European Cystic Fibrosis Society Patient Registry
Organization and achievements

JUSTUS-LIEBIG-UNIVERSITÄT GIESSEN

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Polish Cystic Fibrosis Society Meeting—Warsaw- 24.05.2018

Value of a Patient Registry

Patients & their families	Information about outcomes in country => discuss with doctor Enhance CF-care, access to new therapies
Patient Advocacy groups	Lobby for CF-care with heathcare authorities and other parties
CF centres	Monitor quality of care & identify areas for improvement Improve CF-care
Researchers	Longitudinal and large-scale epidemiological research Identify disease modifying factors
Healthcare authorities	Information about CF and CF-care in country
Industry	Preparation landscape for clinical trials Monitor effectivess & safety of new therapies

Essential Registry tools

COMMITTMENT – TRUST – GOVERNANCE – INDEPENDENCY - SUSTAINABILITY

- Harmonization of data fields and definitions

  International comparison based on harmonization

  Keep the balance between quality and quantity - Data collection resources

- Data collection method (webbased software tool)
- Data management and data quality controls
- Use of data and dissemination of the results (Annual report)

Viviani et al. Orphanet Journal of Rare Diseases 2014, 9:81

ECFSPR

Introduction

A platform for the collection of CF data

- Anonymised data
- Consenting patients with CF
- Agreed inclusion criteria, variables and definitions
- Cooperation with national and rare disease registries (ERN)

Background:

Start in 2003

Part of the European Cystic Fibrosis Society

ECFSPR | Mission

Compare aspects of CF and its treatment to…

- Encourage new standards of CF care
- Inform public health planning
- Enable research

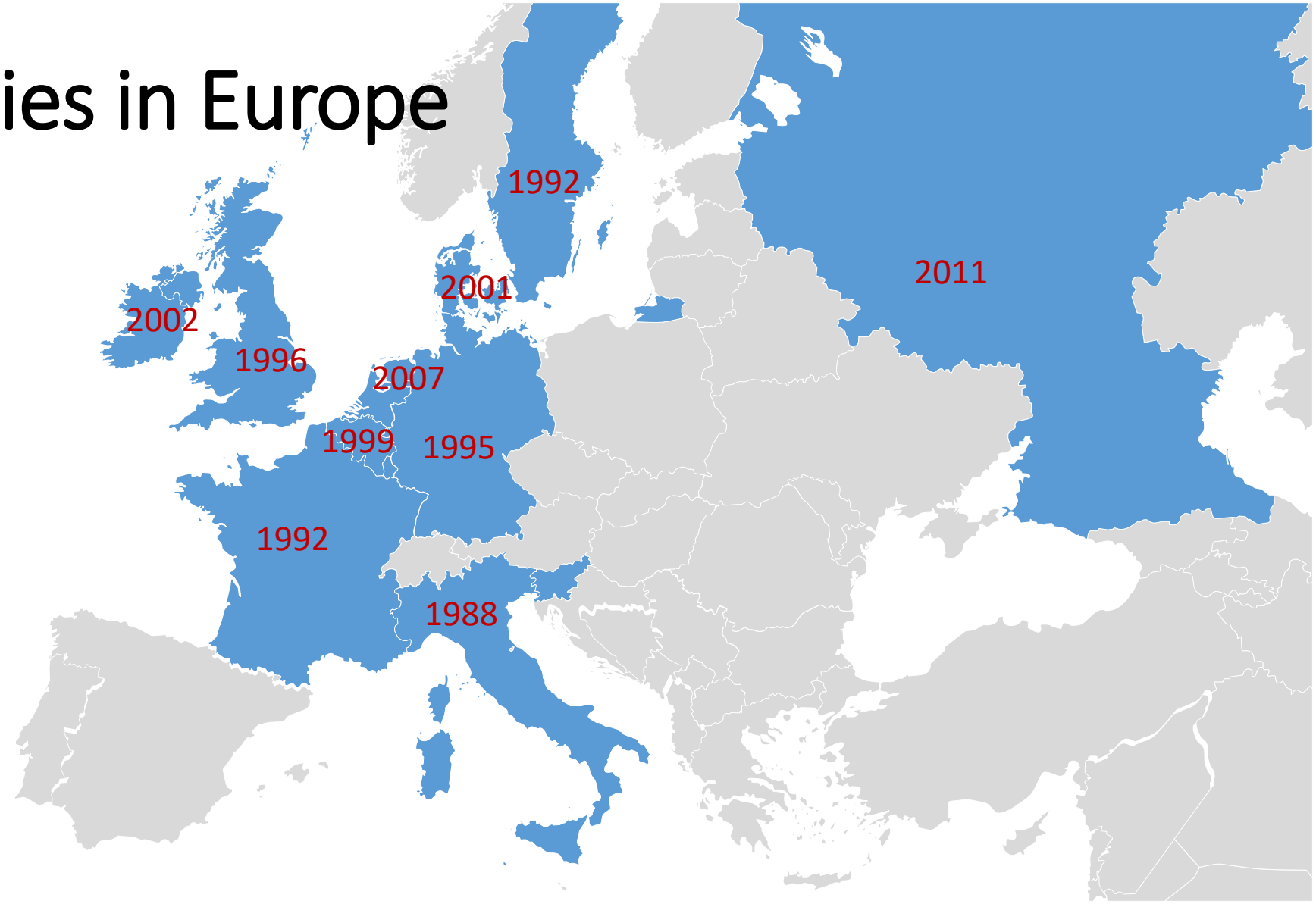
ECFSPR | Agreed Inclusion Criteria

- 2 Sweat tests with values > 60 mmol/L chloride
- 1 sweat test value > 60 mmol/L chloride + 2 identified disease causing CF mutations
- Sweat test values ≤ 60 mmol/L chloride:
  - ✓ DNA analysis: 2 identified disease causing CF mutations
  - ✓ Nasal Potential difference
  - ✓ Clinical presentation: typical CF features

ECFSPR | Agreed Variables, Definitions, References

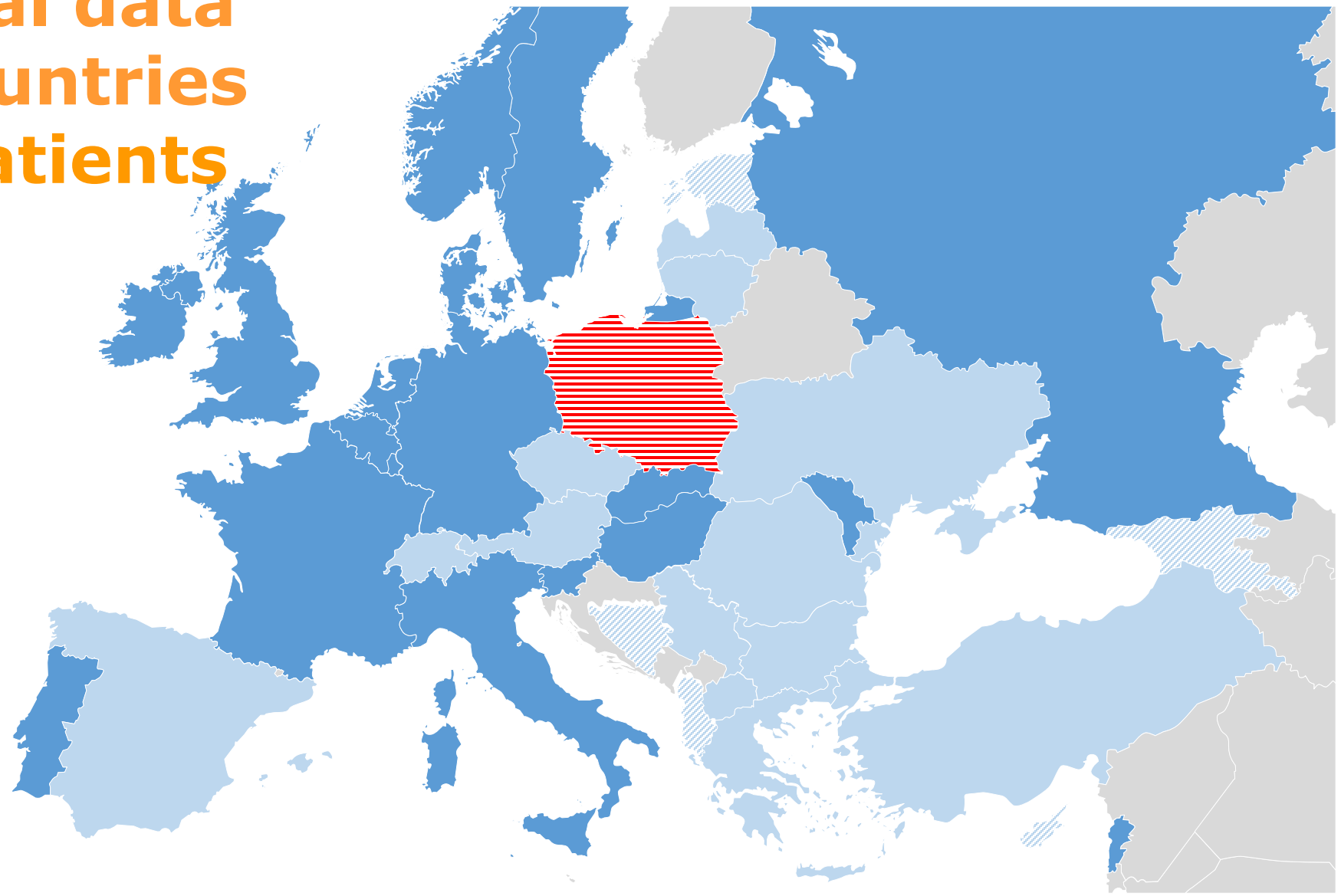
Demographic	age, gender, status of patient
Diagnosis	age at diagnosis, sweat test, meconium Ileus, neonatal screening
Genotype	1st and 2nd mutation
Growth / lung function	value of best FEV1 and FVC, height and weight at best FEV1
Microbiology	Pseudomonas aeruginosa, Staphylococcus aureus, Burkholderia cepacia
Complications	Diabetes, liver disease, pancreatic status, malignancy
Therapy	antibiotic, bronchodilators, oxygen therapy, pancreatic enzymes
Transplant	Lung / liver transplant

CF- Registries in Europe



A.D. Jackson, C. Goss., J Cyst Fibros 2017 in press; RU: Krasovskiy S, J Cyst 2014: S 124;
SE: http://kvalitetsregister.se; DK: Nguyen-Nielsen M, Clin Epidemiol, 2013: 249

ECFSPR:
Longitudinal data
29 (+6) countries
>42.000 patients



Reference: ECFSPR Annual Data Report 2015 + Update (20.05.2018)

ECFSPR

Cooperation with National registries

Model 1 _ Uploading countries

- Own governance
- Own data management and software
- Own budget to maintain this services

Model 2 _ ECFS - Tracker User

- Own governance/country coordinator
- Free use of ECFS-tracker, ECFS-PR service desk/data management
- Option to adapt own variables
- Maintenance cost covered by ECFS

ECFSPR

Cooperation with National registries

Model 1 _ Uploading countries

- Most are established before the ECFSPR started
- Own budget (for example D 5000000 € per year)
  - Data collection/management/software development
- Uploading annual ECFSPR dataset

Model 2 _ ECFS-Tracker User

- Own governance/country coordinator – reassure about data use
- Concentration on data collection and reporting (esp. national report)
- Center are owner of the data

Software | General Features

ECFSTracker
European Cystic Fibrosis Society Patient Registry

A platform for the collection of CF data for all purposes

- ✓ Web-based and open source
- ✓ Designed for the collection of CF data
- ✓ User friendly
- ✓ Remotely managed
- ✓ Data quality checks on different levels
- ✓ Additional variables
- ✓ Possibility add-on modules for data-collection

Software

Data Protection – Security

ECFSTracker
European Cystic Fibrosis Society Patient Registry

- ✓ Advanced Security Technology
- ✓ Controlled user access
- ✓ De-identification of data:

  encryption of data during transmission

  Identification only at a center level
- ✓ Compliant with EU data protection regulations

Software

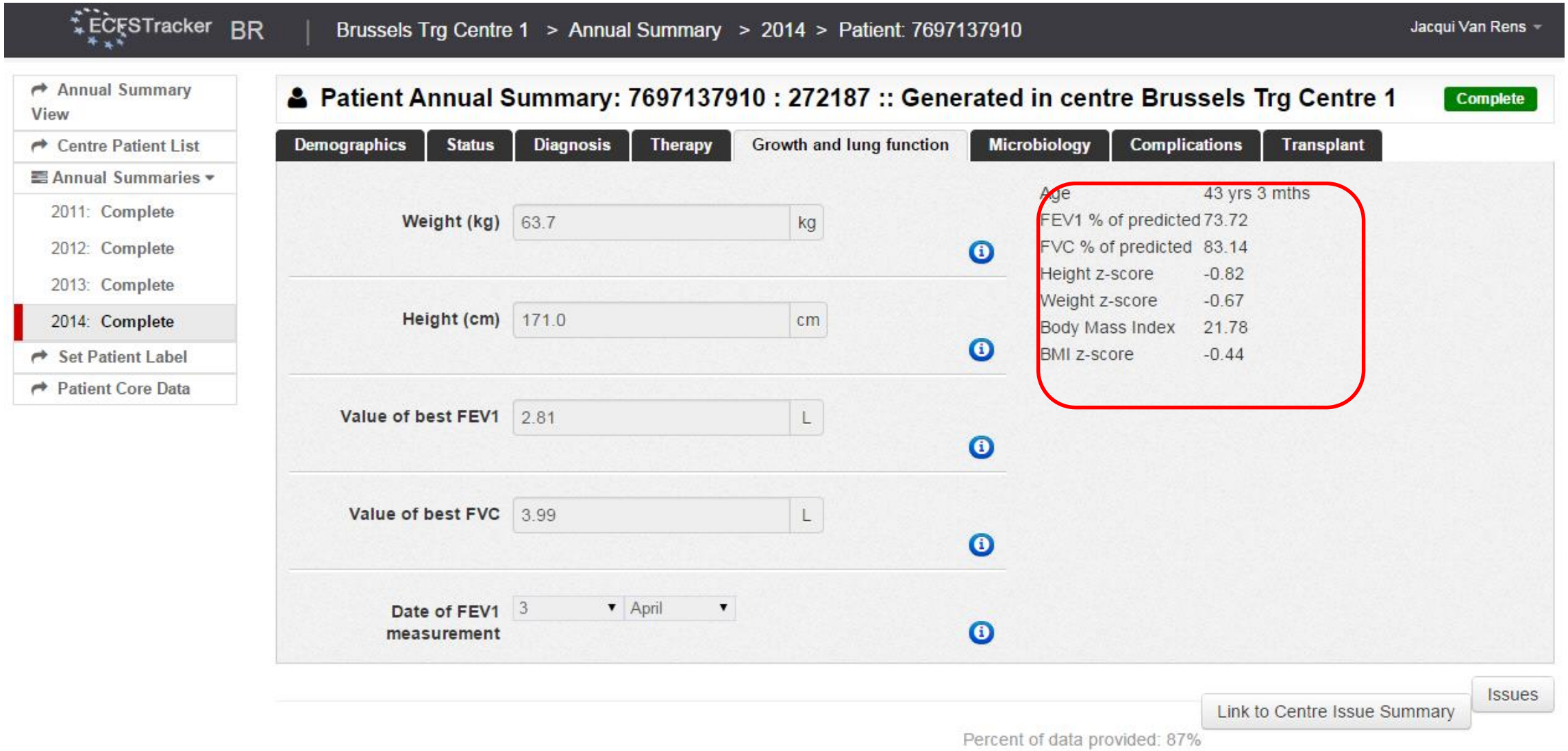
ECFSTracker - homepage

ECFSTracker
European Cystic Fibrosis Society Patient Registry

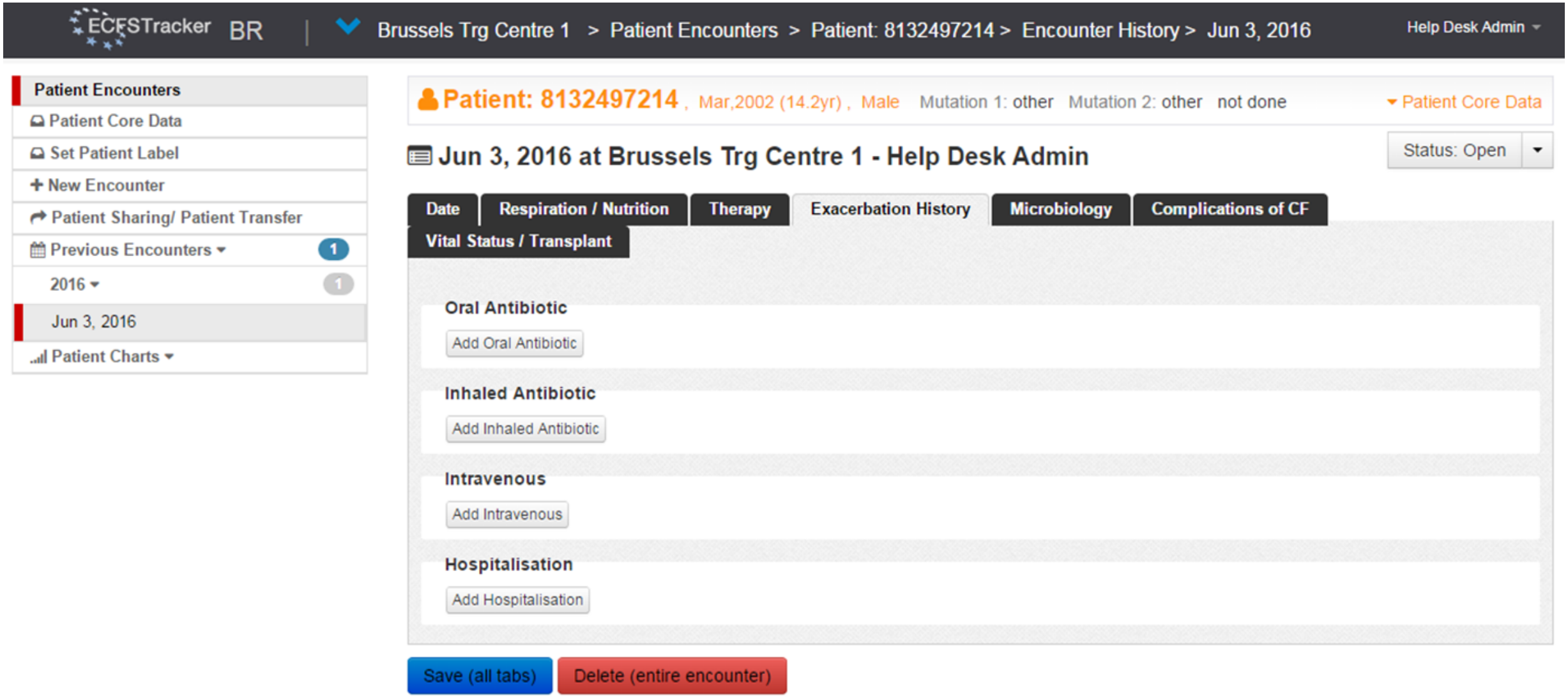
Software

ECFSTracker - dashboard

Software | Annual Summary



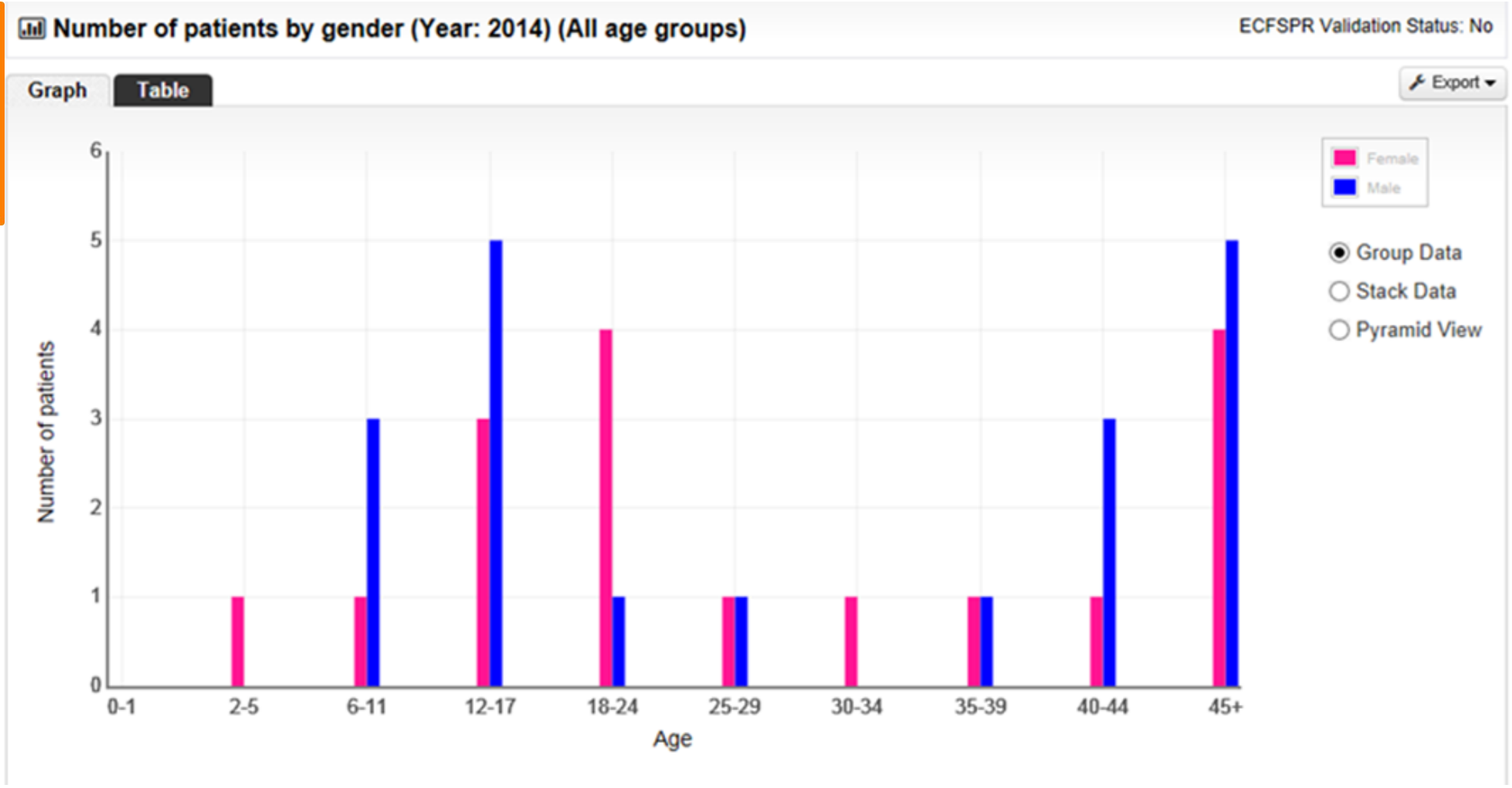
Software | Encounters



Software | Centre Reports

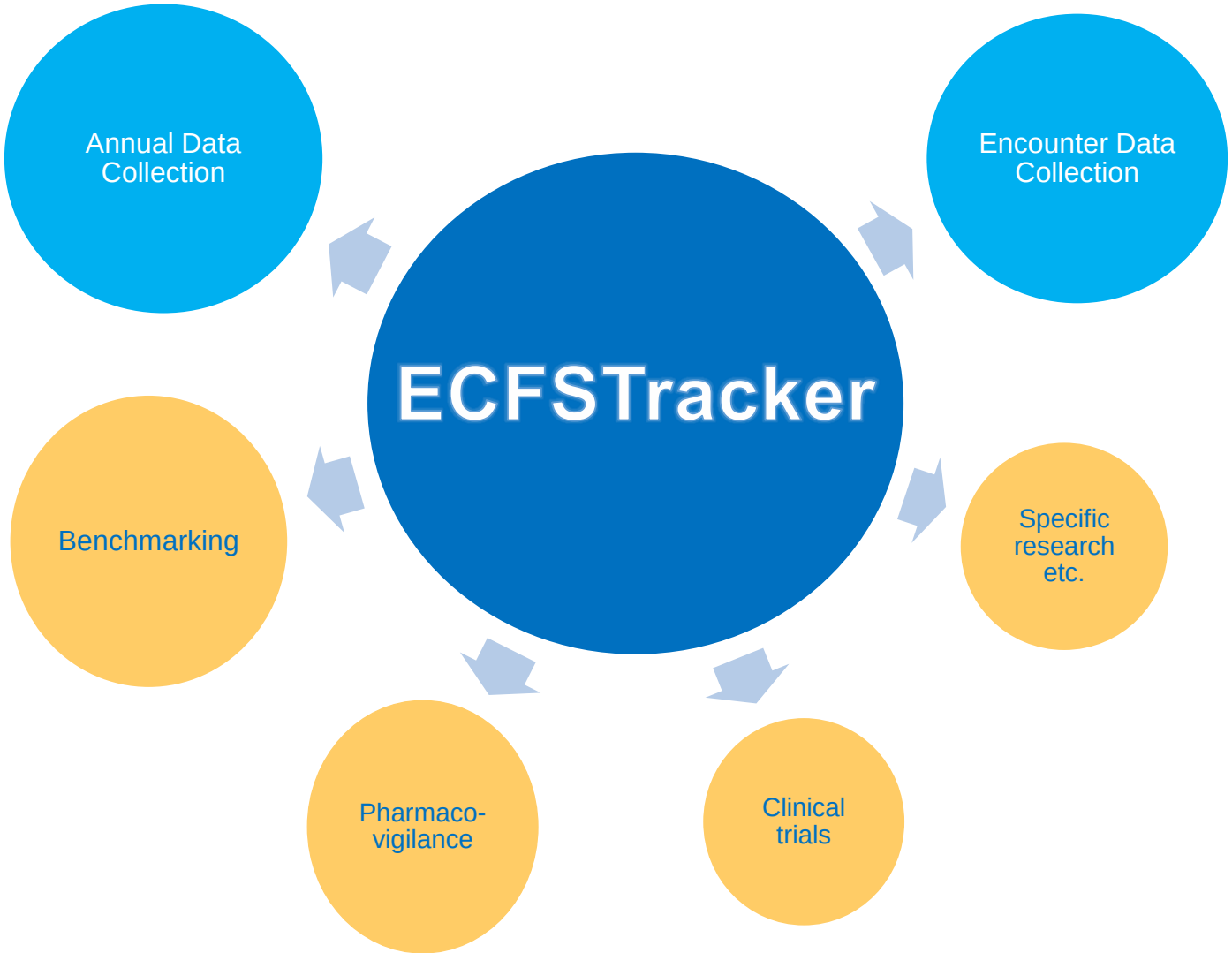
Categories of report

- Number of patients
- Age at follow-up / diagnosis
- Growth and lung function
- Therapy and Microbiology
- Complications



Software | Patient Reports

Software Development



Software

Benchmarking

A module in ECFSTracker to allow cross-comparison of indicators of quality of care (= benchmarks).

Direct feedback to Centre Staff

Identify areas for improvement

A powerful tool to enhance improvement of CF care

Software

Benchmarking

- Compare results between:
  - ✓ Your country with another country / other countries
  - ✓ Your centre with another country / other countries
  - ✓ Your centre with other centres in your country

  Agreement between centres!
- Compare with previous years

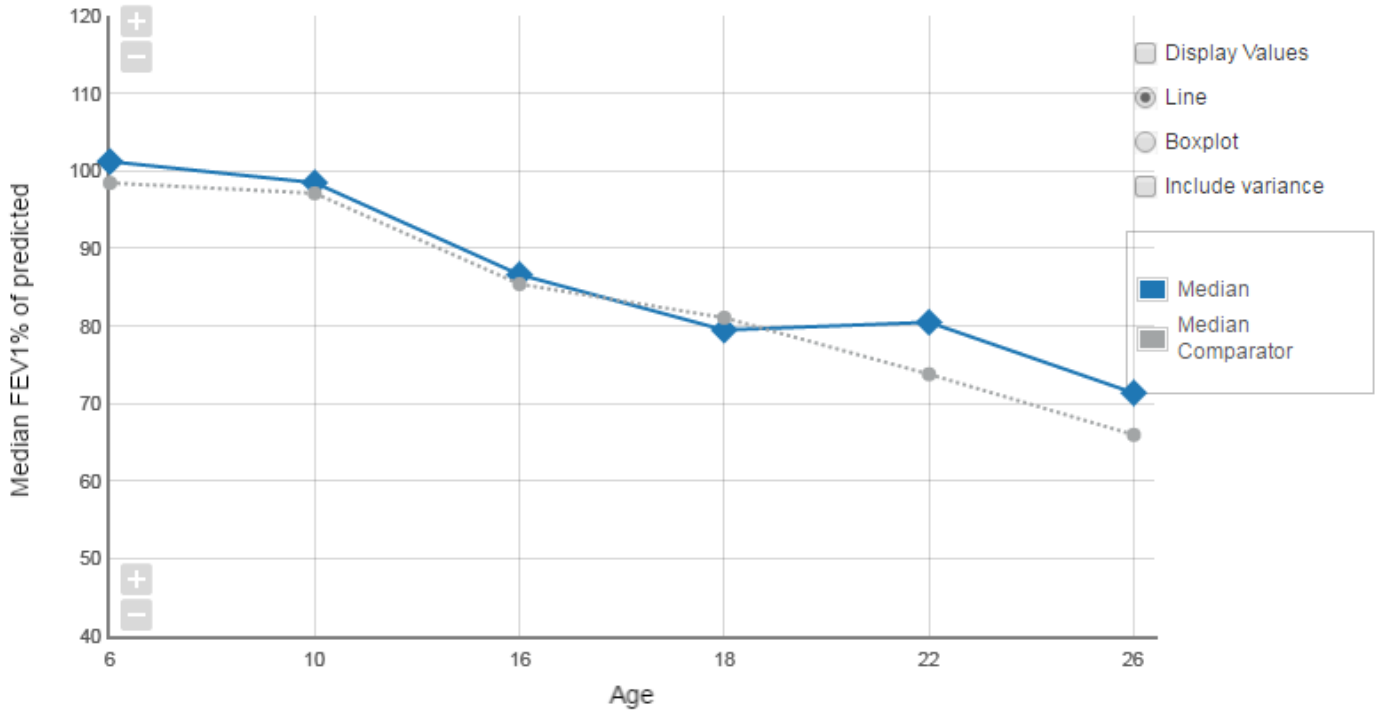
Software | Benchmarking

Median FEV1% of predicted

ECFSPR Validation Status: Yes

Graph | Table

Export



Inclusion criteria:

- Patients with confirmed diagnosis, status alive/deceased, without lung transplantation, with recorded FEV and height value. FEV value only for patients of 6 year and older.

Software

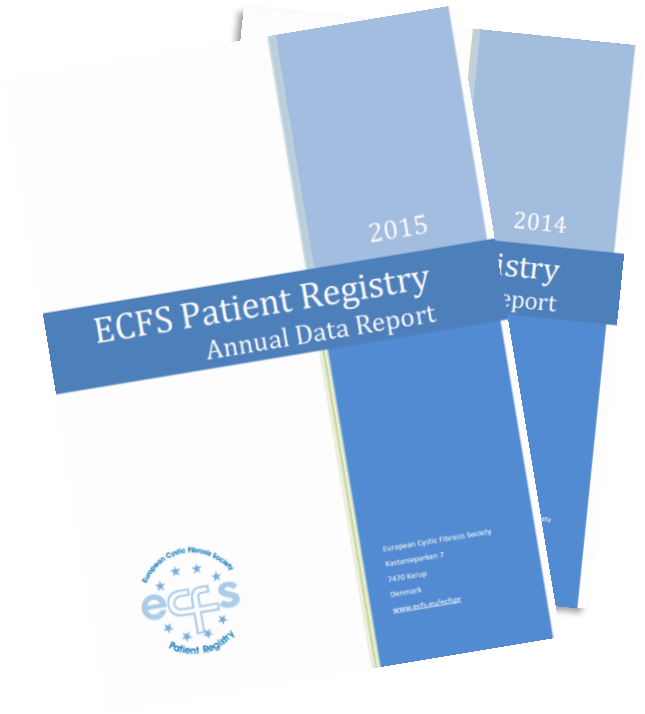
Upgrade to version 2.0

Planning:

- Development: 2017
- Test in pilot countries
- Launch in Europe: 2018

Output

Annual Data Reports

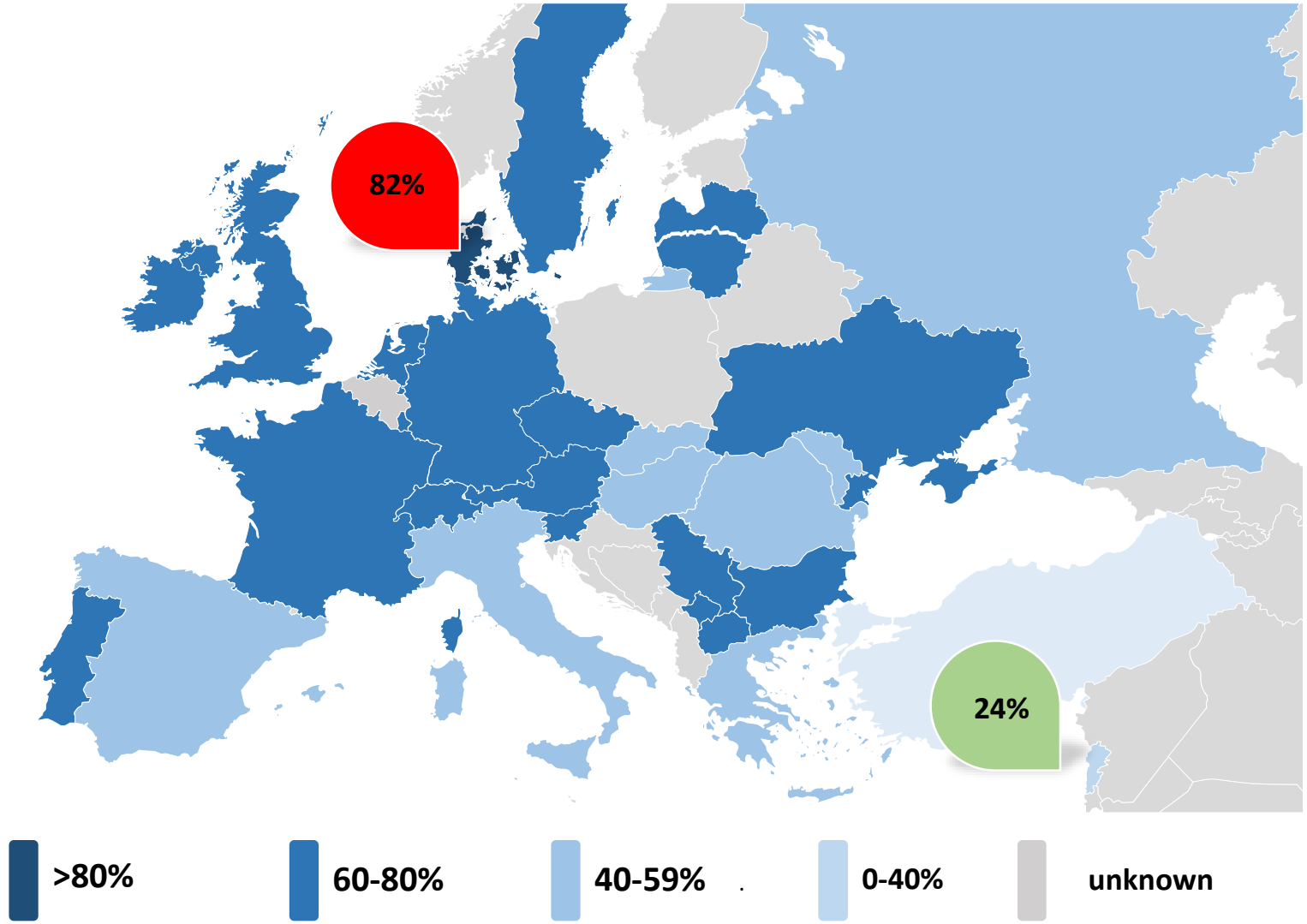


Outcome		Females	Males	Total
Patients registered in the ECFSPR	n (%)	19958 (47.46)	22096 (52.54)	42054
Age at follow-up (in years; patients alive on 31/12/2015)	mean median	20.2 18.1	21.2 19.5	20.7 18.8
Patients ≥ 18 years (patients alive on 1/12/2015)	%	50.3	53.7	52.1
Age at diagnosis*	mean (years) median (months)	4.2 4.6	4.0 4.2	4.1 4.3
Patients with at least one F508del allele recorded*	%	82.1	81.9	82.0
Patients living with lung transplant*	n (%)	975 (5.2)	984 (4.7)	1959 (4.9)
Patients living with liver transplant*	n (%)	86 (0.5)	159 (0.8)	245 (0.6)
Patients deceased in 2015**	n (%)	228 (1.2)	200 (0.9)	428 (1.0)
Age at death (years)**	mean median	30.5 29	31.2 28	30.8 28

Deadline future years: 1 May

Reference: ECFSPR Annual Data Report 2015

Distribution of F508del in Europe



Reference: ECFSPR Annual Data Report 2015

Complication:
Chronic Pseudomonas in children

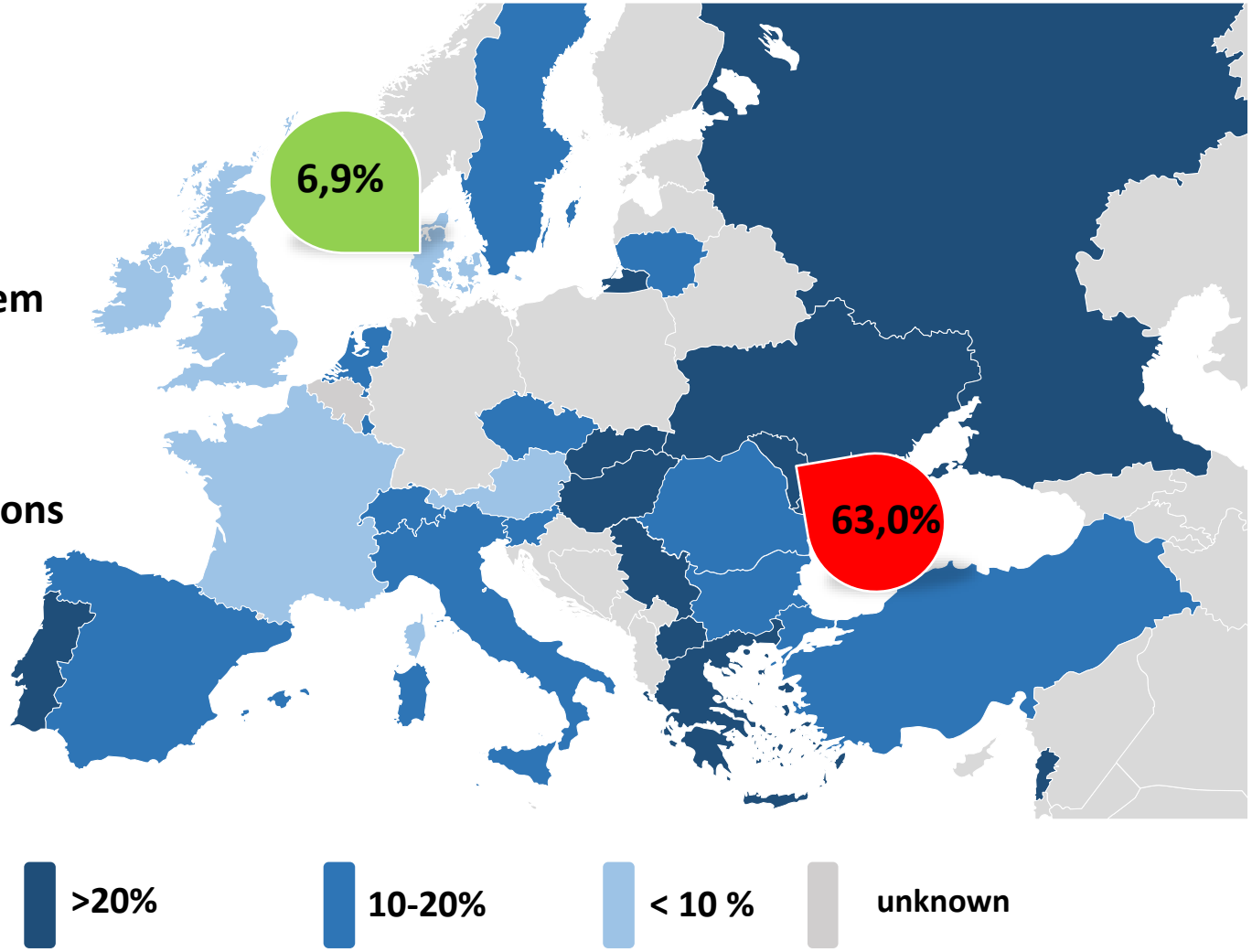
REASONS:

Health care system

Diagnostic tools

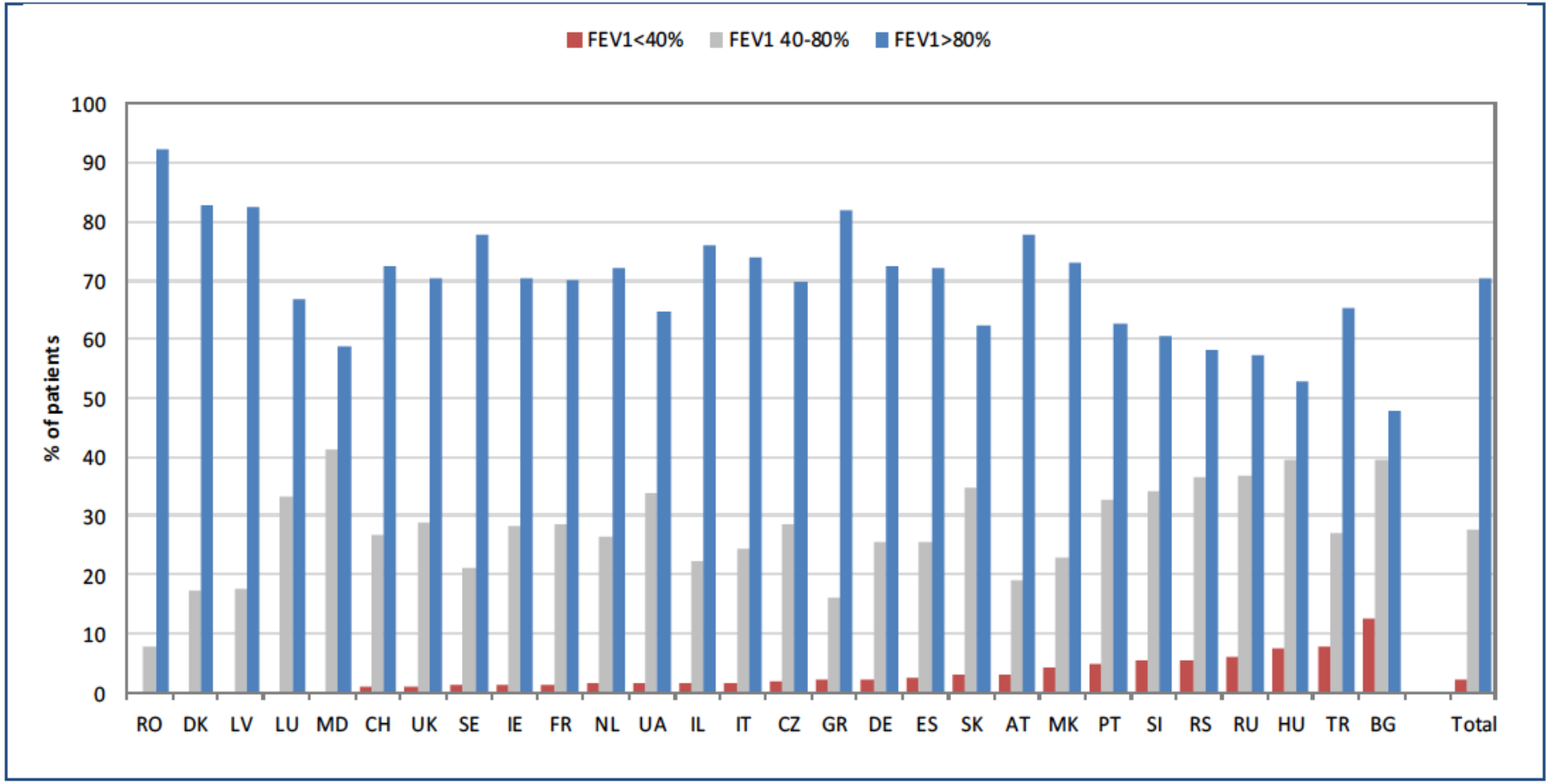
Therapeutic options

Strategy



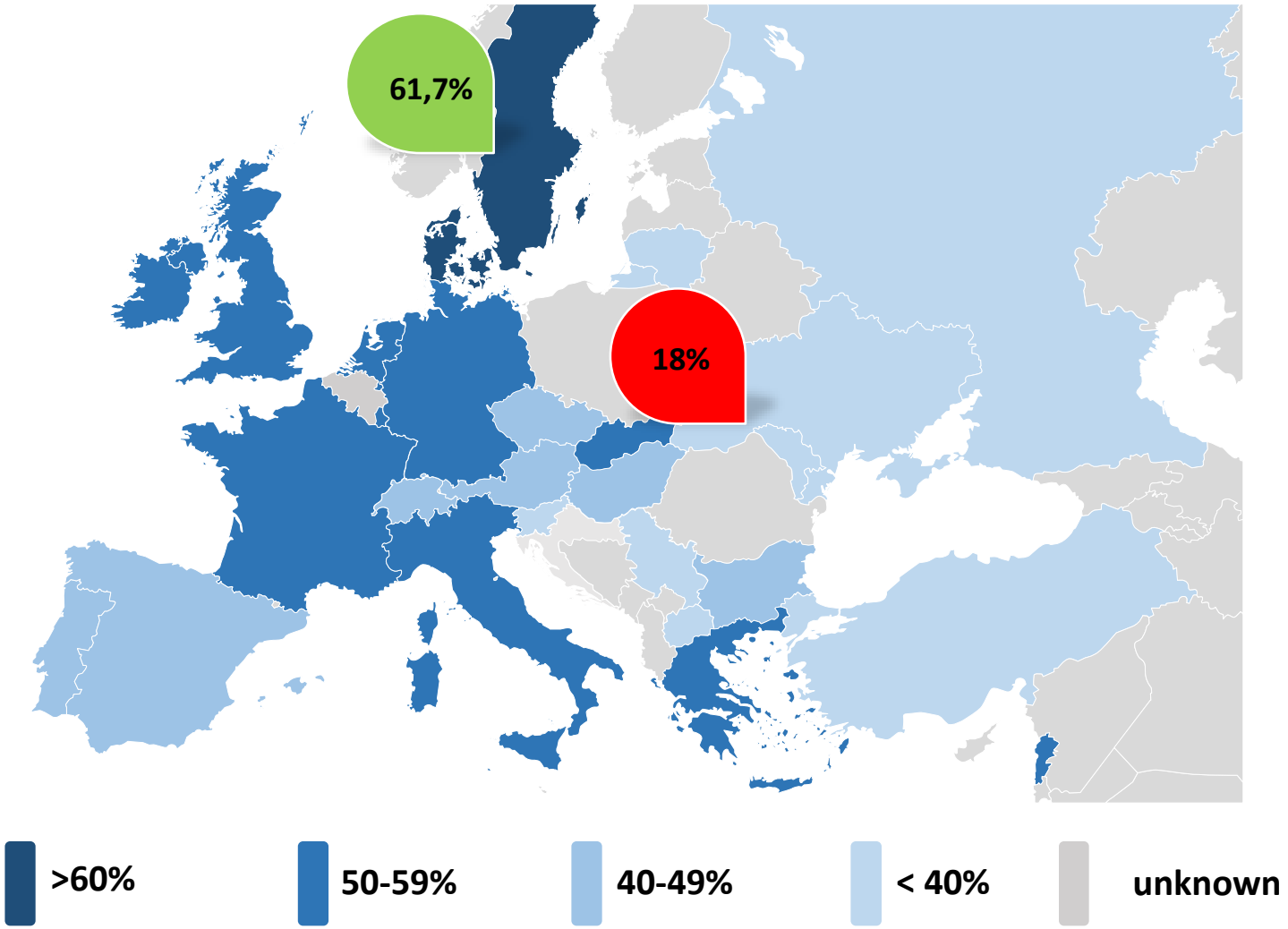
Reference: ECFSPR Annual Data Report 2015

Outcome: Lung function in patients 6-17 year



Reference: ECFSPR Annual Data Report 2015

Outcome: Proportion of adults



Reference: ECFSPR Annual Data Report 2015

Output | Research

Applications for data

Researchers, patient organisations, Industry

Title + Aim + Description of the (research) project

Handling:

- Review by Scientific Committee
- Final Approval by Steering Group for use of data
- Use of data (free for ECFS-PR participants)
- Publication policy

APPLICATION FORM
ECFSPR DATA

All requests for data extractions/data analysis from the European Cystic Fibrosis Society Patient Registry (ECFSPR) must be submitted with this form. We advise you to read all information and complete the form as best as possible to ensure review of your application. You can email the completed form to ecfs-pr@uzleuven.be.

Applicant details			
Name Primary Investigator (incl. title):			
Primary contact (if not PI):			
Institution/Organisation:			
Position:			
Address:			
Email:		Phone:	
Date of request:			

Disclosure
Please disclose any associations with private companies, especially pharmaceutical companies:

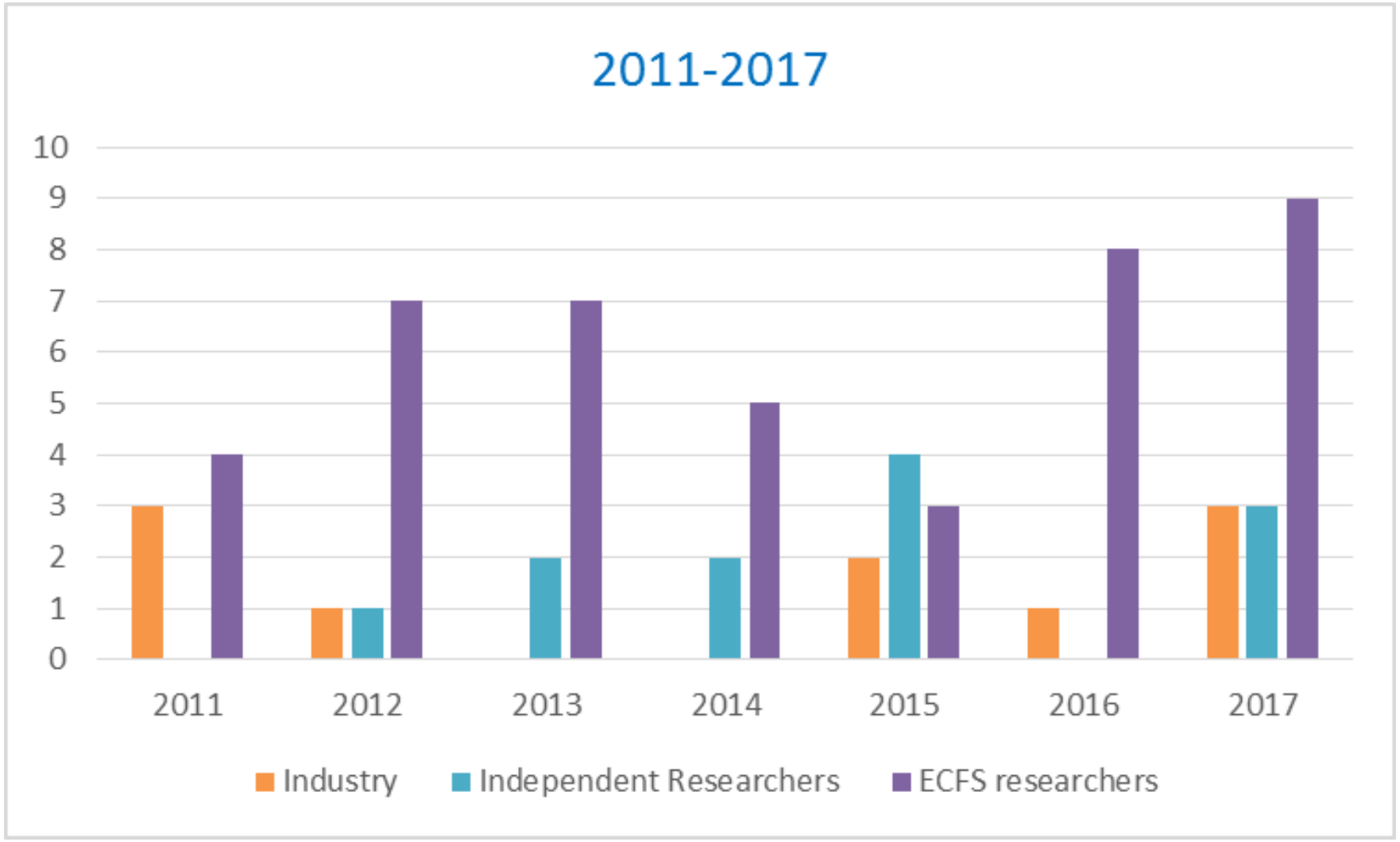
Research Project Information	
Project Name:	
Project Objective(s):	
Description of the Project:	
Brief Background Information (incl. justification of the clinical relevance):	
Research Question/Hypothesis:	
Study Design:	
Cohort Definition:	
Method of Analysis:	
Start and End Date:	

3

www.ecfs.eu/projects/ecfs-patient-registry/data-request-application

Output

Research



Future Trends in CF demographics ERS/ECFFS Task force

Group	Country	Children age ⩽17 years			Adults age ⩾18 years			Total		
		2010	2025	Growth rate %	2010	2025	Growth rate %	2010	2025	Growth rate %
A	Belgium	559	661	18.3	615	1093	77.7	1174	1754	49.4
	Czech Republic	293	313	6.8	230	372	61.7	523	685	31.0
	Denmark	192	192	0.0	265	337	27.2	457	529	15.8
	France	3040	3599	18.4	2718	4776	75.7	5758	8375	45.5
	UK	4435	5539	24.9	4,950	8876	79.3	9385	14 415	53.6
	The Netherlands	591	659	11.5	715	1402	96.1	1306	2061	57.8
	All in group	9110	10 963	20.3	9493	16 856	77.6	18 603	27 819	49.5
B	Germany	2413	2976	23.3	2590	4380	69.1	5003	7356	47.0
	Hungary	339	388	14.5	218	506	132.1	557	894	60.5
	Ireland	527	640	21.4	554	915	65.2	1081	1555	43.9
	Israel	268	327	22.0	284	476	67.6	552	803	45.5
	Latvia	22	19	−13.6	8	12	50.0	30	31	3.3
	Moldova	34	36	5.9	8	25	212.5	42	61	45.2
	Serbia	86	109	26.7	35	94	168.6	121	203	67.8
	Sweden	264	315	19.3	329	523	59.0	593	838	41.3
	Slovenia	55	74	34.6	25	66	164.0	80	140	75.0
	Slovakia	151	202	33.8	182	292	60.4	333	494	48.4
	All in group	4159	5086	22.3	4233	7289	72.2	8392	12 375	47.5

Increase in the CF population by 50%
corresponding by 25% in children and 75% in adults
Impact on care structures

Burgel P, ERJ 2015:133. Based on data 2010

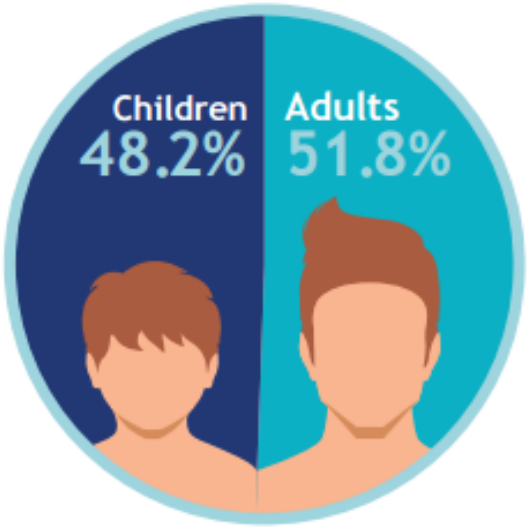
Output

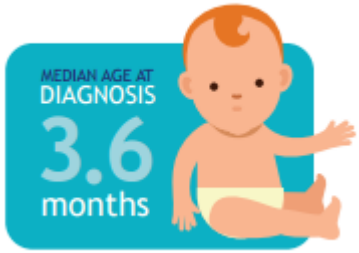
Manuscripts in the pipeline

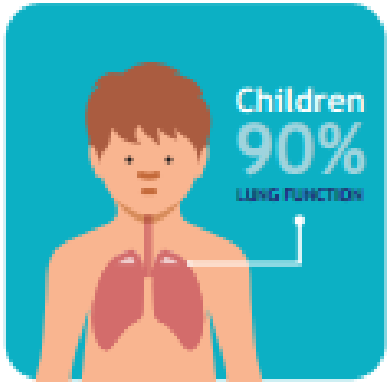
- International and pan-European comparison of survival in CF.
- Changes in demography and clinical outcomes in CF in Europe.
- Mortality during pediatric age in patients with CF in Europe.
- The effect of CFTR nonsense mutations on phenotype and mortality in patients with CF.
- The effect of DNase on longitudinal lung function in patients with CF.
- Clinical characteristics of CFRD: Lessons from the ECFSPR.
- The effect of Allergic Bronchopulmonary Aspergillosis on lung function in children and adolescents with CF: analysis of the ECFSPR data.
- CF-specific reference equations for FEV1 and BMI : an updated analysis.
- Cancer in adult people with CF in Europe.

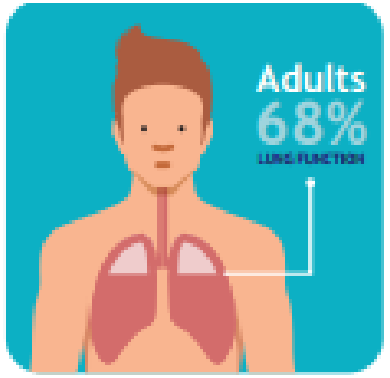
Output

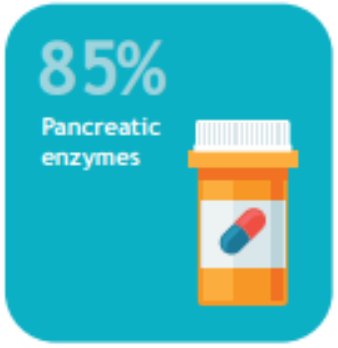
At-a-Glance Reports

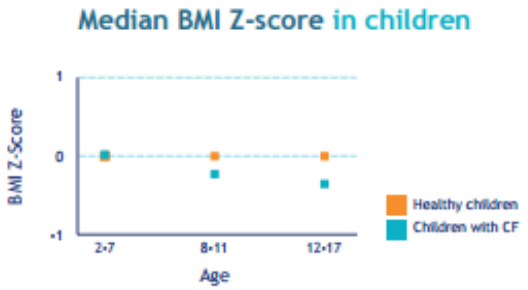


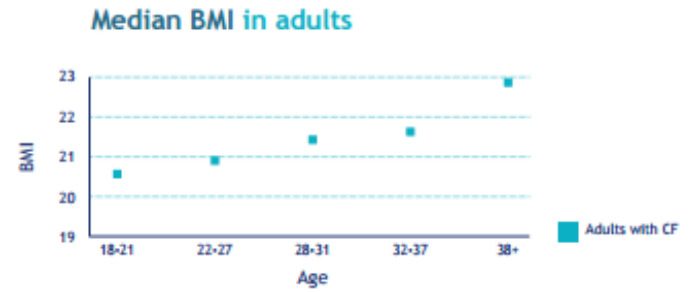


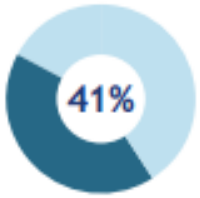




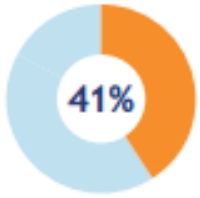




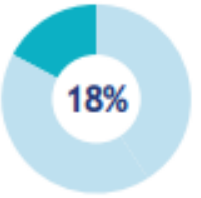




F508del homozygote



F508del heterozygote



Other mutations

POSTER

El Registro de Pacientes de la Sociedad Europea de Fibrosis Quística

¿Por qué es necesario un Registro Europeo de pacientes con FQ?

La Fibrosis Quística (FQ) FQ es una enfermedad rara. Para tener un buen panorama de la FQ en Europa necesitamos los máximos datos posibles. Los datos ayudarán a la comprensión de la enfermedad, a la elaboración de nuevos estándares asistenciales europeos, a la investigación, y a la planificación de la Sanidad Pública.

El Registro de Pacientes de la Sociedad Europea de Fibrosis Quística (ECFSPR)

Recoge, mide, y compara datos de niños y adultos con fibrosis quística que viven en Europa y países vecinos que acceden a estar en el Registro. La información se utiliza para mejorar la salud y el bienestar de las personas con FQ.

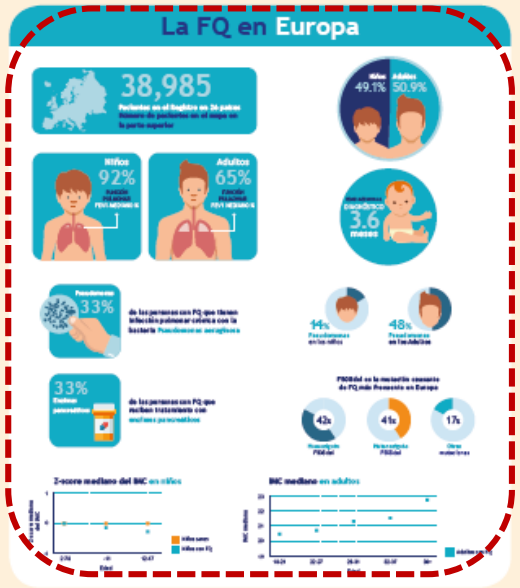
¿Como puedo utilizar la información del Registro?

El ECSPR publica: Informes anuales con indicadores demográficos y clínicos a lo largo de Europa e informes resumidos con información clave acerca de la FQ en Europa.

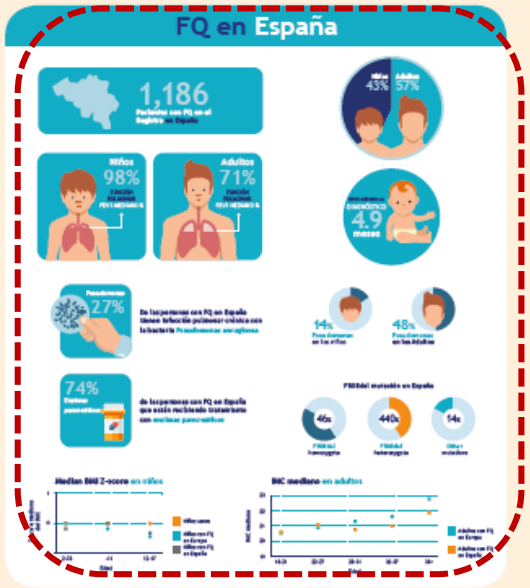
Estos informes son unas herramientas valiosas para:

- las organizaciones locales de pacientes, para discutir como mejorar la asistencia a la FQ en cada país, con las autoridades sanitarias y otras partes relevantes.
- las Unidades de FQ para compararse con otros países e identificar aspectos a mejorar.
- Poder discutir los indicadores y resultados con tu doctor.

La FQ en Europa



FQ en España



Mediana [illegible]

ITC [illegible] peso talla²

Z-score [illegible]

Función Pulmonar:

- **FEV1** Es un indicador de la función pulmonar, es la cantidad máxima de aire que se puede exhalar en un segundo haciendo una espiración forzada después coger el máximo aire posible.
- **FEV1%** Es un porcentaje del valor promedio de personas sanas de la misma edad, sexo, y talla que se considera es 100%.

Las personas con FQ tienen dos mutaciones causantes de FQ, una heredada del padre, y la otra de la madre.

Homozigoto: ambas mutaciones son iguales.

Heterozigoto: las dos mutaciones son diferentes.

¿Qué datos se recogen?

- año/mes del nacimiento, sexo
- genotipo, síntomas al diagnóstico
- Función pulmonar, peso, talla, tipos deinfecciones, tratamientos, algunas complicaciones

Los datos son anónimos, y se guardan en una base de datos segura. Utilizamos normativas bien definidas para el manejo de los datos y estamos supervisados por un comité de expertos.

¿Cómo puedo llegar a formar parte del ECFSPR?

Consúltalo con tu Unidad de FQ local, si la Unidad participa en el ECFSPR, se te debería incluir si firmas una hoja de consentimiento informado.

Si tu Unidad de FQ no participa, pídele a tu Médico que contacte con nosotros, o enviamos tus detalles de contacto y nos pondremos en comunicación contigo.

UNIVERSITÀ DEGLI STUDI DI MILANO · GILEAD · PTC THERAPEUTICS · VERTEX

contacto: ecfs-pr@uzleuven.be página web: www.ecfs.eu/projects/ecfs-patient-registry/

European Cystic Fibrosis Society ecfs Patient Registry

Projects | Overview

1. **Definitions Group**
   Review variables and definitions
2. **Global CF harmonisation project**
   Harmonise variables & definitions to allow comparison ww
3. **Data Quality Group**
   Ensure accuracy and quality of data
4. **Patient awareness project**
   Joint effort with CF Europe to bring data closer to patients

Governance | Organisation

Contributors

CF centres national registries

Data

Steering Group

Country representatives

Strategy

Executive Committee

Steering Group representatives

Management

Scientific Comm.

Steering Group representatives

Data custodian

Staff

Coordinator

Statisticians

Service Desk

Interaction

Governance | Organisation

Terms of Reference: Registry's structure

Code of Conduct: roles and responsibilities

Standard Operating Procedures:

- Data Collection & Error reporting
- Data Access
- Use of data

Business Plan 2018 - 2020

Cooperation with rare disease registries

European rare network (ERN /ERN-LUNG)
- Registry overarching disease areas
- Based on disease-specific registries
- Interaction to fullfill these goals
- No substitute for disease-specific registries

CFTR 2
- Regular data request - cooperation

Governance | Clinical trials

Pharmavigilance _ Longterm safety/efficiency

Cooperation with EMA and industry

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 Procedure No.: EMEA/H/SAB/080/1/QA/2017
2 EMA/CHMP/SAWP/802259/2017
3 Product Development and Scientific Support Department

4 Qualification Opinion
5 The European Cystic Fibrosis Society Patient Registry (ECFSPR)

6 Draft for consultation

„Rare events meet large populations“

- Guidance for decison making
- Specific problem follow-up
- Toolbox registry

European Cystic Fibrosis Society ecfs Patient Registry

Registry

How to join the ECFSPR?

- ✓ Legal and Ethical approval
- ✓ Informed Patients Consents
  - ECFSPR templates on website
  - Meet requirements of your local legal and ethics laws
  - Translate to your own language

ECFSPR

Conclusion

ECFS-PR offer a whole registry infrastructure for free

- FLEXIBLE (National registry/Individual centres)
- Including options for national adaptation
- Including options for national reporting
- Including handling of data requests

Alternative to own national registries with upload of data

- Need for own data collection tools/data management/reporting
- Start-ups costs – Governance – Maintenance costs

Partners & Sponsors

Thank you!