6	-1.3	-0.5	0.2	2.8
Italy	349	-0.7	-7.9	-1.3	-0.6	0.0	2.4
Latvia	6	-2.3	-3.0	-2.5	-2.3	-2.1	-1.5
Rep of Moldova	3	-0.2	-0.6	-0.6	-0.4	0.4	0.4
The Netherlands	600	-0.2	-4.9	-0.8	-0.2	0.4	2.2
Portugal	31	-1.0	-3.3	-2.1	-0.9	-0.4	0.8
Serbia	33	-1.1	-5.5	-1.7	-0.6	-0.1	0.7
Slovenia	12	-0.6	-2.7	-1.3	-0.2	0.3	0.6
Spain	269	-0.7	-6.3	-1.3	-0.6	0.1	3.3
Sweden	262	-0.1	-3.2	-0.6	-0.1	0.5	2.9
Switzerland	16	-0.7	-1.8	-1.2	-0.8	-0.1	0.8

Note: patients seen in 2008 for Ireland.

[1]Belgium: last weight of the year for all patients.

This table reports the median z-score for weight (the value that separates the highest and lowest half of the patients), the mean z-score for weight (the average) and other descriptive statistics for adults (18 years or older).

Figure 6.4 Median z-scores for weight by age group and by country. All patients seen in 2009.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the analyses those age groups where the number of patients was <10.

This graph shows the median z-scores for weight by age group. Each country is represented by a dot (in blue) and the overall estimate is in red. Overall the median z-scores for weight slightly decrease from the youngest age group to the second youngest, probably because some patients are underweight before diagnosis; afterwards the weight decreases again until the 20-24 year age group before it increases in the older age groups. Again, 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.

Table 6.7 Z-scores for weight: descriptive statistics by age group. All patients seen in 2009.

Age at weight measurement	N	Mean	Min	25th pctl	Median	75th pctl	Max
0-4	2039	-0.4	-6.0	-1.2	-0.3	0.4	9.3
5-9	2573	-0.4	-5.8	-1.0	-0.4	0.3	3.2
10-14	2692	-0.7	-6.3	-1.4	-0.6	0.1	2.3
15-19	2611	-0.8	-8.5	-1.4	-0.7	0.0	2.6
20-24	2108	-0.9	-7.0	-1.6	-0.8	-0.1	3.3
25-29	1609	-0.8	-7.9	-1.5	-0.7	-0.0	2.9
30-34	1084	-0.6	-6.3	-1.2	-0.5	0.2	2.8
35-39	798	-0.5	-6.8	-1.1	-0.4	0.3	2.5
40-44	554	-0.3	-4.0	-1.0	-0.2	0.4	2.5
45+	482	-0.2	-4.6	-0.8	-0.2	0.7	2.9

Note: patients seen in 2008 for Ireland.

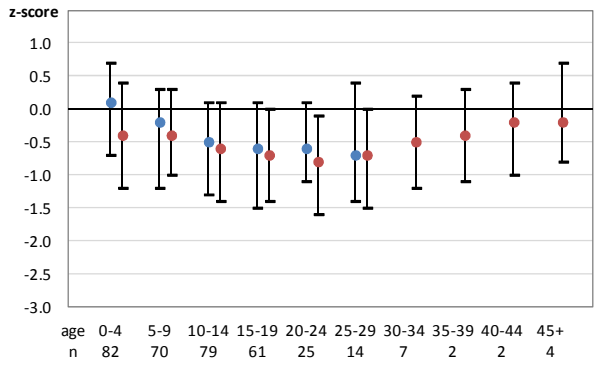
This table reports the median z-score for weight and other descriptive statistics by age group for all the patients seen in 2009. The median values reported in this table are shown as red dots in fig 6.4.

Figure 6.5 Quartiles of z-scores for weight by age group and by country. All patients seen in 2009.

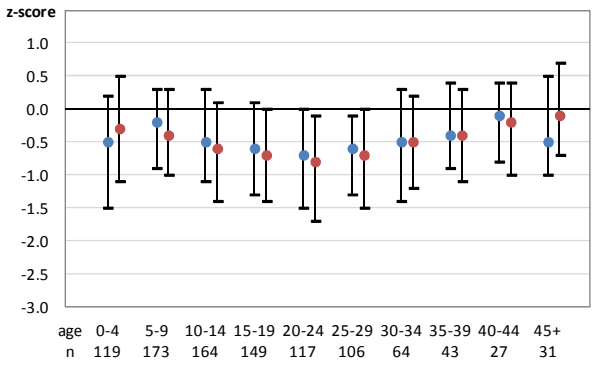
The figures below show the z-scores for weight by country. The dot is the median, and the whiskers show the 25th and 75th percentiles. In blue are the quartiles for the country, in red are the pooled quartiles computed on all other countries (i.e. excluding that country). We did not compute quartiles 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 Latvia and the Republic of Moldova from the graphs because none of the age groups had more than 10 patients.

Note: patients seen in 2008 for Ireland.
Note. Belgium: last weight of the year for all patients.

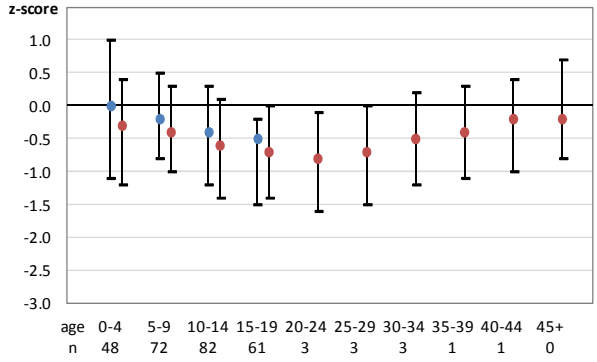
Quartiles of z-scores for weight: Austria



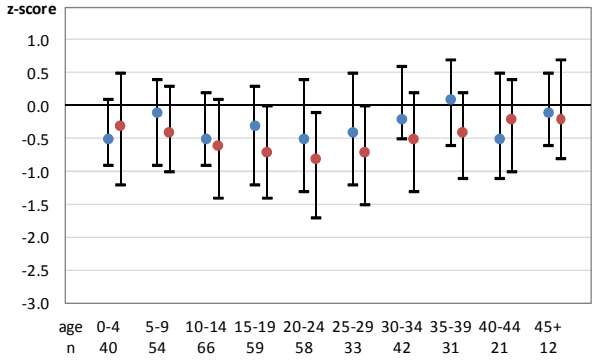
Quartiles of z-scores for weight: Belgium[1]



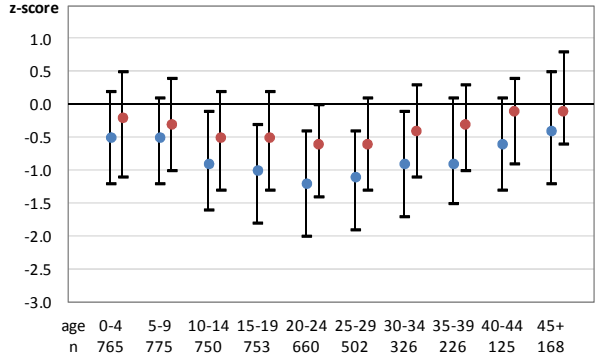
Quartiles of z-scores for weight: Czech Republic



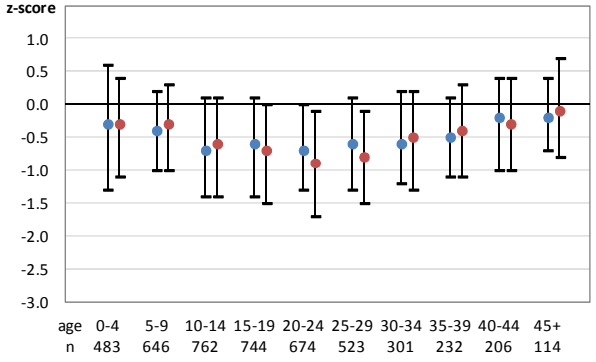
Quartiles of z-scores for weight: Denmark



Quartiles of z-scores for weight: France



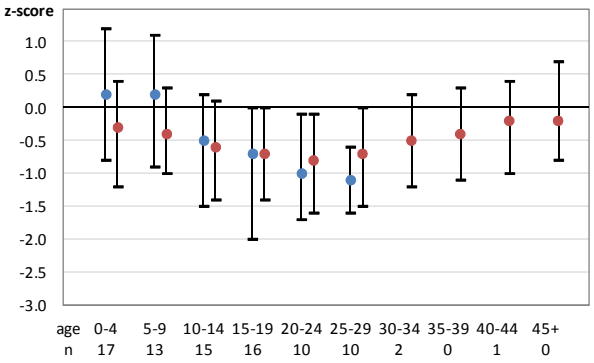
Quartiles of z-scores for weight: Germany



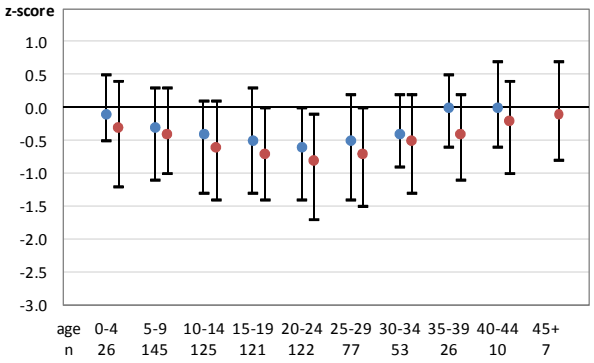
[1]Belgium: last weight of the year for all patients.

[figure 6.5 continued]

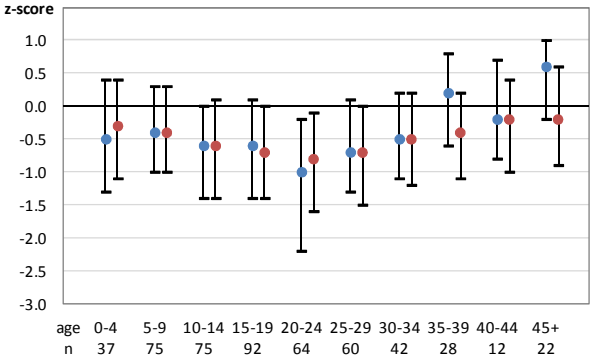
Quartiles of z-scores for weight: Greece



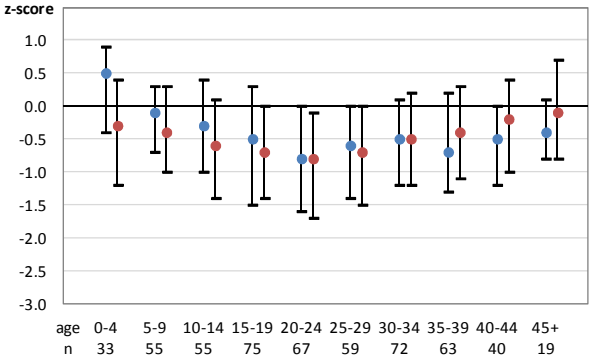
Quartiles of z-scores for weight: Ireland



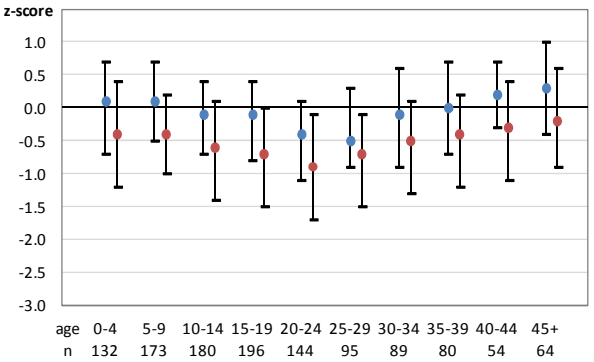
Quartiles of z-scores for weight: Israel



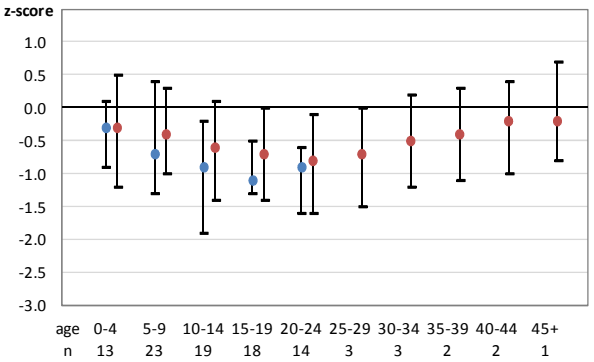
Quartiles of z-scores for weight: Italy



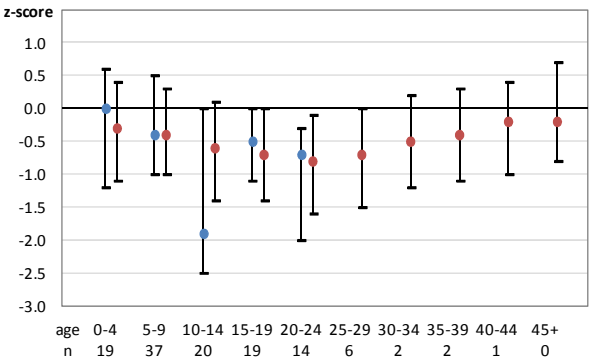
Quartiles of z-scores for weight: The Netherlands



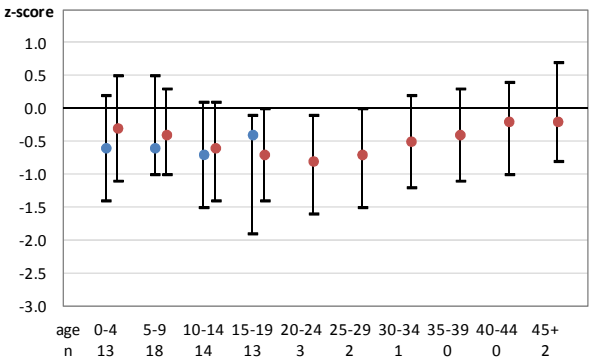
Quartiles of z-scores for weight: Portugal



Quartiles of z-scores for weight: Serbia

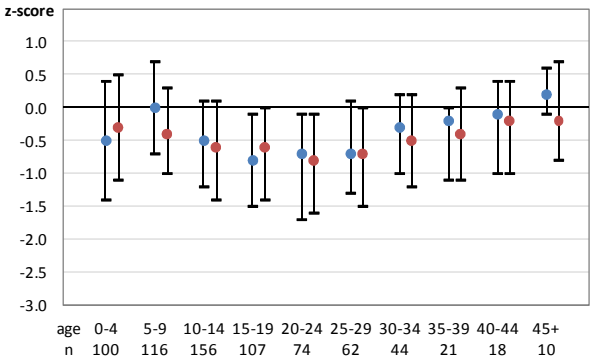


Quartiles of z-scores for weight: Slovenia

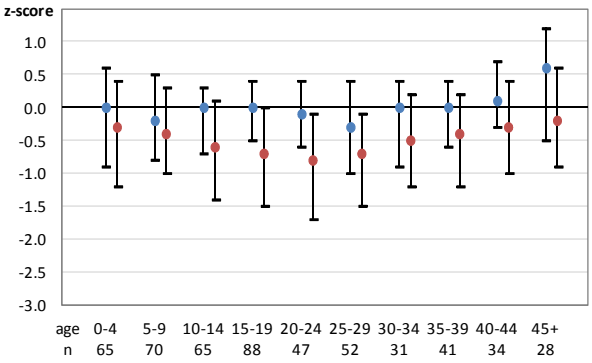


[figure 6.5 continued]

Quartiles of z-scores for weight: Spain



Quartiles of z-scores for weight: Sweden



Quartiles of z-scores for weight: Switzerland

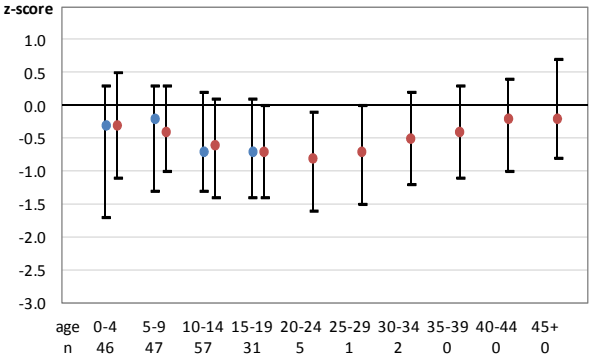


Table 6.8 Z-scores for BMI: descriptive statistics by country. All patients seen in 2009 aged 2-17 years.

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
Austria	245	0	-0.4	-4.1	-1.0	-0.3	0.3	2.1
Belgium	515	1	-0.4	-6.6	-1.0	-0.3	0.3	2.2
Czech republic	232	6	-0.5	-4.0	-1.1	-0.5	0.3	1.9
Denmark	184	0	-0.4	-2.8	-0.9	-0.4	0.2	1.6
France	2455	23	-0.5	-7.7	-1.2	-0.5	0.2	3.3
Germany	2204	64	-0.5	-6.9	-1.1	-0.5	0.2	2.5
Greece	53	0	-0.1	-2.4	-1.1	-0.2	0.9	4.2
Hungary	-	-	-	-	-	-	-	-
Ireland	365	6	-0.1	-4.4	-0.7	-0.1	0.5	2.4
Israel	244	0	-0.2	-2.9	-0.7	-0.1	0.5	2.1
Italy	171	0	-0.2	-4.0	-0.8	-0.2	0.4	2.0
Latvia	14	0	-1.5	-2.9	-2.1	-1.6	-0.9	0.7
Rep of Moldova	12	0	-1.8	-3.8	-2.4	-1.6	-1.2	-0.5
The Netherlands	561	0	-0.2	-3.9	-0.7	-0.1	0.4	3.7
Portugal	64	0	-0.4	-3.8	-1.1	-0.4	0.5	1.9
Serbia	79	0	-0.6	-7.1	-1.6	-0.3	0.5	2.9
Slovenia	48	0	-0.7	-2.8	-1.4	-0.8	-0.2	2.0
Spain	403	0	-0.2	-3.6	-0.8	-0.1	0.5	3.2
Sweden	238	0	-0.0	-2.5	-0.6	-0.0	0.5	2.4
Switzerland	156	0	-0.4	-3.8	-1.1	-0.4	0.2	2.5

Note: patients seen in 2008 and aged 2-17 years for Ireland.

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 6.9 BMI: descriptive statistics by country. All patients seen in 2009 aged 18 years or older.

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	72	0	20.6	15.2	18.7	20.2	22.3	31.2
Belgium	439	3	21.2	14.1	19.1	20.7	22.9	42.5
Czech Republic	28	45	20.6	15.6	18.5	20.3	22.3	27.5
Denmark	221	0	21.6	14.2	19.2	21.3	23.0	38.2
France	2287	49	20.5	12.6	18.5	20.1	22.0	44.9
Germany	2321	93	20.8	13.7	18.8	20.5	22.3	36.1
Greece	30	0	20.6	17.1	18.4	20.0	22.1	26.3
Hungary	-	-	-	-	-	-	-	-
Ireland	328	20	21.7	15.5	19.7	21.3	23.4	43.1
Israel	255	0	22.1	14.7	19.7	21.6	23.9	39.8
Italy	349	0	21.1	12.4	19.2	20.7	22.7	38.8
Latvia	6	0	16.4	14.7	15.6	16.3	17.5	17.8
Rep of Moldova	3	0	20.2	19.7	19.7	20.4	20.6	20.6
The Netherlands	600	14	21.6	14.7	19.7	21.4	23.2	37.3
Portugal	31	0	20.7	15.2	18.8	20.1	22.4	27.5
Serbia	33	0	19.5	14.5	17.1	19.7	21.1	26.1
Slovenia	12	0	20.4	16.2	18.5	20.4	22.6	24.2
Spain	269	0	21.8	14.5	19.5	21.5	23.5	42.5
Sweden	261	38	22.1	13.3	19.9	21.8	23.8	34.5
Switzerland	16	0	20.1	16.7	18.9	20.4	21.3	22.9

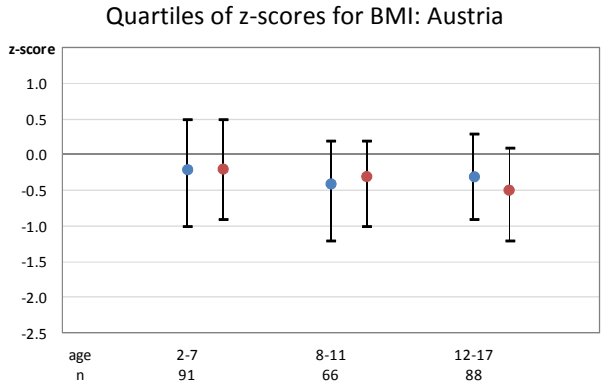
Note: patients seen in 2008 and aged 18 years or more for Ireland.

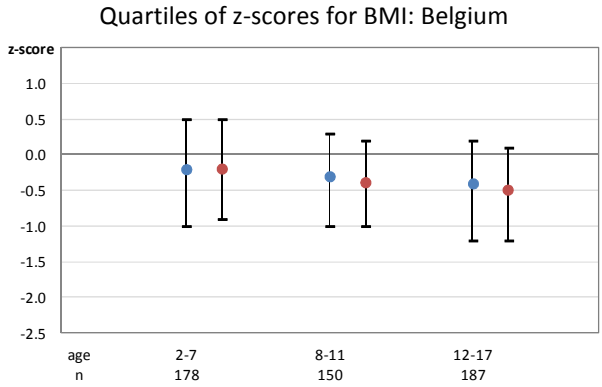
This table reports the median BMI (expressed as absolute values, not as z-scores), the mean BMI and other descriptive statistics for patients aged 18 years or older, by country.

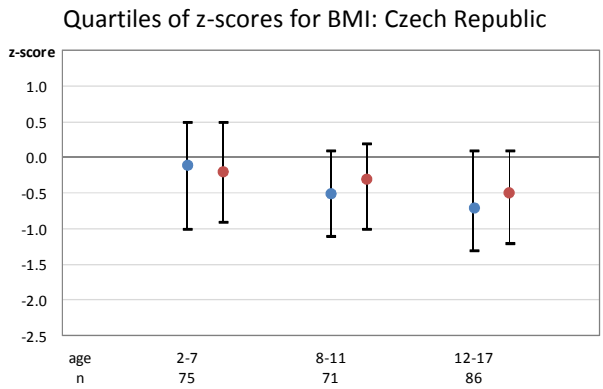
Figure 6.6 Quartiles of z-scores for BMI by age group and country. Patients aged 2-17 years in 2009.

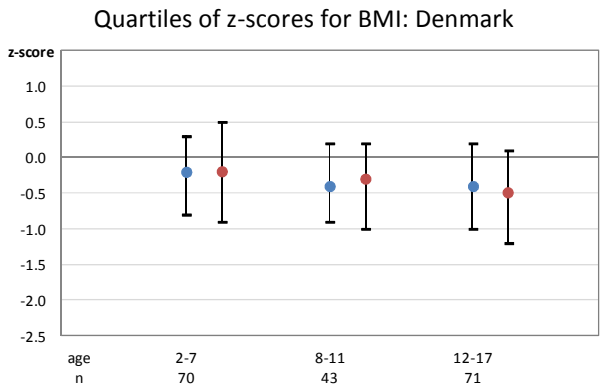
The figures below show the z-scores for weight by country. The dot is the median, and the whiskers show the 25th and 75th percentiles. In blue are the quartiles for the country, in red are the pooled quartiles computed on all other countries (i.e. excluding that country). We did not compute quartiles 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 Latvia and the Republic of Moldova from the graphs because none of the age groups had more than 10 patients.

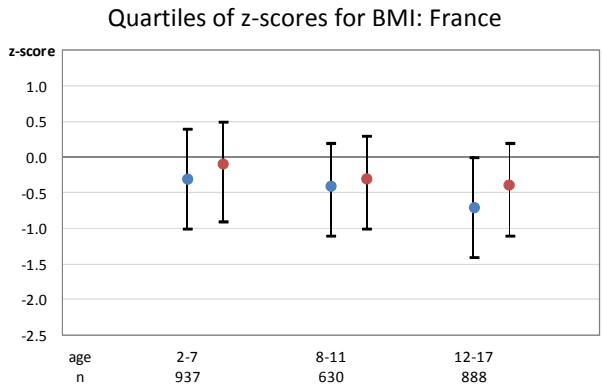
Note: patients aged 2-17 years in 2008 for Ireland.

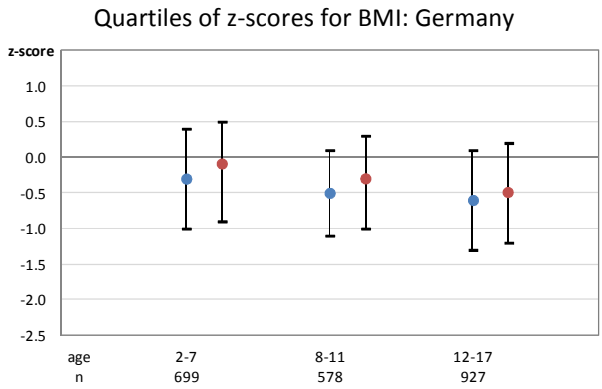






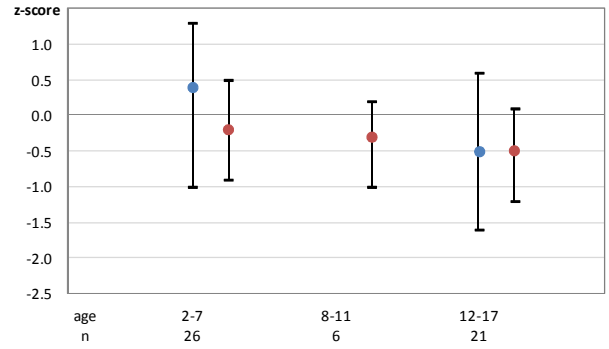




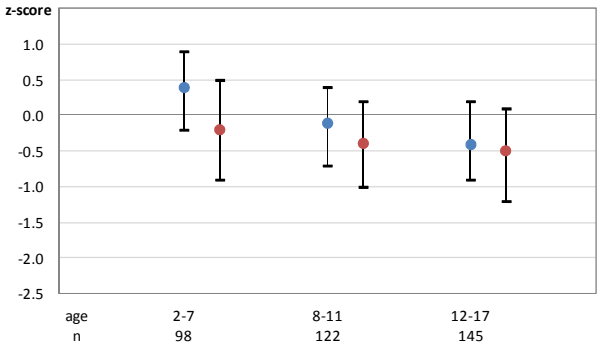


[figure 6.6 continued]

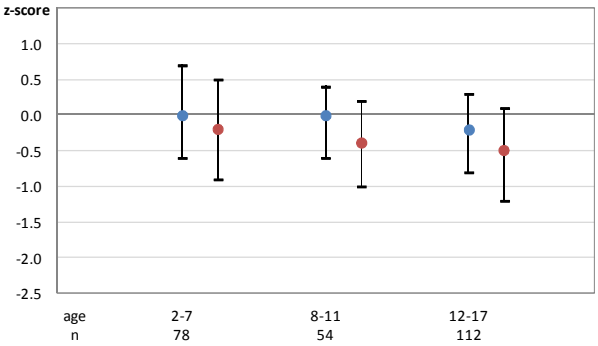
Quartiles of z-scores for BMI: Greece



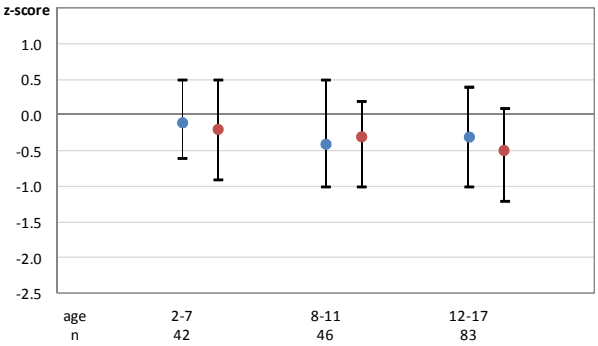
Quartiles of z-scores for BMI: Ireland



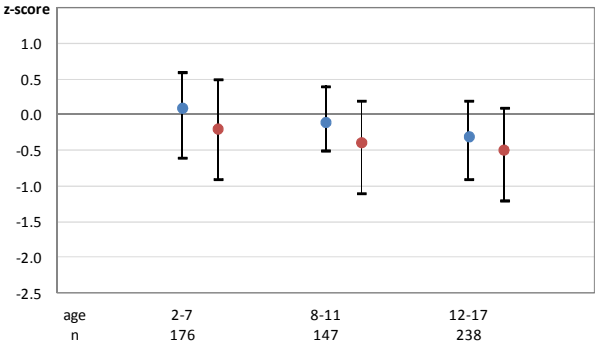
Quartiles of z-scores for BMI: Israel



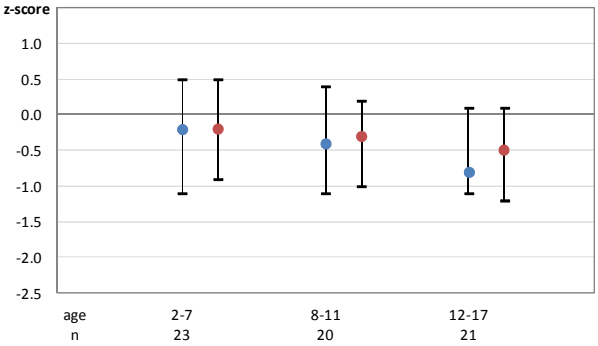
Quartiles of z-scores for BMI: Italy



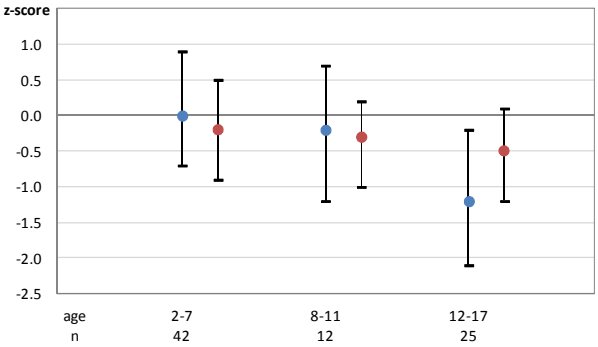
Quartiles of z-scores for BMI: The Netherlands



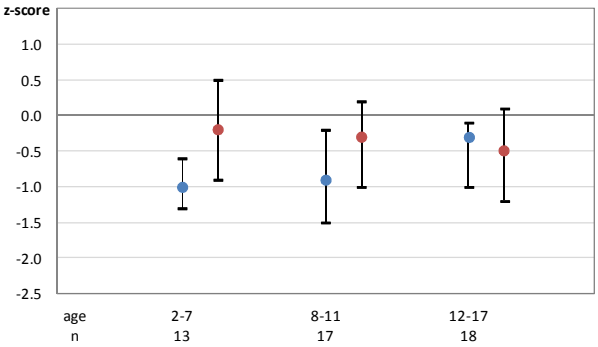
Quartiles of z-scores for BMI: Portugal



Quartiles of z-scores for BMI: Serbia

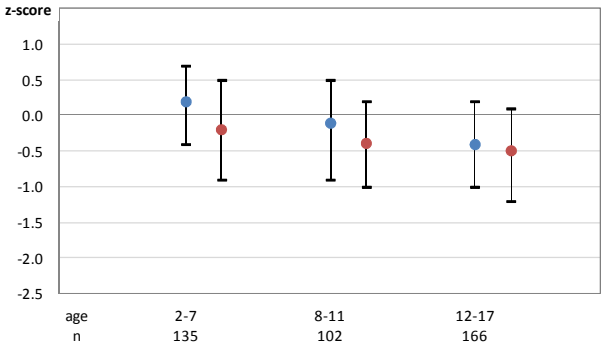


Quartiles of z-scores for BMI: Slovenia

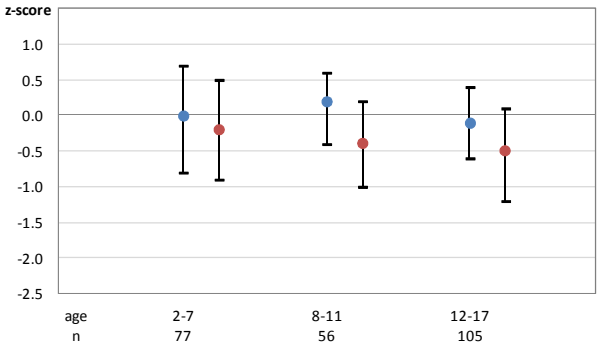


[figure 6.6 continued]

Quartiles of z-scores for BMI: Spain



Quartiles of z-scores for BMI: Sweden



Quartiles of z-scores for BMI: Switzerland

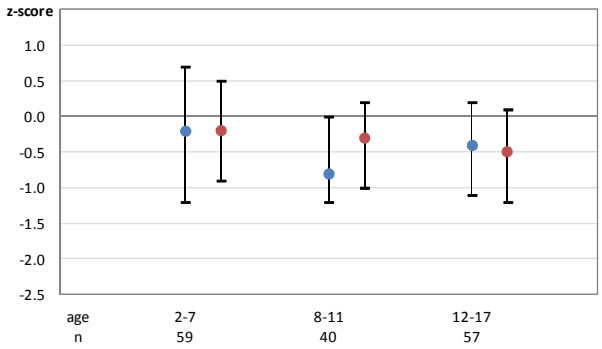
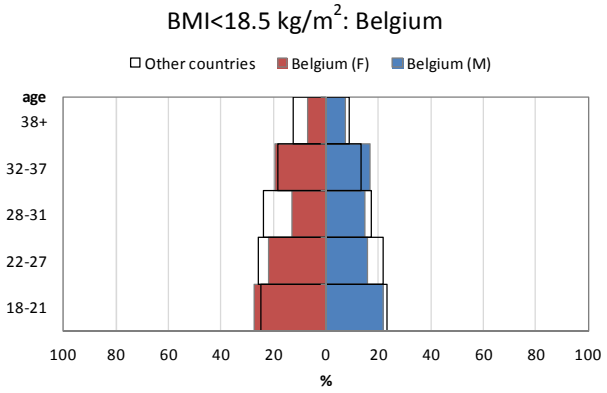
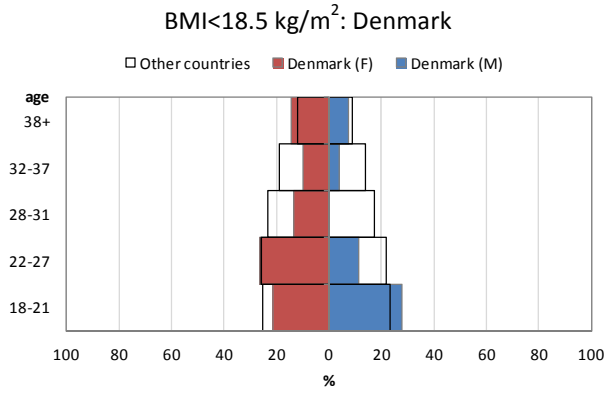


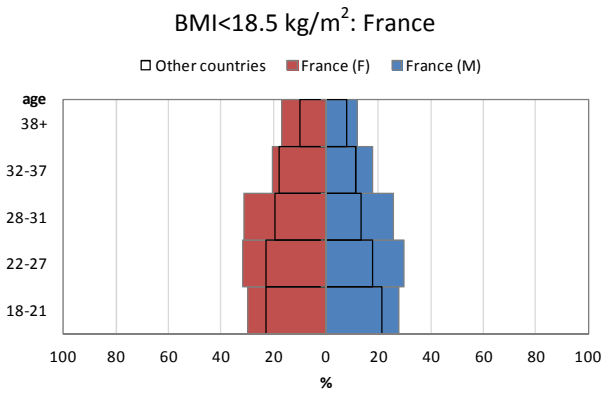
Figure 6.7 Proportion of adult patients underweight (BMI<18.5): age and sex pyramids, by country and overall. Patients aged 18 years or older in 2009.

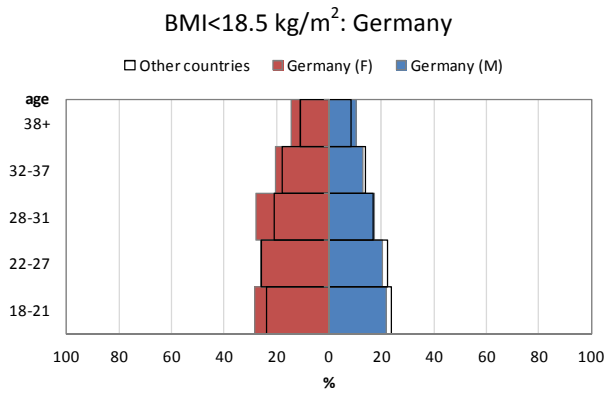
The coloured bars (red for females, blue for males) represent the percentage of underweight patients in the selected country, whereas the uncoloured bars represent the percentage of underweight patients in all the remaining countries (i.e. excluding that country). We excluded from the analyses those age groups where the number of patients was <10. We therefore excluded from the graph Austria, the Czech Republic, Greece, Latvia, Portugal, the Republic of Moldova, Serbia, Slovenia and Switzerland because none of the age groups had more than 10 patients.

Note: patients aged 18 years or more in 2008 for Ireland.

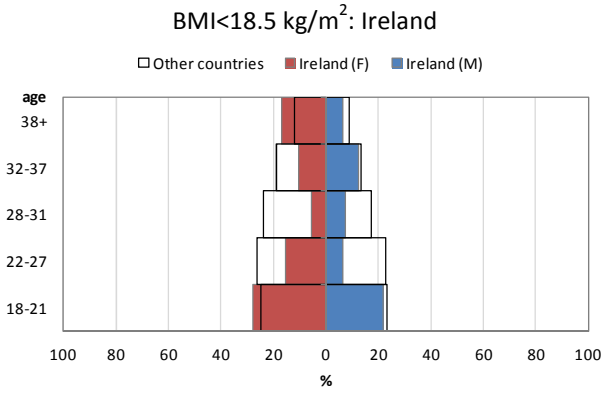


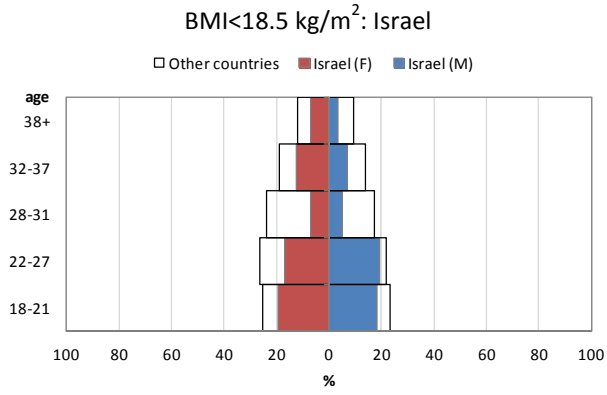


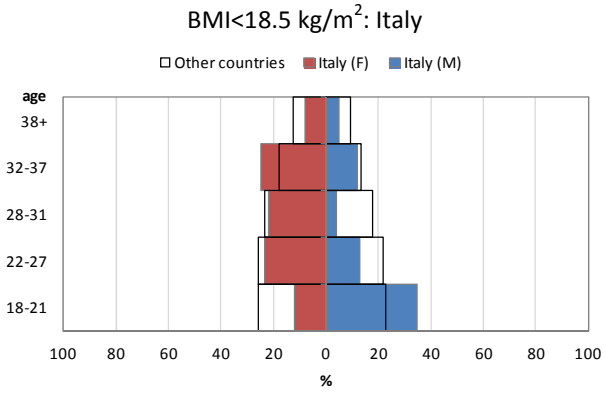


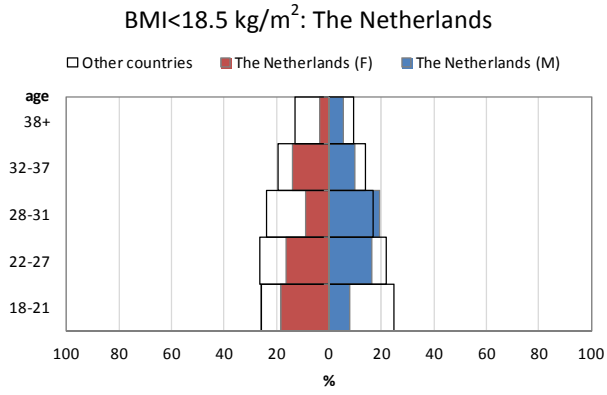


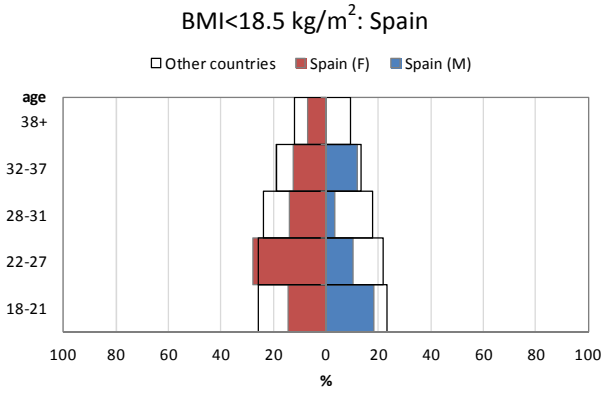
[figure 6.7 continued]

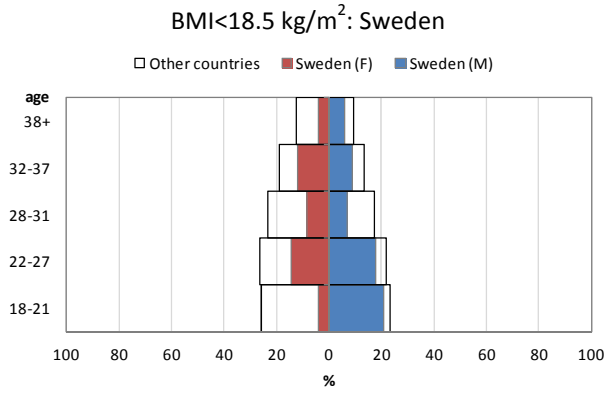












7. Complications and therapy

We collect data on a variety of complications, like CF related diabetes (CFRD), liver disease and allergic broncho-pulmonary aspergillosis (ABPA). This section suffers from a partial lack of information either because national registries do not collect data about the complication, because they use a different definition or because the status of the complication is truly unknown (e.g. liver disease, where the definition requires ultrasound examination). Therefore, in the tables we show the number of missing values of the various complications, but in the graphs we have only included countries where less than 10% of the data were missing. For a full list of complications and definitions please see Appendix 2.

In this section we also present data on selected therapies. We collected information on therapies using the generic name of the drug (i.e. the un-branded name), in order to avoid data collection biases due to brand names. For example, we ask whether the patient has been taking ”inhaled antibiotics more than three months this year”, instead of naming individual antibiotics.

Like the complications section, the therapy section also suffers from a partial lack of information, and we will show only selected results, according to the same criteria used for complications.

Table 7.1 Prevalence of allergic broncho-pulmonary aspergillosis (all patients seen in 2009) and CF related diabetes treated with insulin in 2009 (patients aged 10 years or older), by country.

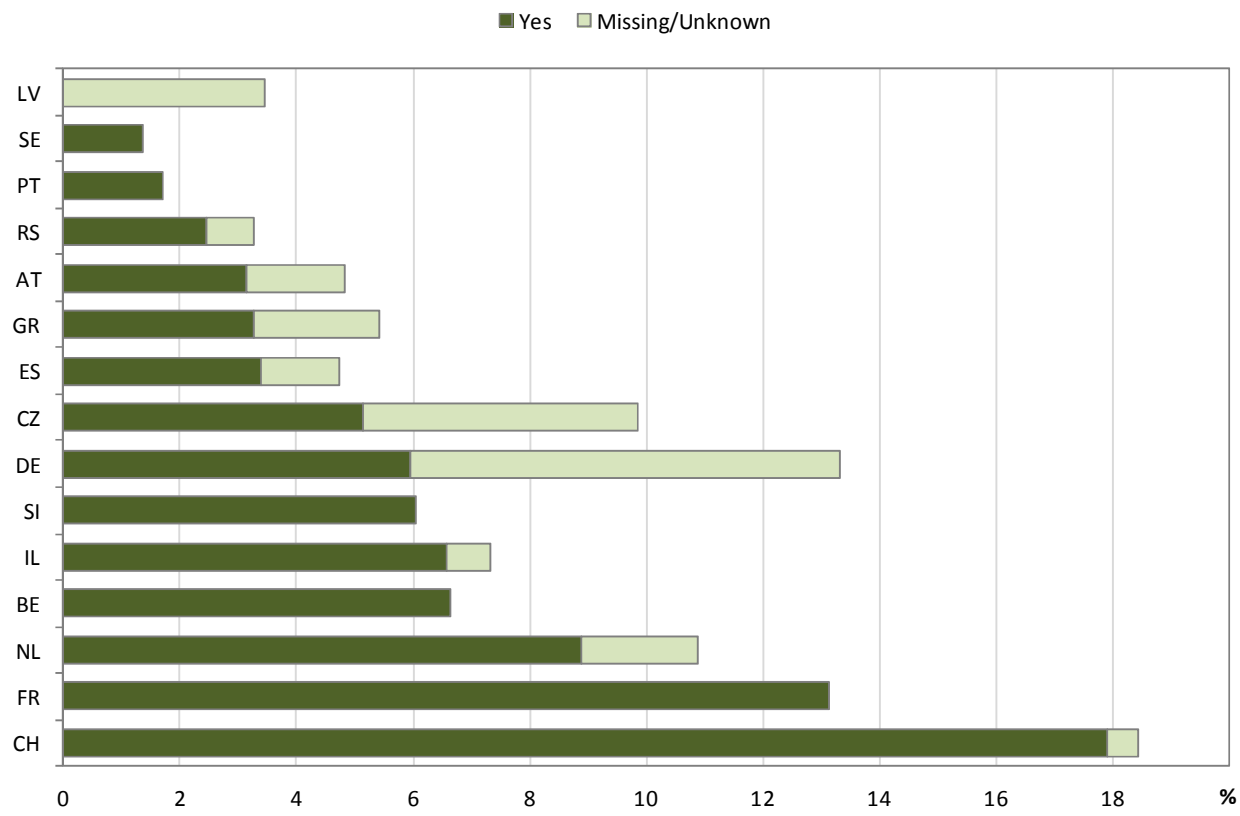
Country	ABPA this year number (%)			CF related diabetes with daily use of insulin this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	6 (1.7)	335 (95.2)	11 (3.1)	6 (2.9)	178 (85.6)	24 (11.5)
Belgium	0 (0)	1054 (93.4)	75 (6.6)	0 (0.0)	739 (86.5)	115 (13.5)
Czech Republic	24 (4.7)	457 (90.1)	26 (5.1)	22 (6.0)	274 (75.1)	69 (18.9)
Denmark	451 (100)	-	-	0 (0)	266 (74.5)	91 (25.5)
France[1]	0 (0)	4900 (86.9)	740 (13.1)	0 (0)	3264 (84.1)	619 (15.9)
Germany	371 (7.3)	4376 (86.7)	301 (6.0)	308 (7.9)	2840 (72.6)	764 (19.5)
Greece	2 (2.2)	87 (94.6)	3 (3.3)	2 (3.2)	52 (83.9)	8 (12.9)
Hungary	555 (100)	-	-	0 (0)	343 (90.0)	38 (10.0)
Ireland	209 (20.5)	789 (77.3)	23 (2.2)	168 (22.2)	496 (65.5)	93 (12.3)
Israel	4 (0.7)	494 (92.7)	35 (6.6)	3 (0.7)	323 (79.2)	82 (20.1)
Italy	539 (100)	-	-	0 (0)	367 (80.0)	92 (20.0)
Latvia	1 (3.4)	28 (96.6)	0 (0)	1 (6.7)	13 (86.7)	1 (6.7)
Rep of Moldova	41 (100)	-	-	0 (0)	16 (100)	0 (0)
The Netherlands	25 (2.0)	1113 (89.1)	111 (8.9)	18 (1.9)	729 (75.2)	222 (22.9)
Portugal	0 (0)	1158 (98.3)	2 (1.7)	0 (0)	69 (90.8)	7 (9.2)
Serbia	1 (0.8)	118 (96.7)	3 (2.5)	0 (0)	57 (89.1)	7 (10.9)
Slovenia	0 (0)	62 (93.9)	4 (6.1)	0 (0)	33 (82.5)	7 (17.5)
Spain	10 (1.4)	705 (95.3)	25 (3.4)	6 (1.2)	447 (85.6)	69 (13.2)
Sweden	0 (0)	570 (98.6)	8 (1.4)	1 (0.2)	361 (79.5)	92 (20.3)
Switzerland	1 (0.5)	155 (81.6)	34 (17.9)	0 (0)	95 (96.0)	4 (4.0)

Note: patients seen in 2008 for Ireland.

[1]France: ABPA was collected as: Aspergillosis (ABPA and other).

This table shows the frequency of allergic broncho-pulmonary aspergillosis (ABPA see Appendix 2 for definitions) and CF related diabetes (here defined as treated daily with insulin) by country. For CFRD only patients 10 years or older are included.

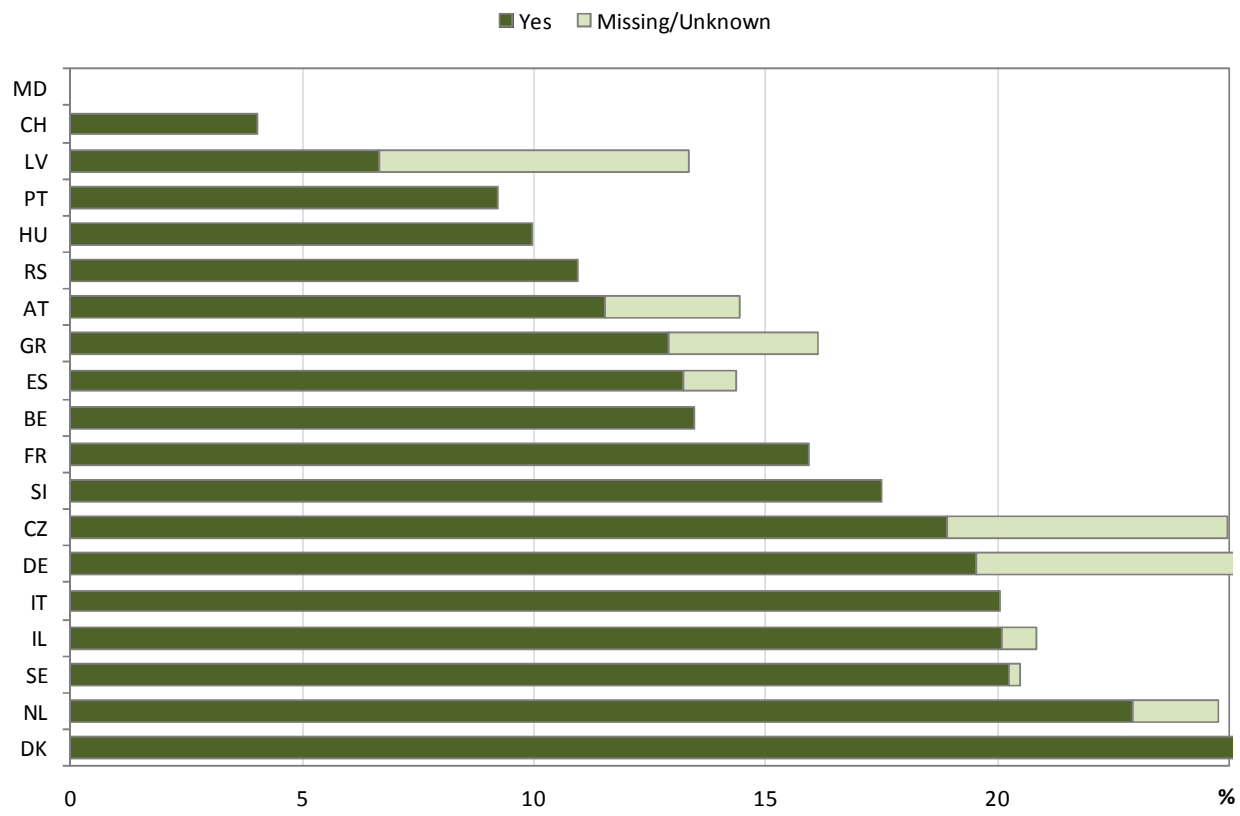
Figure 7.1 Prevalence of allergic broncho-pulmonary aspergillosis in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on allergic broncho-pulmonary aspergillosis was missing for more than 10% of the patients.
Note: France collected ABPA as Aspergillosis (ABPA and other).

This graph shows the frequency of allergic broncho-pulmonary aspergillosis by country. For the definition of ABPA see Appendix 2. 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 was missing.

Figure 7.2 Prevalence of CFRD requiring daily insulin treatment, by country. All patients seen in 2009 aged 10 years or older.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on CFRD was missing for more than 10% of the patients.

This graph shows the prevalence of CF related diabetes (CFRD) by country. CFRD is recorded differently in different national registries. As an alternative, we have collected data on the use of insulin on a daily basis as a substitute marker of diabetes. The dark green part of the bar shows the percentage of patients who use insulin daily, the light green part shows the percentage of patients for which this information was missing. Only patients aged 10 years or older were included in this graph.

Table 7.2 Prevalence of pneumothorax, hemoptysis and malignancy in all patients seen in 2009, by country.

Country	Pneumothorax requiring chest tube this year number (%)			Hemoptysis major over 250 ml this year number (%)			Malignancy occurred this year number(%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	7 (2.0)	344 (97.7)	1 (0.3)	6 (1.7)	346 (98.3)	0 (0)	8 (2.3)	343 (97.4)	1 (0.3)
Belgium	0 (0)	1125 (99.6)	4 (0.4)	0 (0)	1127 (99.8)	2 (0.2)	1127 (99.8)	0 (0)	2 (0.2)
Czech Rep	26 (5.1)	477 (94.1)	4 (0.8)	27 (5.3)	474 (93.5)	6 (1.2)	24 (4.7)	483 (95.3)	0 (0)
Denmark	451 (100)	-	-	451 (100)	-	-	451 (100)	-	-
France[1]	0 (0)	5576 (98.9)	64 (1.1)	0 (0)	5342 (94.7)	298 (5.3)	0 (0)	5630 (99.8)	10 (0.2)
Germany	383 (7.6)	4632 (91.8)	33 (0.6)	377 (7.5)	4585 (90.8)	86 (1.7)	5048 (100)	-	-
Greece	2 (2.2)	90 (97.8)	0 (0)	2 (2.2)	89 (96.7)	1 (1.1)	2 (2.2)	90 (97.8)	0 (0)
Hungary	0 (0)	550 (99.1)	5 (0.9)	555 (100)	-	-	555 (100)	-	-
Ireland	208 (20.4)	808 (79.1)	5 (0.5)	209 (20.5)	811 (79.4)	1 (0.1)	209 (20.5)	811 (79.4)	1 (0.1)
Israel	4 (0.7)	528 (99.1)	1 (0.2)	8 (1.5)	517 (97.0)	8 (1.5)	4 (0.7)	529 (99.3)	0 (0)
Italy	0 (0)	537 (99.6)	2 (0.4)	0 (0)	539 (100)	0 (0)	0 (0)	539 (100)	0 (0)
Latvia	1 (3.4)	27 (93.1)	1 (3.4)	1 (3.4)	27 (93.1)	1 (3.4)	1 (3.4)	28 (96.6)	0 (0)
Rep of Moldova	0 (0)	41 (100)	0 (0)	0 (0)	41 (100)	0 (0)	0 (0)	41 (100)	0 (0)
The Netherlands[2]	326 (26.1)	915 (73.3)	8 (0.6)	21 (1.7)	1205 (96.5)	23 (1.8)	276 (22.1)	967 (77.4)	6 (0.5)
Portugal	1 (0.8)	115 (98.3)	1 (0.8)	1 (0.8)	113 (96.6)	3 (2.6)	1 (0.8)	116 (99.2)	0 (0)
Serbia	0 (0)	122 (100)	0 (0)	2 (1.6)	120 (98.4)	0 (0)	3 (2.5)	119 (97.5)	0 (0)
Slovenia	0 (0)	66 (100)	0 (0)	0 (0)	66 (100)	0 (0)	0 (0)	66 (100)	0 (0)
Spain	8 (1.1)	725 (98.0)	7 (1.0)	18 (2.4)	707 (95.6)	15 (2.0)	9 (1.2)	724 (97.8)	7 (1.0)
Sweden	0 (0)	577 (99.8)	1 (0.2)	0 (0)	574 (99.3)	4 (0.7)	0 (0)	570 (98.6)	8 (1.4)
Switzerland	4 (2.1)	186 (97.9)	0 (0)	4 (2.1)	185 (97.4)	1 (0.5)	1 (0.5)	189 (99.5)	0 (0)

Note: patients seen in 2008 for Ireland.

[1] France: hemoptysis, no quantification

[2] The Netherlands: hemoptysis, no quantification

This table shows the frequency of three rare complications: Pneumothorax (collapsed lung) requiring chest tube, hemoptysis (coughing up blood) more than 250 ml and occurrence of malignancy (cancer). All these complications are extremely rare.

Table 7.3 Prevalence of liver disease and use of ursodeoxycholic acid in all patients seen in 2009, by country.

Country	Liver disease this year number (%)						Ursodeoxycholic acid this year number (%)		
	Missing/ unknown	No liver disease	Cirrhosis			Liver disease without cirrhosis	Missing/ unknown	No	Yes
			Cirrhosis with hypertension/ hypersplenism	Cirrhosis no hypertension/ hypersplenism	Cirrhosis, hypertension unknown				
Austria	6 (1.7)	217 (61.7)	7 (2.0)	4 (1.1)	1 (0.3)	117 (33.2)	6 (1.7)	202 (57.4)	144 (40.9)
Belgium[1]	1105 (97.9)	0 (0)	24 (2.1)	0 (0)	0 (0)	0 (0)	108 (9.6)	735 (65.1)	286 (25.3)
Czech Republic	197 (38.9)	191 (37.7)	4 (0.8)	3 (0.6)	0 (0)	112 (22.1)	24 (4.7)	265 (52.3)	218 (43.0)
Denmark[2]	428 (94.9)	0 (0)	0 (0)	0 (0)	23 (5.1)	0 (0)	0 (0)	344 (76.3)	107 (23.7)
France[3]	0 (0)	5438 (96.4)	0 (0)	0 (0)	202 (3.6)	0 (0)	0 (0)	3930 (69.7)	1710 (30.3)
Germany	5048 (100)	-	-	-	-	-	178 (3.5)	2565 (50.8)	2305 (45.7)
Greece	2 (2.2)	64 (69.6)	0 (0)	0 (0)	0 (0)	26 (28.3)	1 (1.1)	51 (55.4)	40 (43.5)
Hungary	555 (100)	-	-	-	-	-	555 (100)	-	-
Ireland	209 (20.5)	758 (74.2)	4 (0.4)	5 (0.5)	0 (0)	45 (4.4)	254 (24.9)	655 (64.2)	112 (11.0)
Israel	9 (1.7)	416 (78.0)	9 (1.7)	5 (0.9)	2 (0.4)	92 (17.3)	7 (1.3)	416 (78.1)	110 (20.6)
Italy	0 (0)	471 (87.4)	3 (0.6)	0 (0)	0 (0)	65 (12.0)	0 (0)	387 (71.8)	152 (28.2)
Latvia	3 (10.3)	13 (44.8)	0 (0)	0 (0)	0 (0)	13 (44.8)	3 (10.3)	19 (65.5)	7 (24.1)
Rep of Moldova	0 (0)	27 (65.9)	0 (0)	0 (0)	0 (0)	14 (34.1)	0 (0)	22 (53.7)	19 (46.3)
The Netherlands	143 (11.4)	960 (76.9)	57 (4.6)	7 (0.6)	74 (5.9)	8 (0.6)	176 (14.1)	760 (60.8)	313 (25.1)
Portugal	3 (2.6)	98 (83.8)	0 (0)	1 (0.8)	0 (0)	15 (12.8)	4 (3.4)	81 (69.2)	32 (27.4)
Serbia	1 (0.8)	87 (71.3)	7 (5.7)	22 (18.0)	0 (0)	5 (4.1)	0 (0)	88 (72.1)	34 (27.9)
Slovenia	3 (4.5)	38 (57.6)	1 (1.5)	1 (1.5)	0 (0)	23 (34.9)	0 (0)	37 (56.1)	29 (43.9)
Spain	11 (1.5)	578 (78.1)	10 (1.3)	5 (0.7)	9 (1.2)	127 (17.2)	8 (1.1)	535 (72.3)	197 (26.6)
Sweden	2 (0.3)	444 (76.8)	8 (1.4)	4 (0.7)	93 (16.1)	27 (4.7)	0 (0)	450 (77.9)	128 (22.2)
Switzerland	3 (1.6)	169 (89.0)	5 (2.6)	0 (0)	2 (1.0)	11 (5.8)	0 (0)	147 (77.4)	43 (22.6)

Note: patients seen in 2008 for Ireland.

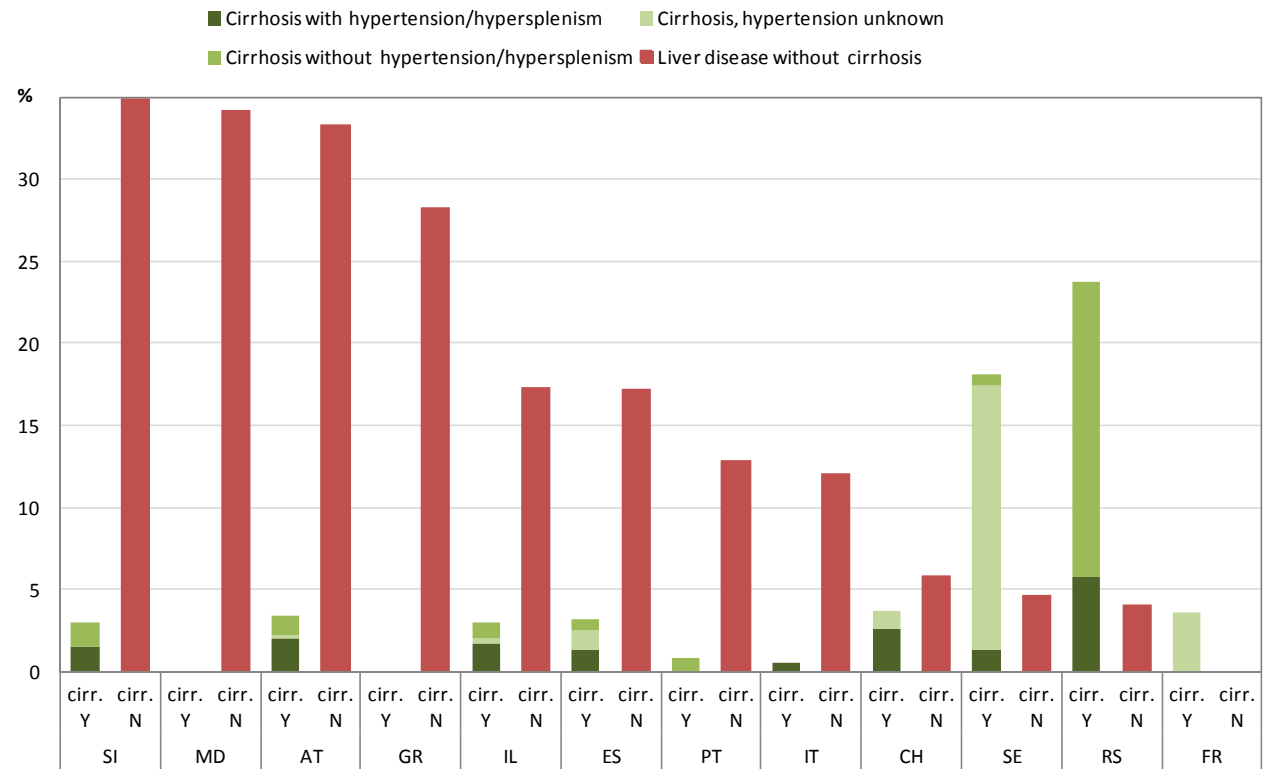
[1] Belgium: collects only cirrhosis with portal hypertension. Missing/unknown therefore means NO cirrhosis with portal hypertension, but other liver disease unknown.

[2] Denmark: collects only cirrhosis. Missing/unknown therefore means NO cirrhosis, but other liver disease unknown.

[3] France: collects cirrhosis/liver disease – these have been pooled under cirrhosis, hypertension unknown.

This table shows the frequency and severity of liver disease according to the ECFSPR definitions (see Appendix 2) and use of ursodeoxycholic acid, a liver-protective drug. The frequency and severity of liver disease differs greatly, and does not correspond to the number of patients on ursodeoxycholic acid.

Figure 7.3 Prevalence and severity of liver disease in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on liver disease was missing for more than 10% of the patients.
Note: France: collects cirrhosis/liver disease – these have been pooled under cirrhosis, hypertension unknown

This graph 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 2). 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.

Figure 7.4 Use of ursodeoxycholic acid in all patients seen in 2009, by country.

Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on ursodeoxycholic acid was missing for more than 10% of the patients.

This graph shows how many patients used ursodeoxycholic acid during the survey year. 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 which this information is missing.

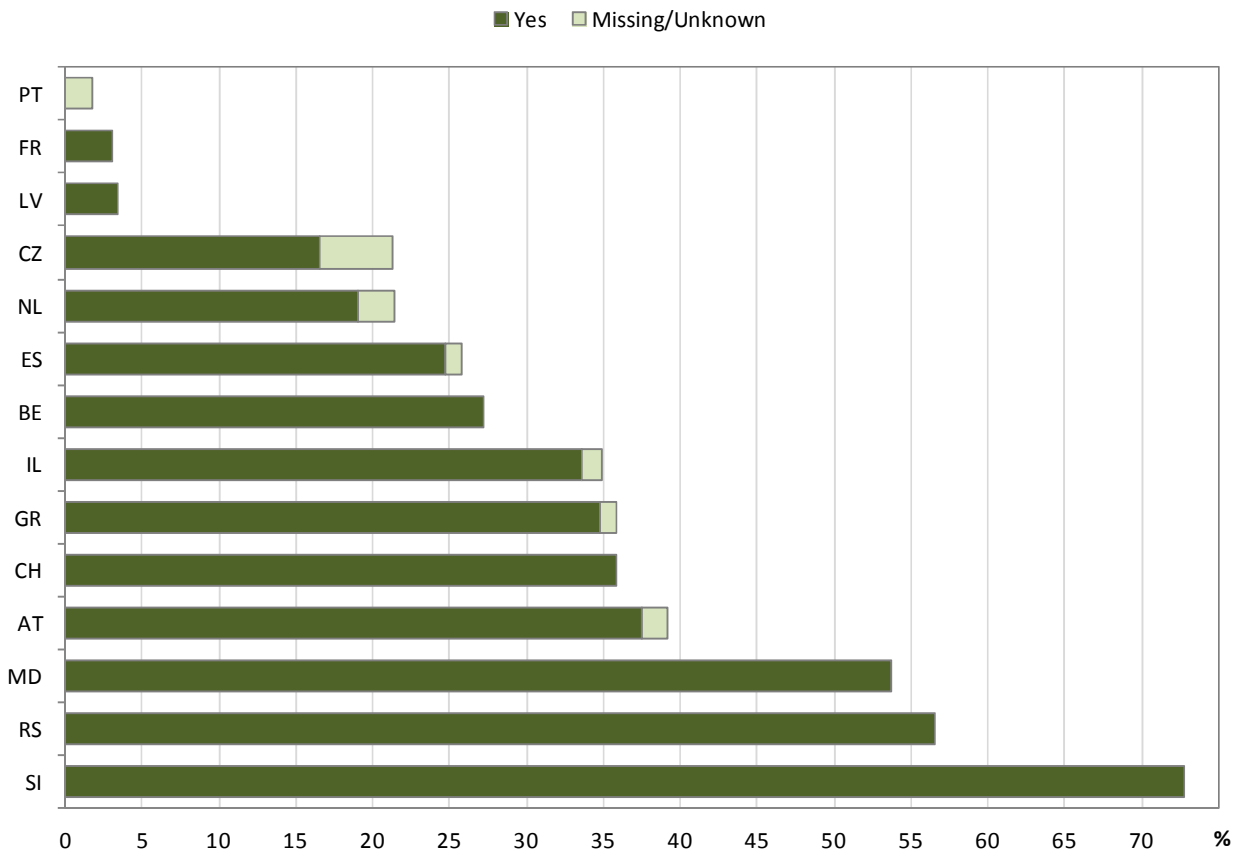
Table 7.4 Use of hypertonic saline, rhDNase and bronchodilators in all patients seen in 2009, by country.

Country	Hypertonic saline (NaCl) inhaled > 3 months this year number (%)			rhDNase inhaled > 3 months this year number (%)			Bronchodilators inhaled > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	6 (1.7)	214 (60.8)	132 (37.5)	7 (2.0)	156 (44.3)	189 (53.7)	7 (2.0)	34 (9.7)	311 (88.3)
Belgium	0 (0)	822 (72.8)	307 (27.2)	0 (0)	535 (47.4)	594 (52.6)	0 (0)	408 (36.1)	721 (63.9)
Czech Republic	24 (4.7)	399 (78.7)	84 (16.6)	24 (4.7)	194 (38.3)	289 (57.0)	24 (4.7)	273 (53.9)	210 (41.4)
Denmark	451 (100)	-	-	0 (0)	85 (18.8)	366 (81.2)	451 (100)	-	-
France	0 (0)	5470 (97.0)	170 (3.0)	0 (0)	3199 (56.7)	2441 (43.3)	0 (0)	2876 (51.0)	2764 (49.0)
Germany	5048 (100)	-	-	226 (4.5)	2525 (50.0)	2297 (45.5)	5048 (100)	-	-
Greece	1 (1.1)	59 (64.1)	32 (34.8)	1 (1.1)	35 (38.0)	56 (60.9)	1 (1.1)	41 (44.6)	50 (54.4)
Hungary	555 (100)	-	-	555 (100)	-	-	555 (100)	-	-
Ireland	998 (97.7)	0 (0)	23 (2.3)	254 (24.9)	510 (50.0)	257 (25.2)	254 (24.9)	323 (31.6)	444 (43.5)
Israel	7 (1.3)	347 (65.1)	179 (33.6)	7 (1.3)	289 (54.2)	237 (44.5)	13 (2.4)	214 (40.2)	306 (57.4)
Italy	539 (100)	-	-	0 (0)	375 (69.6)	164 (30.4)	539 (100)	-	-
Latvia	0 (0)	28 (96.6)	1 (3.4)	0 (0)	12 (41.4)	17 (58.6)	0 (0)	0 (0)	29 (100)
Rep of Moldova	0 (0)	19 (46.3)	22 (53.7)	0 (0)	41 (100)	0 (0)	0 (0)	26 (63.4)	15 (36.6)
The Netherlands	29 (2.3)	982 (78.6)	238 (19.1)	27 (2.2)	488 (39.1)	734 (58.8)	26 (2.1)	682 (54.6)	541 (43.3)
Portugal	2 (1.7)	115 (98.3)	0 (0)	3 (2.6)	51 (43.6)	63 (53.8)	4 (3.4)	77 (65.8)	36 (30.8)
Serbia	0 (0)	53 (43.4)	69 (56.6)	0 (0)	62 (50.8)	60 (49.2)	0 (0)	5 (4.1)	117 (95.9)
Slovenia	0 (0)	18 (27.3)	48 (72.7)	0 (0)	40 (60.6)	26 (39.4)	0 (0)	63 (95.5)	3 (4.5)
Spain	8 (1.1)	549 (74.2)	183 (24.7)	7 (1.0)	524 (70.8)	209 (28.2)	9 (1.2)	230 (31.1)	501 (67.7)
Sweden	143 (24.7)	239 (41.4)	196 (33.9)	2 (0.4)	469 (81.1)	107 (18.5)	5 (0.9)	52 (9.0)	521 (90.1)
Switzerland	0 (0)	122 (64.2)	68 (35.8)	0 (0)	129 (67.9)	61 (32.1)	0 (0)	20 (10.5)	170 (89.5)

Note: patients seen in 2008 for Ireland.

This table shows the use of three different inhaled medications: hypertonic saline, rhDNase (Pulmozyme®) and bronchodilators (see page 11 for abbreviations). All of these medications are widely used, but still with marked differences between the countries.

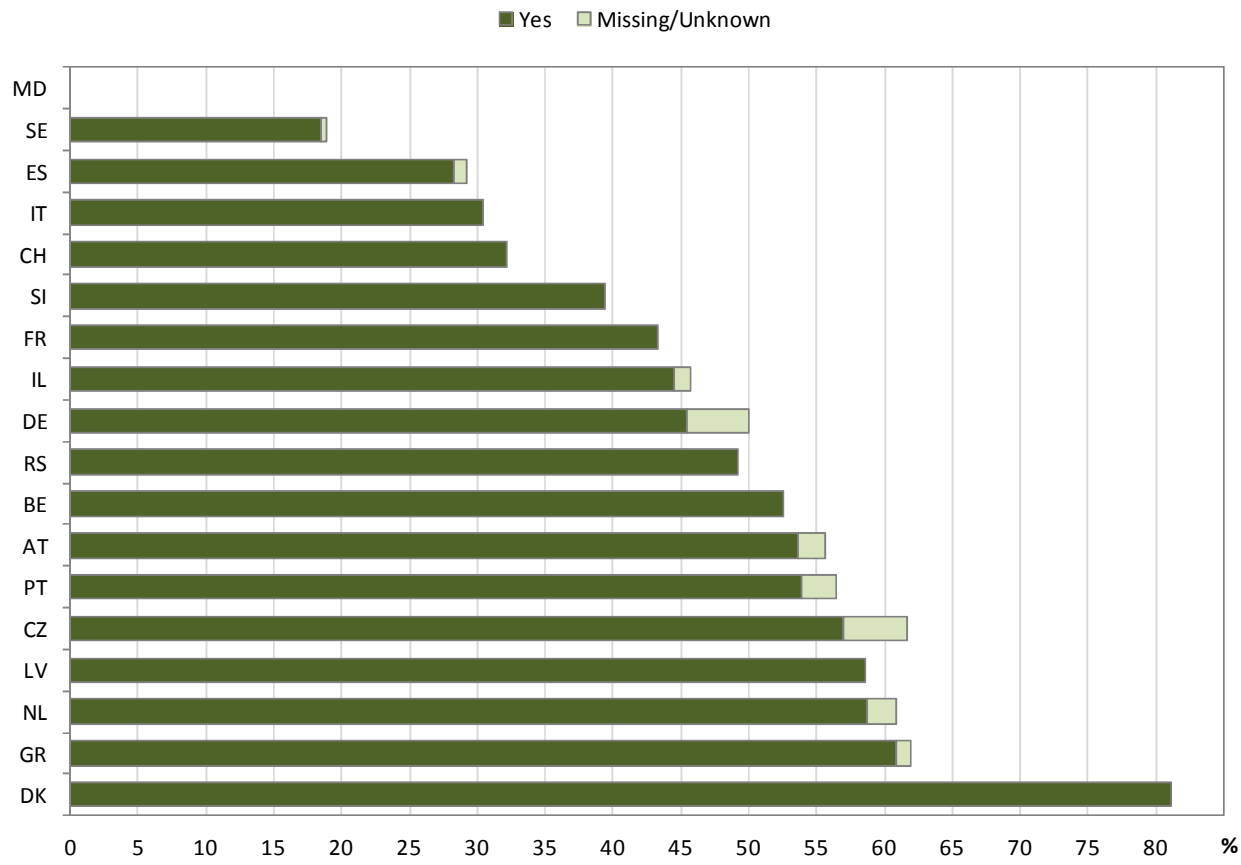
Figure 7.5 Use of inhaled hypertonic saline in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on inhaled hypertonic saline was missing for more than 10% of the patients.

This table 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 this drug, the light green part shows the percentage of patients for which this information is missing.

Figure 7.6 Use of rhDNase in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on rhDNase was missing for more than 10% of the patients.

This graph shows the use of rhDNase (marketed as Pulmozyme®) 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 which this information is missing.

Figure 7.7 Use of bronchodilators in all patients seen in 2009, by country.

Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on use of bronchodilators was missing for more than 10% of the patients.

This graph shows the use of bronchodilators (also used as asthma medication) for more than three months during the survey year. This is the most widely used inhaled medication, but still there are large 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 which this information is missing.

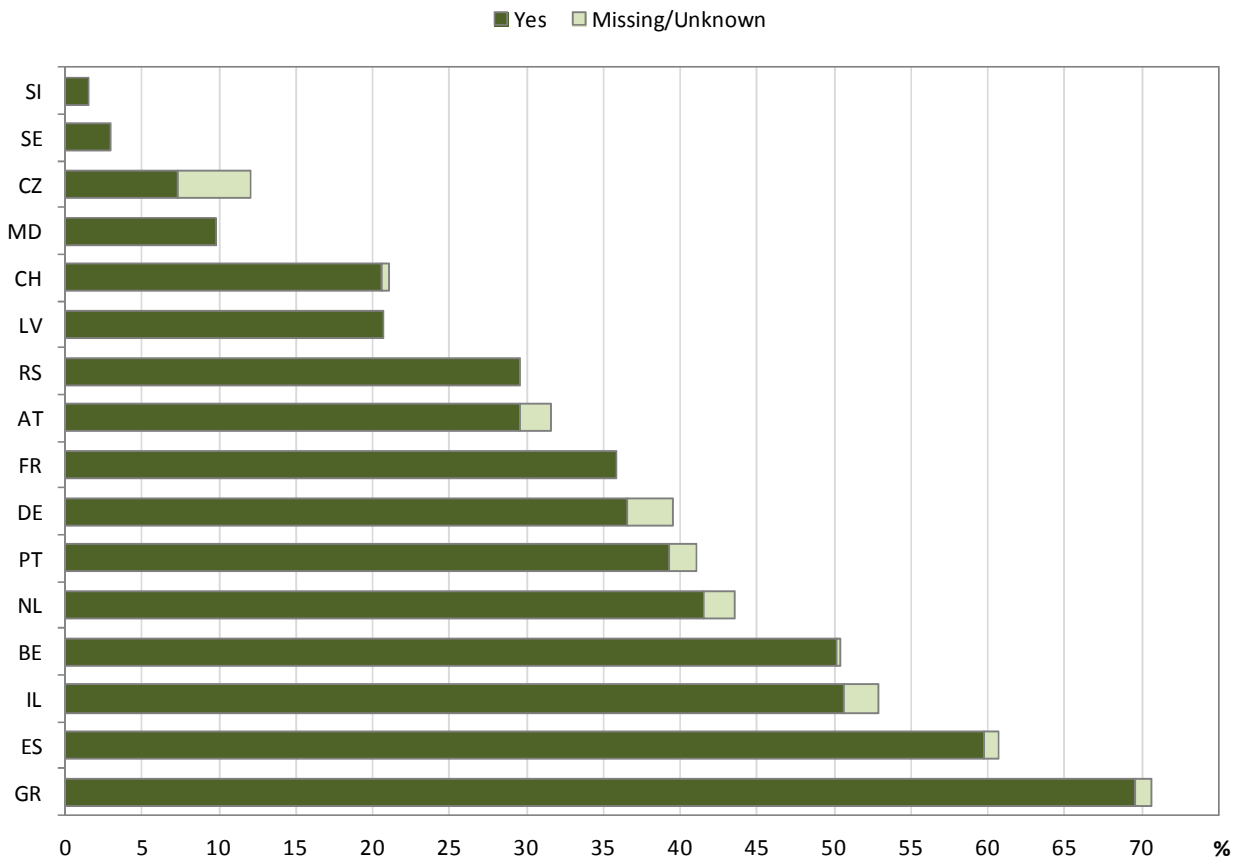
Table 7.5 Use of inhaled antibiotics, macrolides and oxygen in all patients seen in 2009, by country.

Country	Inhaled antibiotics inhaled > 3 months this year number (%)			Oxygen therapy this year number (%)			Macrolides > 3 months this year number (%)		
	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes	Missing/ unknown	No	Yes
Austria	7 (2.0)	241 (68.5)	104 (29.5)	6 (1.7)	335 (95.2)	11 (3.1)	6 (1.7)	310 (88.1)	36 (10.2)
Belgium	3 (0.3)	560 (49.6)	566 (50.1)	0 (0)	1095 (97.0)	34 (3.0)	0 (0)	702 (62.2)	427 (37.8)
Czech Republic	24 (4.7)	446 (88.0)	37 (7.3)	24 (4.7)	476 (93.9)	7 (1.4)	24 (4.7)	390 (76.9)	93 (18.3)
Denmark	451 (100)	-	-	451 (100)	-	-	451 (100)	-	-
France	0 (0)	3621 (64.2)	2019 (35.8)	0 (0)	5288 (93.8)	352 (6.2)	0 (0)	3357 (59.5)	2283 (40.5)
Germany	154 (3.1)	3051 (60.4)	1843 (36.5)	332 (6.6)	4518 (89.5)	198 (3.9)	5048 (100)	-	-
Greece	1 (1.1)	27 (29.3)	64 (69.6)	1 (1.1)	86 (93.5)	5 (5.4)	1 (1.1)	74 (80.4)	17 (18.5)
Hungary	555 (100)	-	-	555 (100)	-	-	555 (100)	-	-
Ireland	779 (76.3)	39 (3.8)	203 (19.9)	254 (24.9)	748 (73.3)	19 (1.9)	188 (18.4)	670 (65.6)	163 (16.0)
Israel	12 (2.2)	251 (47.1)	270 (50.7)	5 (0.9)	514 (96.4)	14 (2.6)	10 (1.9)	247 (46.3)	276 (51.8)
Italy	539 (100)	-	-	0 (0)	504 (93.5)	35 (6.5)	539 (100)	-	-
Latvia	0 (0)	23 (79.3)	6 (20.7)	0 (0)	27 (93.1)	2 (6.9)	3 (10.3)	17 (58.6)	9 (31.0)
Rep of Moldova	0 (0)	37 (90.2)	4 (9.8)	0 0)	36 (87.8)	5 (12.2)	0 (0)	19 (46.3)	22 (53.7)
Netherlands	26 (2.1)	705 (56.4)	518 (41.5)	38 (3.0)	1145 (91.7)	66 (5.3)	29 (2.3)	670 (53.6)	550 (44.0)
Portugal	2 (1.7)	69 (59.0)	46 (39.3)	2 (1.7)	112 (95.7)	3 (2.6)	2 (1.7)	85 (72.7)	30 (25.6)
Serbia	0 (0)	86 (70.5)	36 (29.5)	(0)	113 (92.6)	9 (7.4)	0 (0)	108 (88.5)	14 (11.5)
Slovenia	0 (0)	65 (98.5)	1 (1.5)	0 (0)	66 (100)	0 (0)	0 (0)	58 (87.9)	8 (12.1)
Spain	7 (1.0)	291 (39.3)	442 (59.7)	7 (1.0)	703 (95.0)	30 (4.0)	7 (1.0)	489 (66.0)	244 (33.0)
Sweden	0 (0)	561 (97.1)	17 (2.9)	0 (0)	571 (98.8)	7 (1.2)	5 (0.9)	354 (61.2)	219 (37.9)
Switzerland	1 (0.5)	150 (79.0)	39 (20.5)	1 (0.5)	189 (99.5)	0 (0)	1 (0.5)	169 (89.0)	20 (10.5)

Note: patients seen in 2008 for Ireland.

This table shows the use of three treatments: inhaled antibiotics for more than 3 months during the survey year (any kind); macrolides (e.g. azithromycin) for more than three months; and oxygen for home treatment. Both inhaled antibiotics and macrolides are frequently used but with marked differences between countries. Oxygen is used less frequently (severe lung disease).

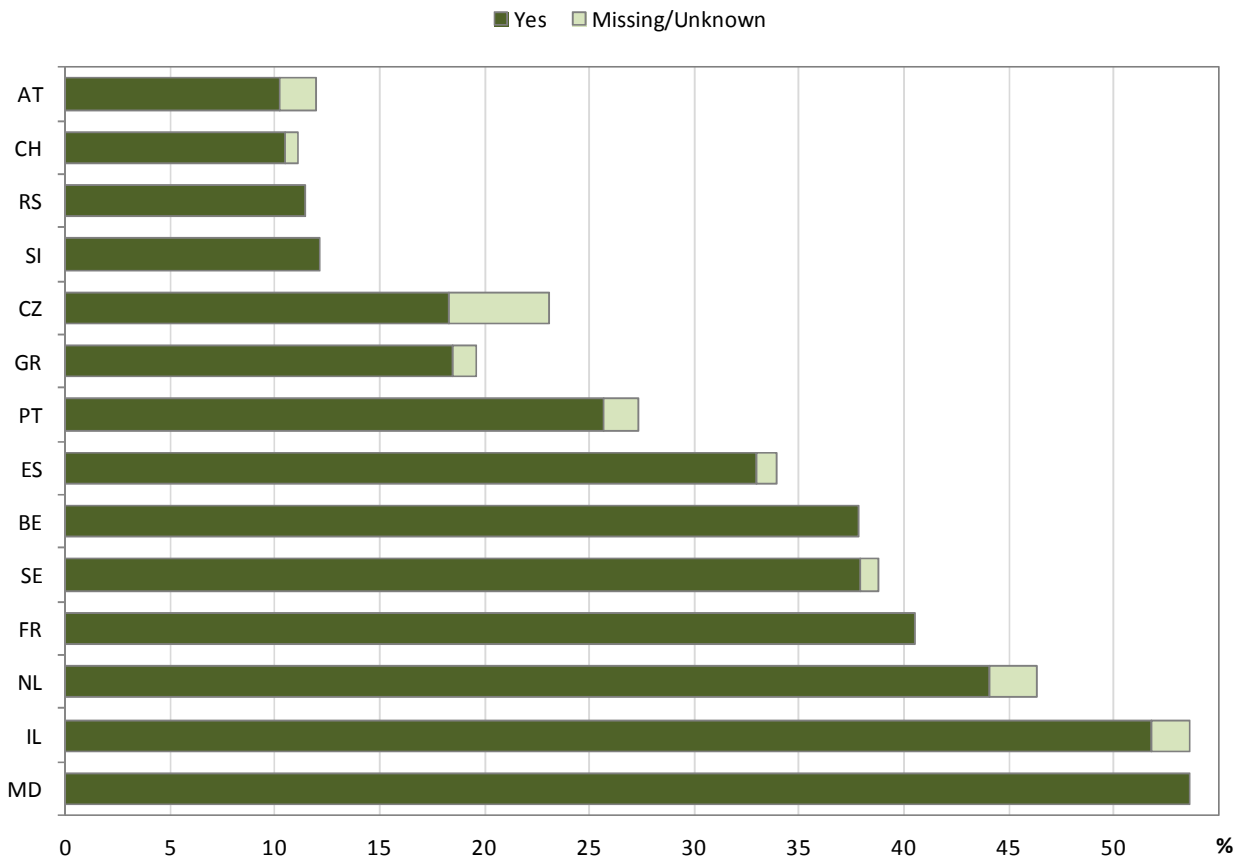
Figure 7.8 Use of inhaled antibiotics in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on inhaled antibiotics was missing for more than 10% of the patients.

This graph shows the use of inhaled antibiotics (of any kind) for more than three months during the survey year. The frequency ranges widely, from 10 to 70%. 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 which this information is missing.

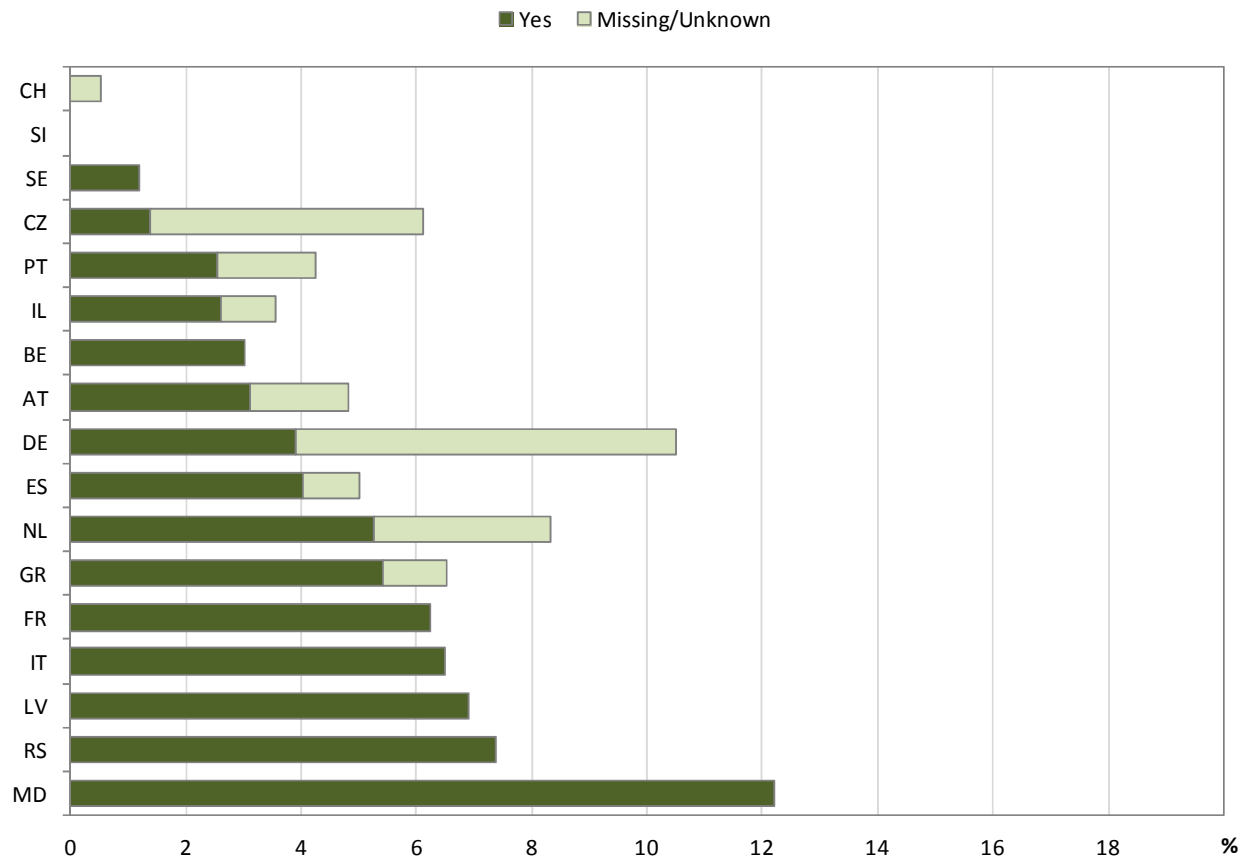
Figure 7.9 Use of macrolides in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on use of macrolides was missing for more than 10% of the patients.

This graph shows the use of macrolides for more than 3 months during the survey year (e.g. azithromycin). Macrolides are antibiotics, but taken continuously they also modulate the immune system. 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 which this information is missing.

Figure 7.10 Use of oxygen in all patients seen in 2009, by country.



Note: patients seen in 2008 for Ireland.
Note: we excluded from the graph the countries for which the information on the use of oxygen was missing for more than 10% of the patients.

This graph shows the use of oxygen at home during the survey year. 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 which this information is missing.

8. Transplantation

In the ECFSPR transplantation section we focus on transplant of two organs that are directly affected by the disease, namely the lungs and the liver. We ask the countries whether their patients are transplanted or not, and if they are, in which year they had their (latest) transplant.

In some countries (such as in The Netherlands) transplanted patients are no longer registered in the CF centres database/CF national registries, usually 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 8. 1 Number of patients living in 2009 with transplanted lung(s), by age and sex.

Age	Males	Females	Total	Transplants performed during the survey year
5-9	1	1	2	0
10-14	5	7	12	4
15-19	23	29	52	15
20-24	49	62	111	34
25-29	77	83	160	30
30-34	90	97	187	25
35-39	74	53	127	11
40-44	43	45	88	9
45+	33	32	65	5
Total	**395**	**409**	**804**	**133**

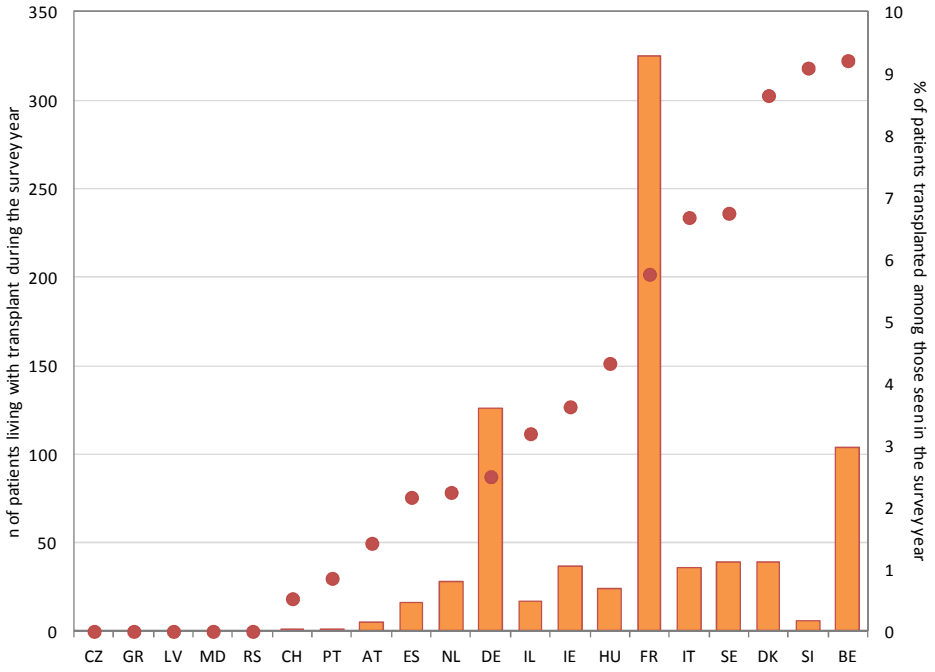
This table shows the number of patients alive in 2009 (2008 for Ireland) who have had a lung transplant at some time in their lives, by age group, as well as the number of patients transplanted during 2009 (2008 for Ireland).

Table 8. 2 Number of patients living in 2009 with transplanted liver, by age and sex.

Age	Males	Females	Total	Transplants performed during the survey year
0-4	0	1	1	1
5-9	0	1	1	0
10-14	6	8	14	1
15-19	12	8	20	3
20-24	14	10	24	0
25-29	8	6	14	2
30-34	6	2	8	0
35-39	2	3	5	0
40-44	2	2	4	0
45+	2	0	2	0
Total	52	41	93	7

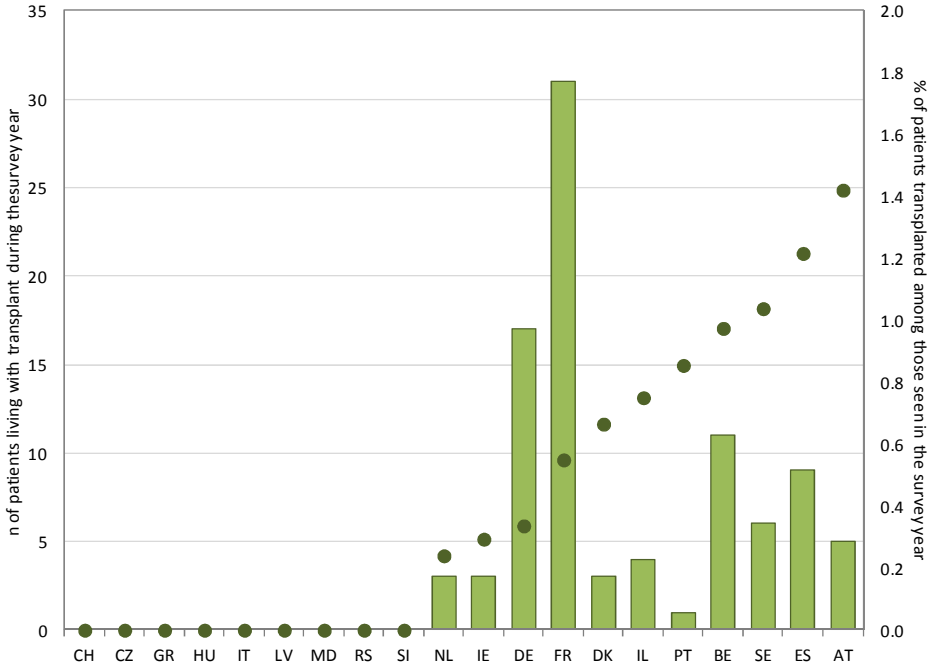
This table shows the number of patients alive in 2009 (2008 for Ireland) who have had a liver transplant at some time in their lives, by age group, as well as the number of patients transplanted during the 2009 (2008 for Ireland).

Figure 8. 1 Number of patients living in 2009 with transplanted lung(s), by country.



This graph shows the number of patients alive in 2009 (2008 for Ireland) with lung transplant (orange bars). The red dots (right axis) show the percentage of patients that are living with lung transplant in 2009 among the patients that were seen in 2009.

Figure 8. 2 Number of patients living in 2009 with transplanted liver, by country.



This graph shows the number of patients alive in 2009 (2008 for Ireland) with liver transplant (green bars). The dark green dots (right axis) show the percentage of patients that are living with liver transplant in 2009 among the patients that were seen in 2009.
Note on the vertical axis that the number of patients with liver transplant is much lower than the number with 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.

9. Mortality

Cystic fibrosis remains a life-shortening disease, but with a steadily increasing expected lifetime. Therefore, we also record patients who died during the survey year, their age at death and the cause of death.

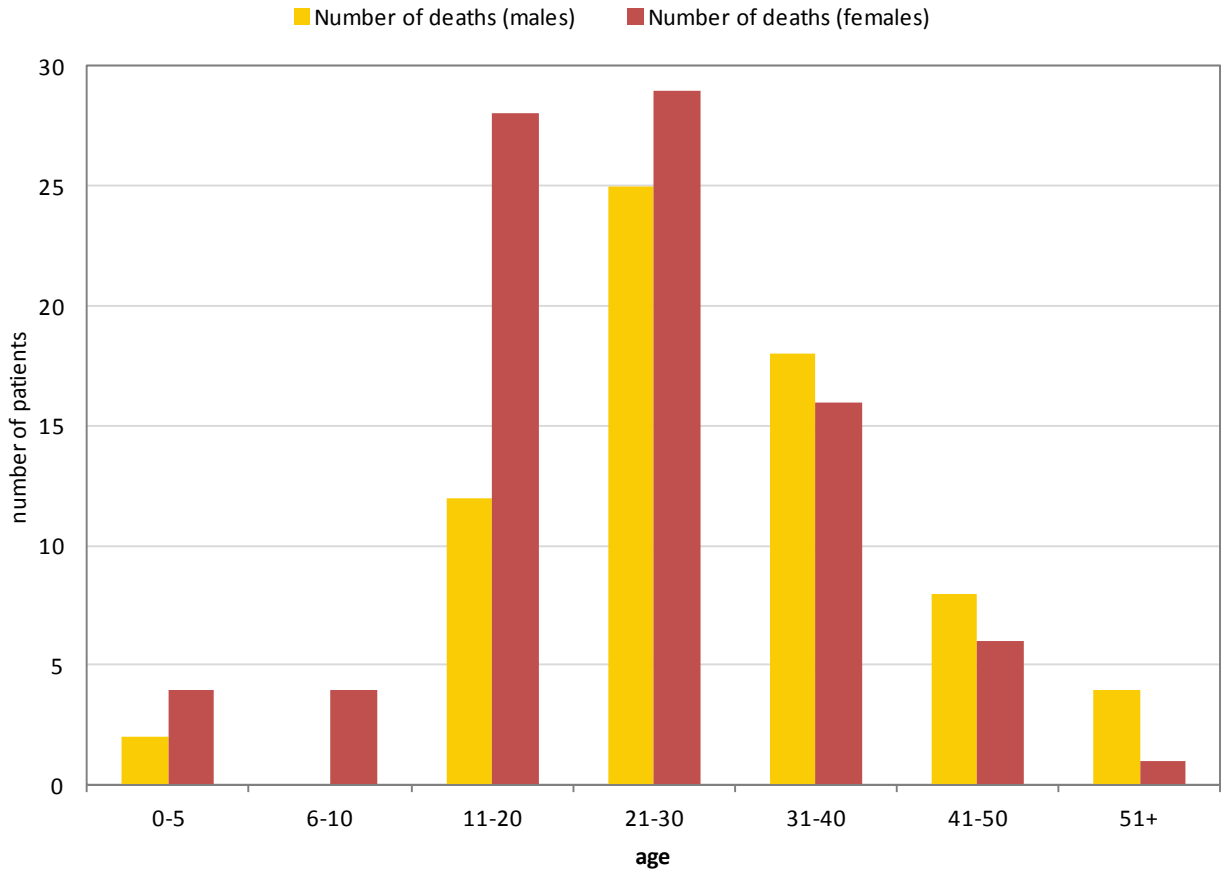
Table 9.1 Number of deaths in 2009, by age and sex.

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	2	2.90	4	4.55	6	3.82
6-10	0	0.00	4	4.55	4	2.55
11-20	12	17.39	28	31.82	40	25.48
21-30	25	36.23	29	32.95	54	34.39
31-40	18	26.09	16	18.18	34	21.66
41-50	8	11.59	6	6.82	14	8.92
51+	4	5.80	1	1.14	5	3.18
Total	69	100.00	88	100.00	157	100.00

Note: we included the number of deaths in 2008 for Ireland.
Note: for 13 patients (7 males and 6 females) date at death, and thereby age at death, was unknown.

This table shows the number of deaths in 2009 by age group and sex. Death in small children is very rare, and the most frequent age of death for both sexes is 21-30 years.

Figure 9.1 Age at death distribution of patients deceased in 2009, by sex.



Note: we included age at death of patients deceased in 2008 for Ireland.

This graph shows the distribution of age at death of patients deceased in 2009, separately by males (yellow) and females (red).

Table 9.2 Cause of death distribution of deaths in 2009.

Cause of death	Number of deaths	Percentage of all deaths
Respiratory disease	77	45.29
Transplantation related	38	22.35
Non-CF related	13	7.65
Liver related	6	3.53
Suicide	2	1.18
Unknown	34	20.00
Total	170	100.00

Note: we included in the table the cause of death of deaths in 2008 for Ireland.

This table shows the list of causes of death for the deceased patients. The most frequent cause of death is respiratory disease. Please note that only a limited number of causes of death are collected, therefore if some deaths are due to rare complications to CF, they may have been classified as “Unknown”.

Publications

The ECFSPR data have been used for research, in accordance with the ECFSPR guidelines (http://www.ecfs.eu/projects/efcs-patient-registry/guidelines).

Three manuscripts are currently in preparation, and updates on their publication will be available on the ECFSPR website.

Two abstracts were accepted for the 6th European Conference on Rare Diseases Orphan Products:

- Viviani L, van Rens J, De Boeck K: The European Cystic Fibrosis Society Patient Registry: a valuable research tool;
- Pypops U, van Rens J, Ravilly S: Information about the European Cystic Fibrosis Society Patient Registry for patients.

Contacts and information

Requests for additional information relating to this report: ecfs-pr@uzleuven.be.

Use of ECFSPR data for research: Executive Coordinator, ecfs-pr@uzleuven.be.

Website: www.ecfs.eu/projects/ecfs-patient-registry/intro.

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IBIS INFORMATICA

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Appendix 1: technical notes

Patient inclusion criteria.

The ECFSPR registers patients diagnosed with CF according to agreed definitions (see Appendix 2). Data of patients with a diagnosis that does not meet the agreed definition are accepted in the database but not included in the analyses.

Data manipulation.

For data anonimisation reasons, we collected only year and month of birth and days of birth were set to 15 (for Belgium month of birth was set to 7 for adults).

Unknown dates of lung function tests and of height/weight measurements were set to July 1st of the survey year.

For pre-natal diagnoses, we set age at diagnosis equal to 0.

We checked for outliers and, whenever possible, we corrected the values according to the national registries'/individual centres' instructions. If, after the data quality controls, aberrant values were still present in the database, we set them to missing for the purposes of this report.

Reference populations used for computing z-scores

The value of a z-score depends on the reference anthropometric chart: the same value of height (or weight or BMI) will result in different values of z-scores if different reference values are used, and these differences might be of clinical importance. 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 forced us to use an international reference to compute z-scores for height, weight and BMI. We decided to use the CDC 2000 reference charts (Kuczmarski RJ, Ogden CL, Guo SS et al. 2000 CDC Growth Charts for the United States: Methods and Development. National Centre for Health Statistics. Vital Health Stat 2002; 11(246):1-190.), which were derived from samples of U.S. healthy individuals[3]. The choice of CDC charts as a reference, although not the most suitable to assess the nutritional status of European CF patients, is justified by the widespread use of these charts at international level.

Reference populations used for computing FEV1 predicted values.

We computed percent of predicted values for FEV1 and FVC using:

- for male children (6-17 years) and female children (6-15 years):
  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.
- for male adults (≥18 years) and female adults (≥16 years):
  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.

Software used for data management and statistical analyses

SAS software, Version 9.2. 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.

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

Appendix 2: list of variables, inclusion criteria and definitions for the ECFSPR

List of the 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

Therapy
Inhaled continuous hypertonic NaCl this year
Inhaled continuous antibiotic this year
Inhaled continuous bronchodilators this year
In Oxygen therapy this year
Use of rhDNase this year
Use of continuous Azithromycin (or other macrolide) this year
Use of ursodeoxycholic acid this year
Use of pancreatic enzymes this year

Diagnosis
Diagnosis confirmed
Age at diagnosis
Type of sweat test
Electrolytes
Chloride value
Meconium Ileus
Neonatal screening

Complications
Allergic broncho-pulmonary aspergillosis this year
Diabetes: daily insulin treated this year
Pneumothorax requiring chest drain this year
Liver disease this year
Hemoptysis major over 250 ml this year
Pancreatic status: faecal elastase
Pancreatic status: faecal fat
Occurrence of malignancy this year

Genotype
First mutation
Second mutation

Microbiology
Chronic *Burkholderia cepacia complex*
Nontuberculous mycobacteria this year
Chronic *Pseudomonas aeruginosa*
Chronic *Staphylococcus aureus*
Stenotrophomonas maltophilia 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
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 (if occurred before or during this year)
Lung transplant
Year of latest lung transplant (if occurred before or during this year)

Inclusion criteria

Only patients who fulfil the diagnostic criteria below should be included the registry.

a. **Two sweat tests value > 60 mmol/L chloride**: CF diagnosis accepted
b. **One sweat test value > 60 mmol/L chloride and DNA Analysis/Genotyping – two identified disease causing CF mutations**: CF diagnosis accepted
c. **Sweat value less than or equal to 60 mmol/L chloride**: if the sweat value is less than or equal to 60 mmol/L chloride, then at least 2 of these should be fulfilled
    i. DNA Analysis/Genotyping – two identified disease causing CF mutations.
    ii. Transepithelial (Nasal) Potential Difference – study consistent with a diagnosis of CF.
    iii. Clinical Presentation – typical features of CF.
d. **Diagnosis reversal**: if the patient's CF diagnosis reversed during the year, identify the reason from the options listed.
    i. DNA Analysis – unable to identify two disease causing CF mutations.
    ii. Transepithelial (Nasal) Potential Difference – study not consistent with a diagnosis of CF.
    iii. Repeat normal sweat testing – confirm with clinical team.

Definitions for EFCSPR

SWEAT TEST

If a sweat test was not performed on a patient, record "not done". If a sweat test is "not done" then two known genotype mutations must be reported.

i. Sweat Test: record the patient's sweat test.
ii. Electolytes: Chloride concentration measurement is the preferred analysis.
iii. Chloride value: report the Chloride value in millimols per liter (mmol/L). If duplicate tests were completed on the same day, report the highest positive value.

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.

SPIROMETRY

The purpose of recording data on spirometry values for the ECFS Patient Registry is to obtain standardized comparable data for comparison with other centers/countries and for use in specific epidemiological studies. Some of the conditions for this (see below) might not be met at every clinic visit for all patients. Therefore, for the purpose of the registry, only the spirometry tests fulfilling the criteria should be recorded/extracted for the ECFS Patient Registry.
For all tests the spirometry should be performed according to the common ATS/ERS guidelines

a. general considerations for lung function testing (http://www.ers-education.org/pages/default.aspx?id=2005&idBrowse=37467&det=1)
b. standardization of spirometry (http://www.ers-education.org/pages/default.aspx?id=2005&idBrowse=37466&det=1)

Furthermore for the values reported to the registry the following criteria should be met

1. Pre-test
    a. date of birth, gender and height should be recorded for calculation of predicted values
    b. all recorded spirometry tests should be pre-bronchodilator* values
        i. short-acting bronchodilators: at least 4 hours pre-test
        ii. long-acting bronchodilators: at least 12 hours pre-test

    *This was decided according to the PortCF official definitions
2. Reported values
    a. for values reported to national registries or to centres and extracted to ECFS Patient Registry, the value in litres of the highest available value of FEV_1% of predicted (according to local references) of the year should be extracted
    b. each patient's FVC and FEV_1 measurement has to be reported in litres (L), with up to two places to the right of the decimal
    c. the FVC measurement must be greater than or equal to the FEV_1 measurement
    d. for each reported spirometry value, the date of the test and the patient's height at that date should be reported in order to perform the calculation of percent of predicted values
    e. only tests deemed valid according to ATC/ERS guidelines should be reported
3. Calculation of percent of predicted values. A common set of reference values will be used
    a. for male children 6-17 yrs and female children 6-15 yrs: Wang et al (1993)
    b. for male adults ≥ 18 yrs and females ≥ 16 yrs: Hankinson et al (1999)
    c. for children < 6 yrs no calculation of percent of predicted values will be performed because of lack of valid

reference values

The definition group considered the issue of race-specific reference values and has decided not to do this calculation and not to record race for European patients

References:
a) Miller et al. Standardisation of spirometry. Eur Respir J 2005; 26: 319–338
b) Miller et al. General considerations for lung function testing. Eur Respir J 2005; 26: 153–161
c) Cystic Fibrosis Foundation Patient Registry User's Guide, Version 4.0. 2006
d) Rosenfeld et al. CFF registry committee task force to evaluate choice of spirometric reference equations for the national patient registry – summary and recommendations
e) 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
f) 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

NUTRITION

Measurements: weight and height are measured according to EuroCareCF guidelines

a. weight: removal of outer clothing, shoes and socks
b. height: without shoes and socks - stadiometer - top of head in contact with head board, slight pressure
c. it should be the value at the day of the recorded FEV_1

z-scores for height, weight and BMI will be calculated using the CDC reference values [Kuczmarski et al (2002)]

References:
a) Kromeyer-Hauschild K, Wabitsch M, Kunze D, Geller F, Geiss HC, Hesse V *et al.* Percentiles of body mass index in children and adolescents evaluated from different regional German studies. Monatsschr Kinderheilkd 2001; 149:807-818
b) Lai H-C, Corey M, FitzSimmons S, Kosorok MR, Farrell M. Comparision of growth status of patients with cystic fibrosis between the United States and Canada. Am J Clin Nutr 1999; 69:531-538
c) Public Use File BGS98, German National Health Interview and Examination Survey 1998, Robert-Koch-Institut, Berlin, Germany, 2000
d) Wiedemann B, Paul KD, Stern M, Wagner TO, Hirche TO, on behalf of the German CFQA Group. Evaluation of body mass index percentiles for assessment of malnutrition in children with cystic fibrosis. Eur J Clin Nutr 2007; 61, 759-768
e) Kuczmarski RJ, Ogden CL, Guo SS et al. 2000 CDC Growth Charts for the United States: methods and development. Vital Health Stat 2002; 11(246): 1-190

DEFINITION OF CHRONIC INFECTION IN THE LOWER AIRWAYS

1. Chronic PA infection should be defined by local physician according to modified Leeds criteria[a] and/or anti-pseudomonas antibodies[b]. Patient should be defined as chronically infected if he/she fulfils the criteria now or in recent years and the physician have no reason to think the status has changed
   a. modified Leeds criteria, chronic infection: >50% of the sputum samples positive, collected during the last 12 months. At least 4 sputum samples during that period
   b. and/or significantly raised anti-pseudomonas antibodies according to local laboratories
2. Chronic infection with other gram-negative bacteria should be recorded by the same criteria as above

References:
a) Lee TWR, Brownlee KG, Conway SP, Denton M, Littlewood JM. Evaluation of a new definition for chronic Pseudomonas aeruginosa in cystic fibrosis patients. J Cystic Fibrosis
b) Proesmans M, Balinska-Miskiewiscz, Dupont L et al. Evaluating the "Leeds criteria" for Pseudomonas aeruginosa infectionin a cystic fibrosis centre. Eur Resp J 2006;27:937-943.
c) Doring G, Conway SP, Heijerman HG, et al. Antibiotic therapy against Pseudomonas aeruginosa in cystic fibrosis: a European consensus. Eur Respir J 2000;16:749-767

ALLERGIC BRINCHO-PULMONARY ASPERGILLOSIS (ABPA)

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 positiv 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:

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. Allergic bronchopulmonary aspergillosis in cystic fibrosis--state of the art: Cystic Fibrosis Foundation Consensus Conference. Clin Infect Dis. 2003 Oct 1;37 Suppl 3:S225-64

LIVER DISEASE

We adopt the definitions for Liver Disease used by the UK Registry. These definitions discriminate patients with severe liver disease (with portal hypertension) from milder cases (cirrhosis without portal hypertension).

Cirrhosis with Hypertension: scaring 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: scaring of the liver relating to underlying CF.

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

PANCREATIC STATUS

Definition:

Stool fat (van de Kamer) > 4-5 g/d in young children, > 7g/d in children above 10 yrs and adults and/or faecal pancreatic elastase-1 < 200 ug/g

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

Pancreatic status will be assessed at the registry level, according to the following:

Pancreatic insufficiency

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

Pancreatic sufficiency

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

*according to definition above

References:

a) Sinaasappel M, Stern M, Littlewood J, Wolfe S, Steinkamp G, Heijerman HGM, Robberecht E, Döring G. Nutrition in patients with cystic fibrosis. A European consensus. J Cystic Fibrosis 2002; 1:51-75.
b) Walkowiak J, Nousia-Arvanitakis S, Henker J, Stern M, Sinaasappel M, Dodge JA. Invited review: Indirect pancreatic function tests in children. J Pediatr Gastroenterol Nutr 2005; 40:107-114.