Patient Registries: Beyond Epidemiology

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CF Society Patient Registry,
Consultant Respiratory Physician,
St. Vincent's University Hospital &
University College Dublin,
Ireland.

Facts about CF Patient Registries

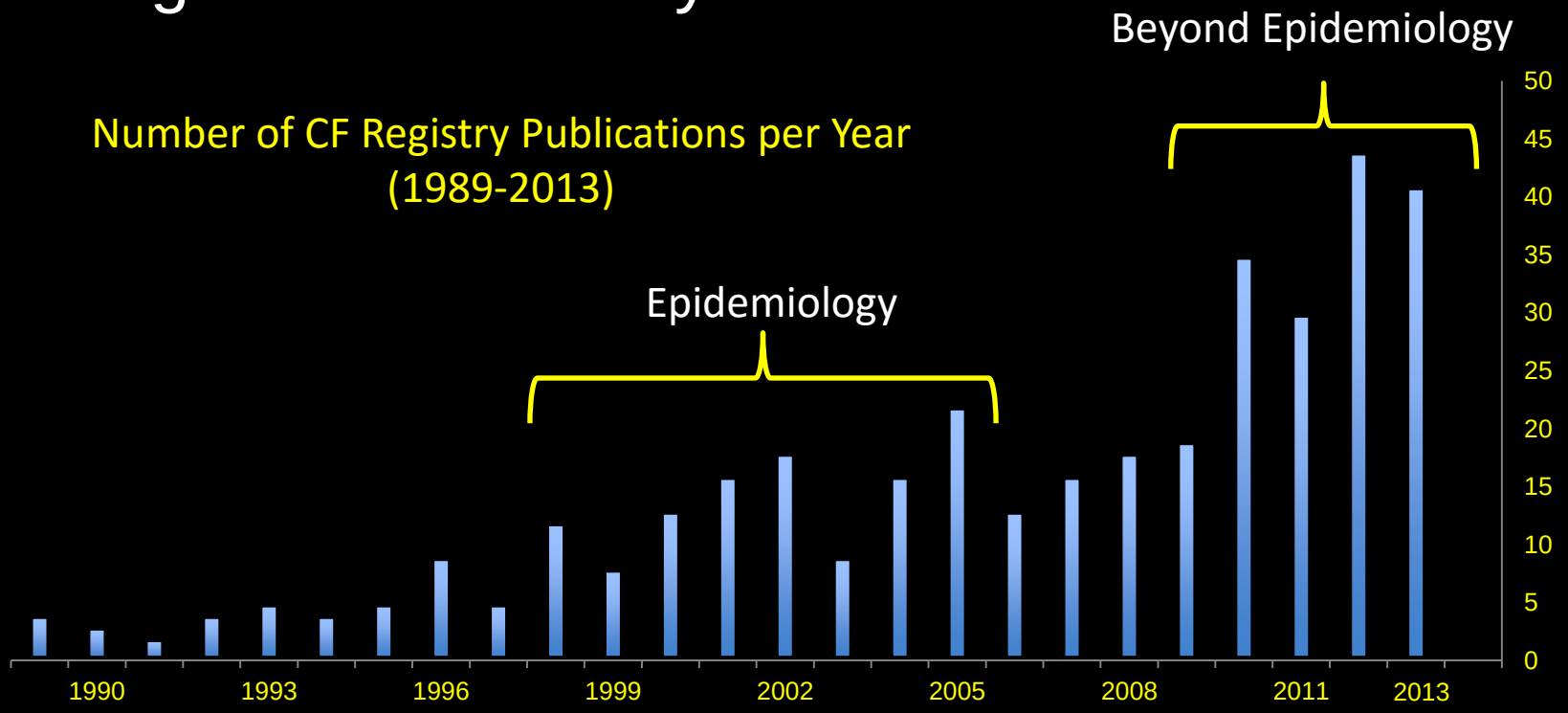
- >65,000 CF patients are currently enrolled in registries throughout the world.

Registry*	Number of Centres	Number of Patients
UK	59	10,078
Germany	80	8,661
Ireland	19	1,200
USA	110	27,804
Australia	23	3,156
Canada	42	3,975
Europe 2013/4	23 countries	32,248

*National registries reports 2014

Facts about CF Patient Registries

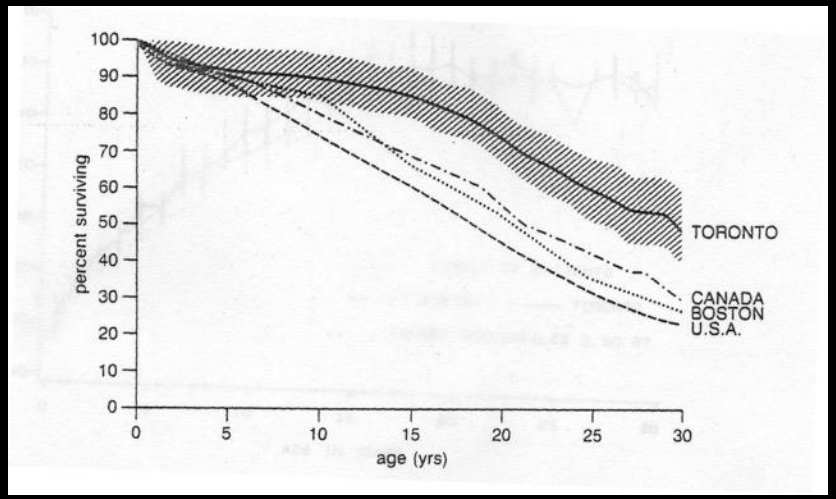
- 398 publications related to cystic fibrosis and registries over the years



Does Registry-based research impact how we care for CF patients?

High-fat Diets Improve Survival

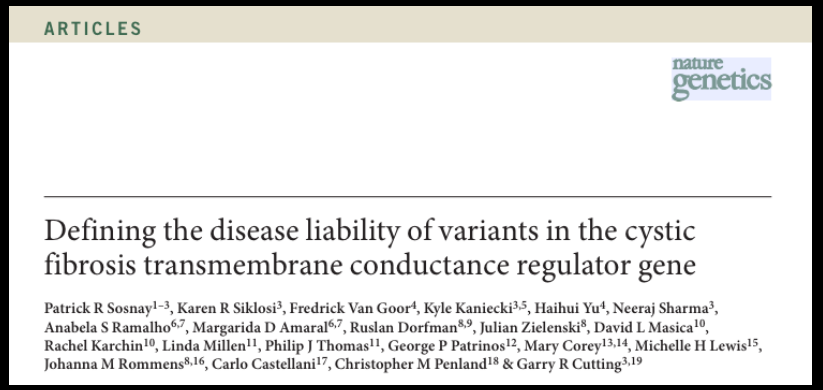
- 1989: Pivotal registry publication comparing outcomes between Toronto and Boston
- Significant survival differences identified
- Attributed to different approach to nutrition with high-fat diet in Toronto.
- Led to changes in how patients with CF were



Corey et al. J Peds. 1989.

CFTR2

- 2013 Nature Genetics Publication
- Most comprehensive genotype/phenotype analysis of 159 CFTR mutations
- Genetic data collated with clinical data from 25 country CF registries throughout the world.
- Led to development of CFTR2 (www.cftr2.org) a resource for clinicians and patients to identify CFTR mutations that cause CF


ARTICLES

nature genetics

Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene

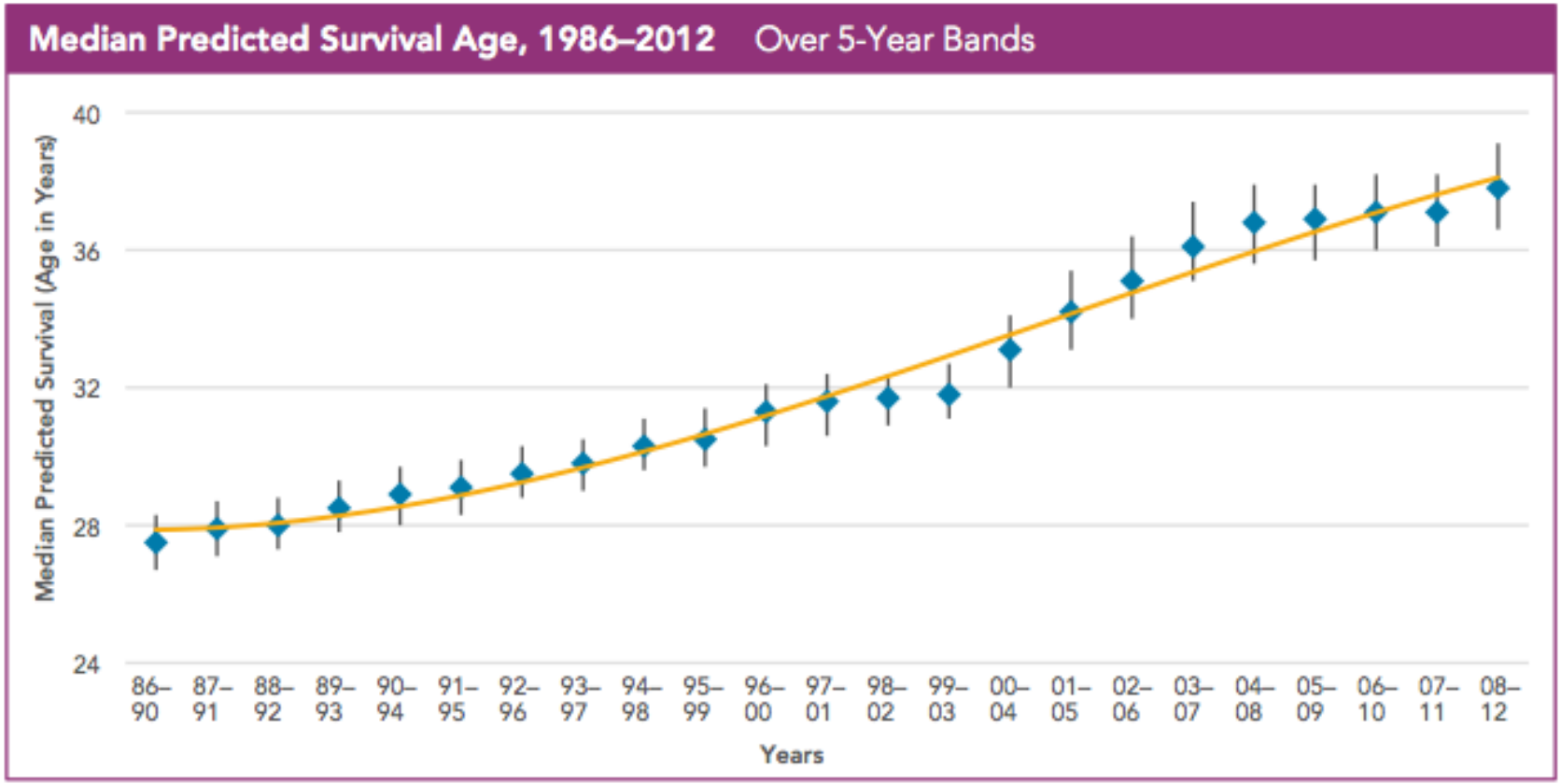
Patrick R Sosnay[1–3], Karen R Siklosi[3], Fredrick Van Goor[4], Kyle Kaniecki[3,5], Haihui Yu[4], Neeraj Sharma[3], Anabela S Ramalho[6,7], Margarida D Amaral[6,7], Ruslan Dorfman[8,9], Julian Zielenski[8], David L Masica[10], Rachel Karchin[10], Linda Millen[11], Philip J Thomas[11], George P Patrinos[12], Mary Corey[13,14], Michelle H Lewis[15], Johanna M Rommens[8,16], Carlo Castellani[17], Christopher M Penland[18] & Garry R Cutting[3,19]

Sosnay et al. Nat Genetics 2013

Other examples of registry research

- Safety of pregnancy in CF. (Goss, Chest 2003)
- Identification of impact of different bacteria (Steno/MRSA) on CF patients. (Goss. AJRCCM, 2002; Dasenbrook JAMA 2010)
- Development of survival tools to predict when to refer for transplantation. (MayerHamlett.,AJRCCM 2002, Liou, AmJEpi. 2001)
- Understanding the natural history of exacerbations (Saunders Pediatr Pulm 2011; Saunders AJRCCM 2010)
- Identifying factors associated with better outcomes in certain CF centers. (Johnson. Chest.2003)
- Understanding why some CF patients get severe disease at a young age and other don't. Vanscoy. AJRCCM. (Vanscoy. AJRCCM.2007; Wright. Nat Genetics.2012)

Registries also inform us whether outcomes are improving in CF



US CFF Annual Report 2012

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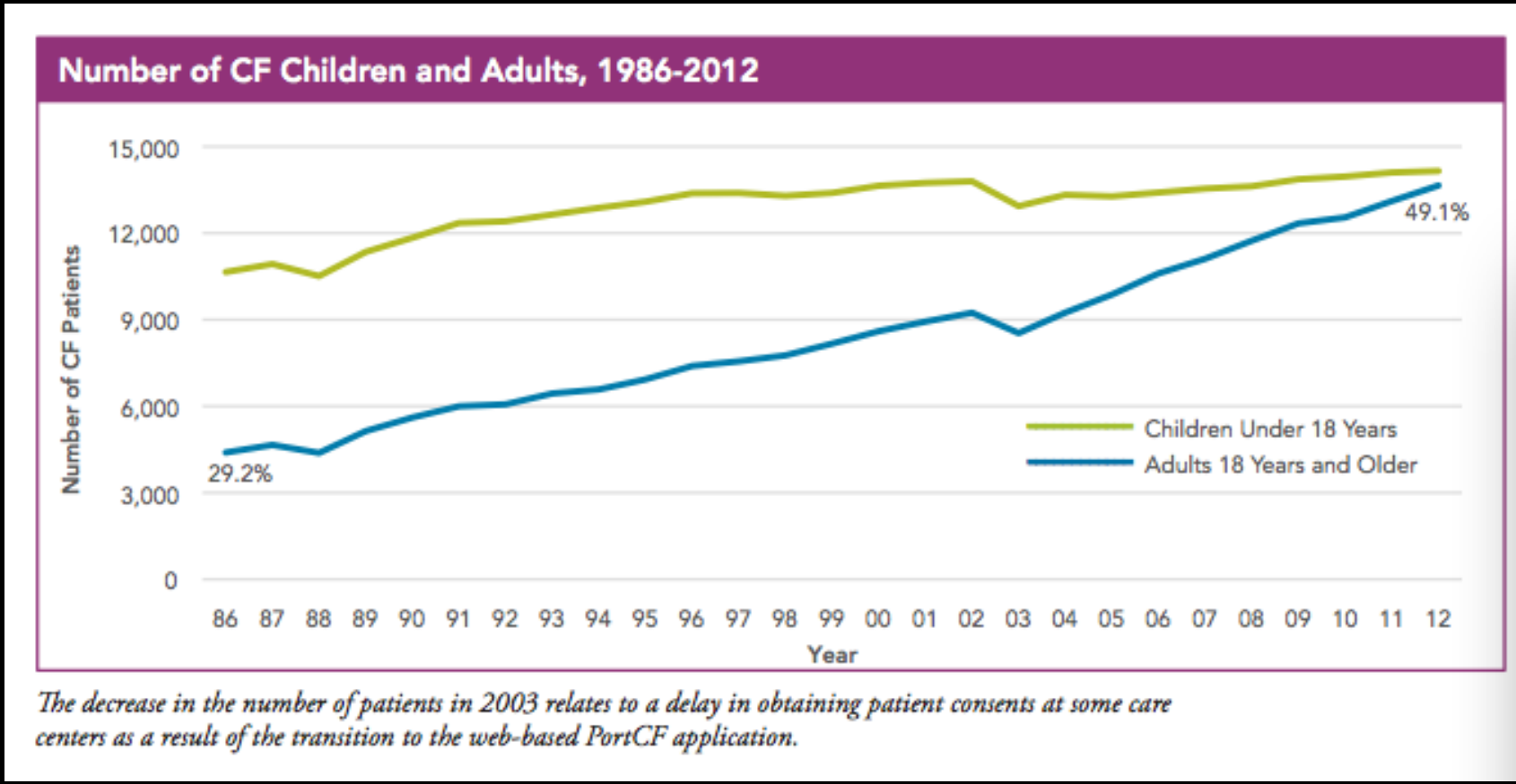
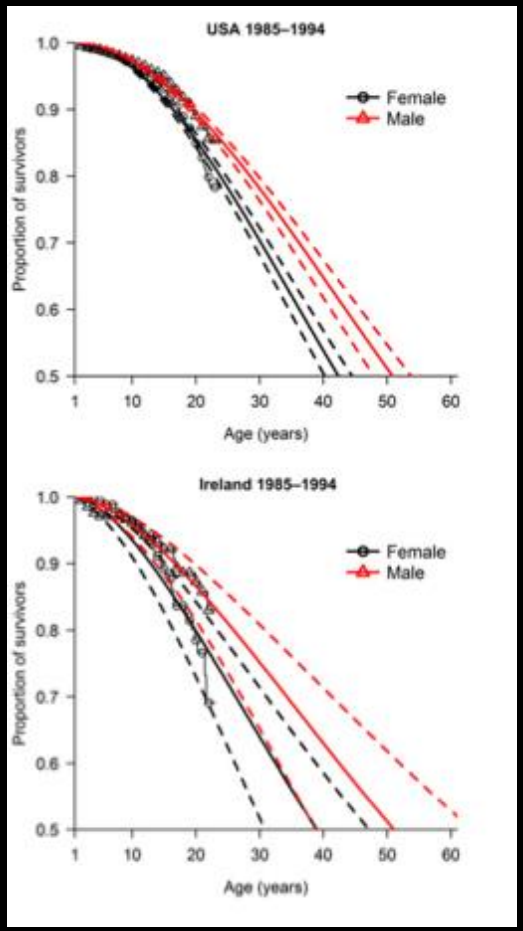


The decrease in the number of patients in 2003 relates to a delay in obtaining patient consents at some care centers as a result of the transition to the web-based PortCF application.

US CFF Annual Report 2012

Registries allow comparison of outcomes across countries

- Irish Registry
  - Mortality outcomes very similar to that seen in United States
  - Certain statistical methods better for compsing outcomes from smaller countries
- Australian Registry
  - Australian new born screened patients did better then not screened.
  - Lung function benefits of NBS not quite as good as seen in US.



Jackson et al. Thorax 2011
Martin et al. Pediatrics 2012

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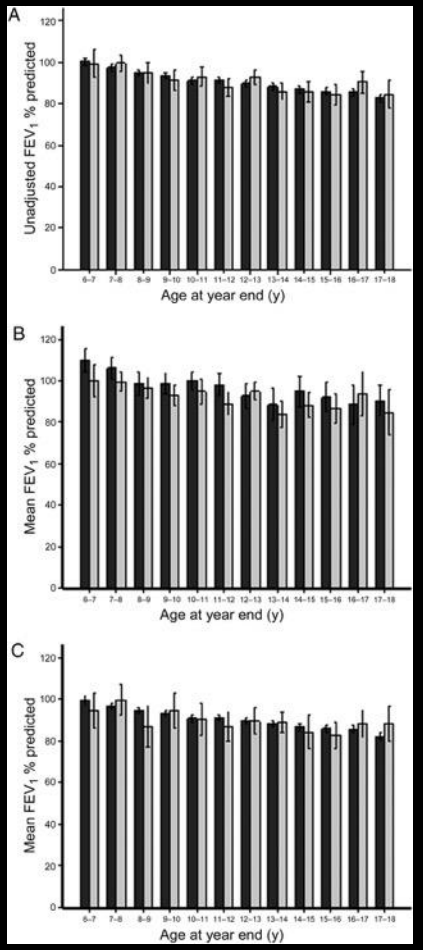


Jackson et al. Thorax 2011
Martin et al. Pediatrics 2012

Beyond Outcomes/Epidemiolgy: Use of Registries

1. Improve CF Care at Centre Level
   - Use as a tool for “real time” monitoring of patients
   - Quality Improvement/Benchmarking
     - Monitor how good your centre’s CF care is
     - Determine areas of weakness
     - Identify whether interventions are improving service
     - Benchmarking against other countries/centers
2. Identify patients for clinical trials and use in clinical trials
3. Monitor the effectiveness of new CF therapies
   - New therapy effectiveness and safety
   - Comparative effectiveness studies

The European CF Registry

ECFSTracker
European Cystic Fibrosis Society Patient Registry

Welcome to the ECFS Patient Registry

The European Cystic Fibrosis Society Patient Registry (ECFSPR) collects demographic and clinical data from consenting cystic fibrosis (CF) patients in Europe. The ECFSPR aims to use the outcomes of data analyses and comparisons to improve standards of care for CF patients, promote innovation and facilitate public health planning and research. See more about the ECFSPR and what happens to the data on the website here.

ECFSTracker

ECFSTracker is the ECFSPR's dedicated data-collection software. Users can input data directly or, alternatively, upload a data file in a compatible format e.g. Excel or XML. The latter is how most national registries choose to present their data.

ECFSTracker also has an option which allows participating centres to record outcomes from individual patient encounters throughout the year. This is very useful for long-term CF clinical monitoring and patient progress can be represented in the form of graphs and tables. Once a year an Annual Summary with anonymised data is extracted and exported to the ECFSPR.

Variables
The ECFSPR has selected a set of key variables and agreed definitions to facilitate the comparison of clinical data throughout the CF community in Europe and worldwide. Click here to open the variables and definitions document.

Uploading in Excel/XML-format
National registries and others who don't input data in the system directly are obliged to perform standard controls on their original data sets before uploading their data to the ECFSPR in Excel or XML format. The controls were defined and approved by consensus of all participating national registries. Click here to open the control document.

User Manual
You can download the ECFSTracker manual here.

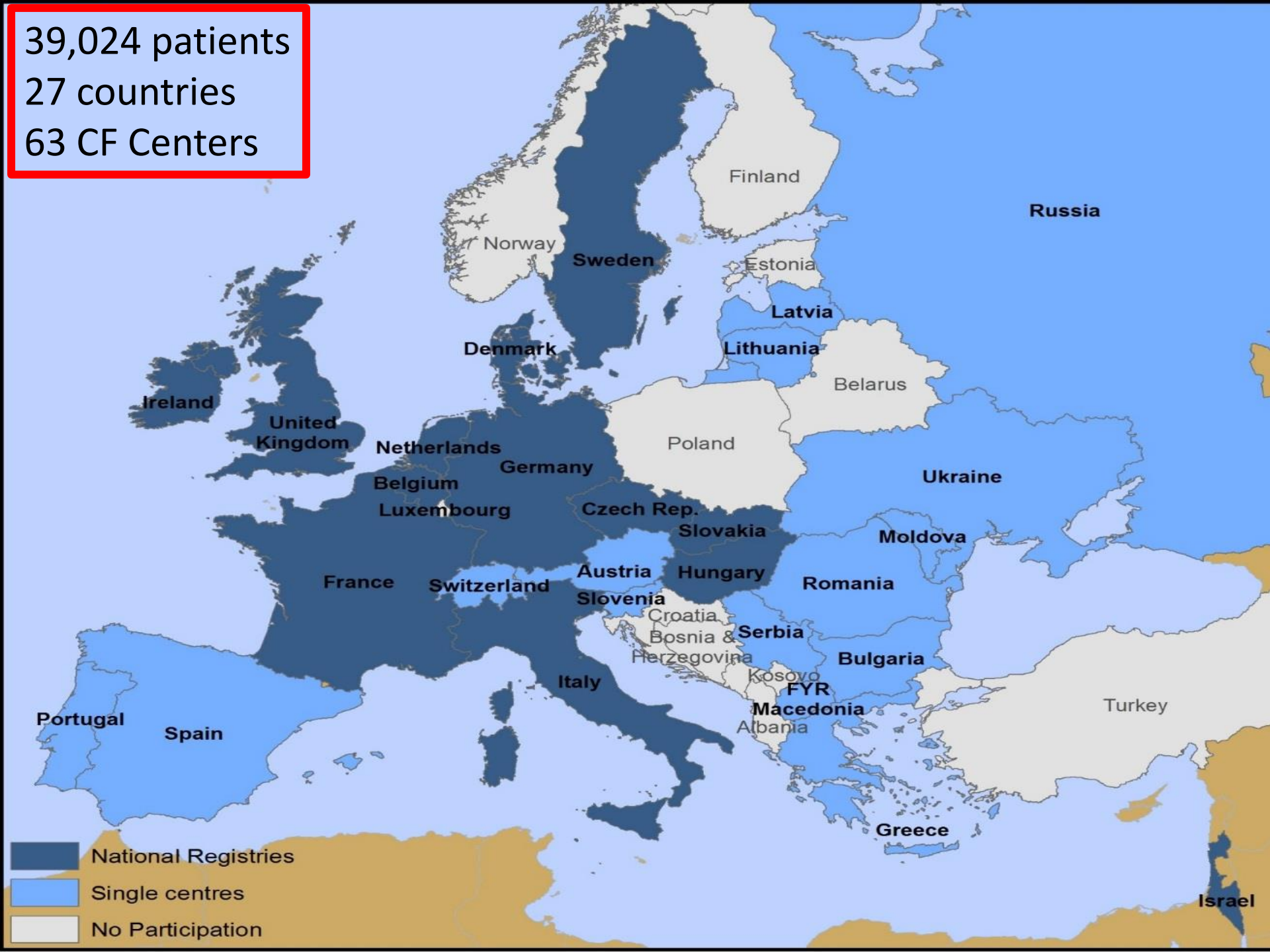
Contact
If you have access problems please contact the Centre Administrator for your centre. If you continue to experience problems please send an email to the ECFSPR Service Desk at: helpdesk@ecfregistry.eu. For general information about the ECFSPR please contact

To log in, please select your country.

EUR
Austria
Belgium
Czech Republic
Denmark
France
Germany
Greece
Hungary
Ireland
Israel
Italy
Latvia
Moldova
Netherlands
Portugal
Russia
Slovakia
Slovenia
Serbia
Spain
Sweden
Switzerland
UK

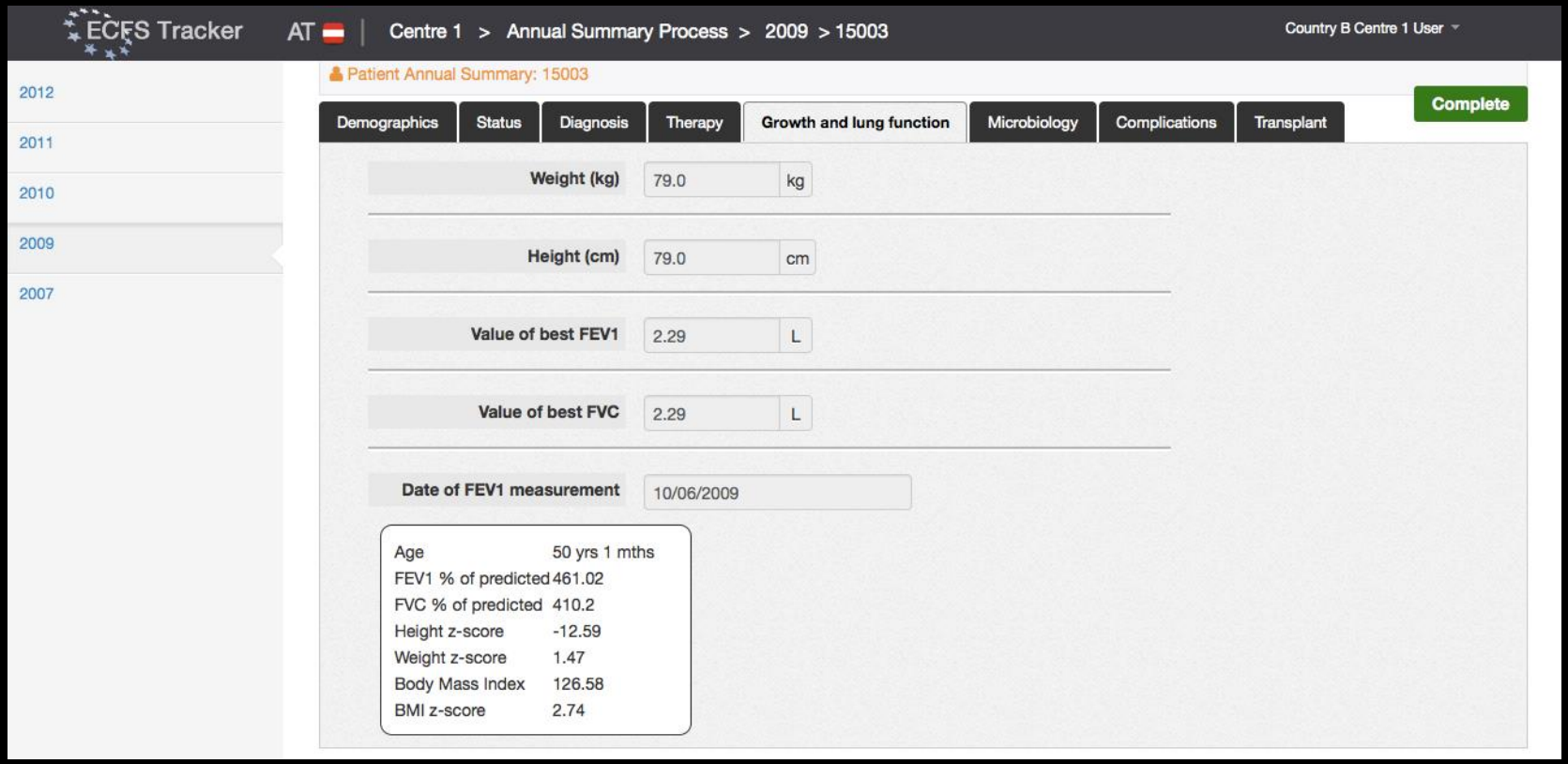
ECFS Tracker

- New software program developed specifically for CF data collection
- Web-based, open source
- Encounter based or annual upload
- Generates annual country/centre reports in real-time
- Launch January 2014


39,024 patients
27 countries
63 CF Centers
Finland
Russia
Norway
Sweden
Estonia
Latvia
Denmark
Lithuania
Belarus
Ireland
United Kingdom
Netherlands
Germany
Poland
Ukraine
Belgium
Luxembourg
Czech Rep.
Slovakia
Moldova
France
Switzerland
Austria
Hungary
Romania
Slovenia
Croatia
Bosnia & Herzegovina
Serbia
Bulgaria
Kosovo
Italy
FYR Macedonia
Albania
Turkey
Portugal
Spain
Greece
Israel
National Registries
Single centres
No Participation

ECFS Tracker
Annual Data Collection

- Tabulated Forms Divided into Different Sections
- Automated Calculations



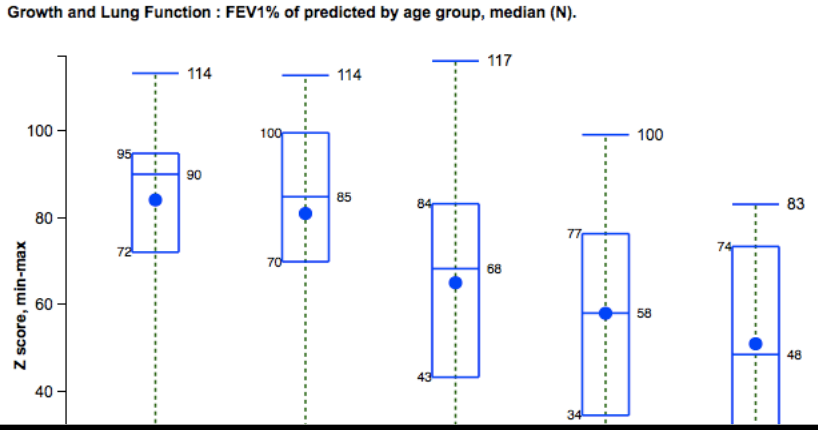
ECFS Tracker
Centre Level Reports

- Built in Function for Generation of Annual Reports by Centre/Country
- Includes average FEV1, BMI, rates of Pseudomonas, MRSA, NTM etc.

ECFS Tracker AT | Centre 1 > Reports > Country B Centre 1 User

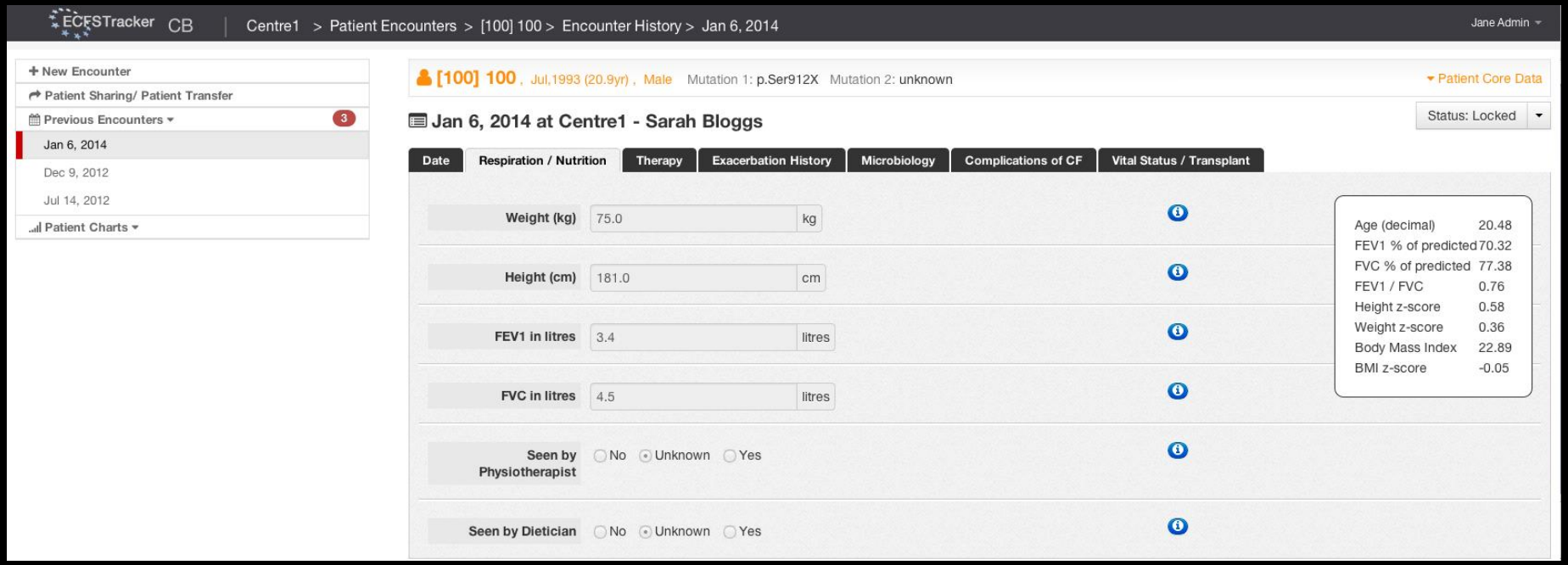
PDF Chart image Export

	Total patients	P25	Median	P75	Mean	Min	Max
6-11	33	72.22	90.48	95.37	84.46	28.50	114.16
12-17	28	69.99	85.20	100.18	81.28	27.54	113.64
18-23	40	42.92	68.35	83.57	65.05	16.91	117.02
24-29	27	33.99	57.94	76.55	57.90	11.94	99.75
30 and older	44	27.16	48.23	73.55	50.75	14.38	83.44



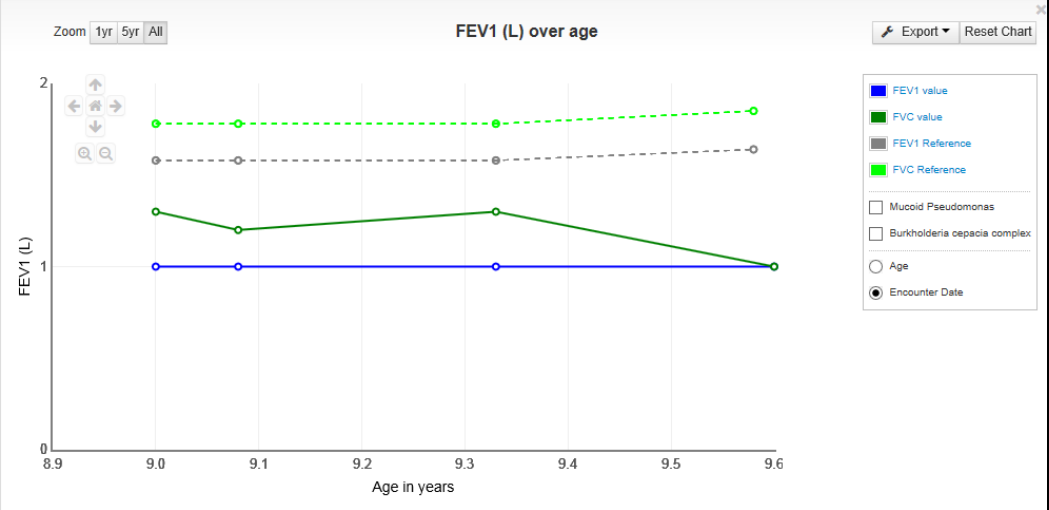
ECFS Tracker
Real-time Encounter Data

- Built in Function for Collection of Clinical Data at each clinic visit
- Clinician and Patient Friendly reports can be generated for use in clinic
- Graphs can be generated looking at longitudinal changes.



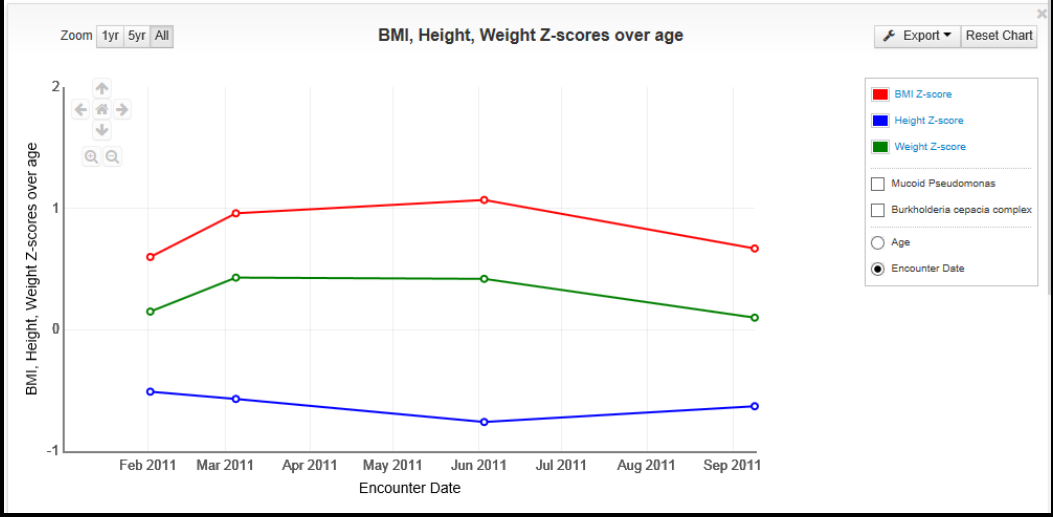
ECFS Tracker
Real-time Encounter Data

FEV1 (%)



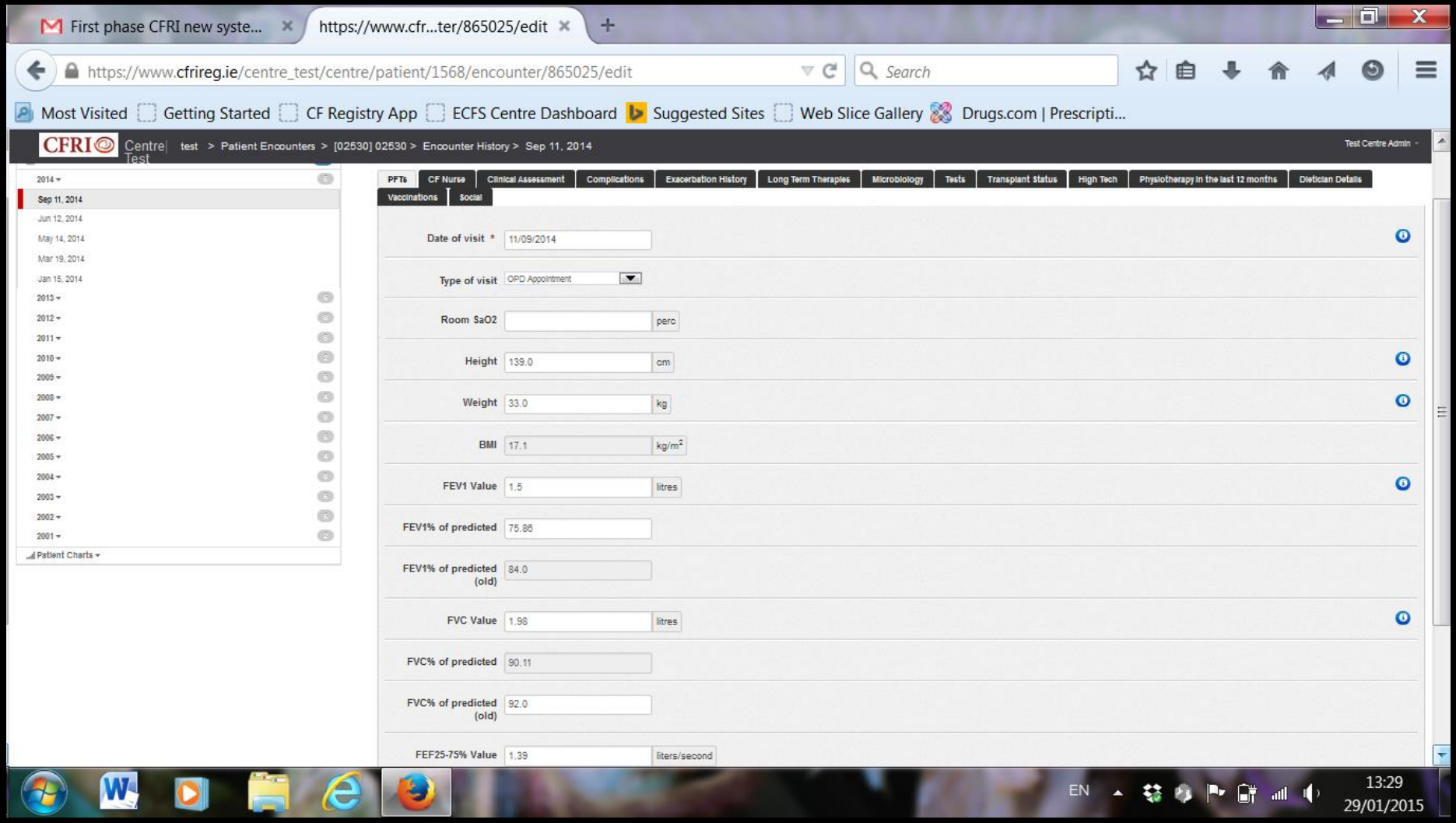
Micro Data can be superimposed

BMI (kg/m^2)



Not real patient data

ECFS Tracker Plus

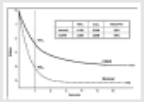


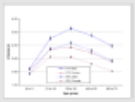
CF Patient Dashboard

Planned for Irish CFR - Shared Enhanced Encounter Mgt

John Doe
DOB 12 Oct 1997
CFRI Id - 12345
12 Main St, Athy, Co Kildare

Key Clinical Indicators





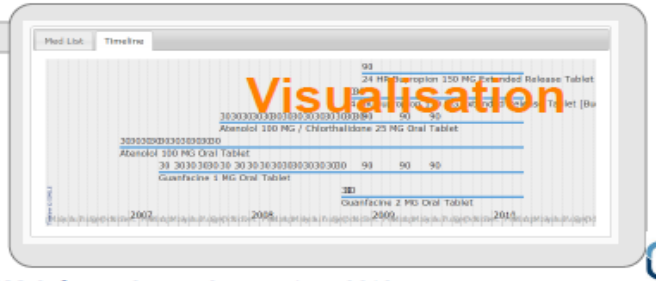
- Hospital MRN
- Next of Kin
- Referring GP etc
- Treating Consultant
- Other provider

Patient Summary
- Some indicators
- Complications
- Patient report

Hospital Data
- Lab test results
- Inpatient encounters

Medications
- Current
- History

Patient Schedule
- Clinic dates (assessments)
- Other

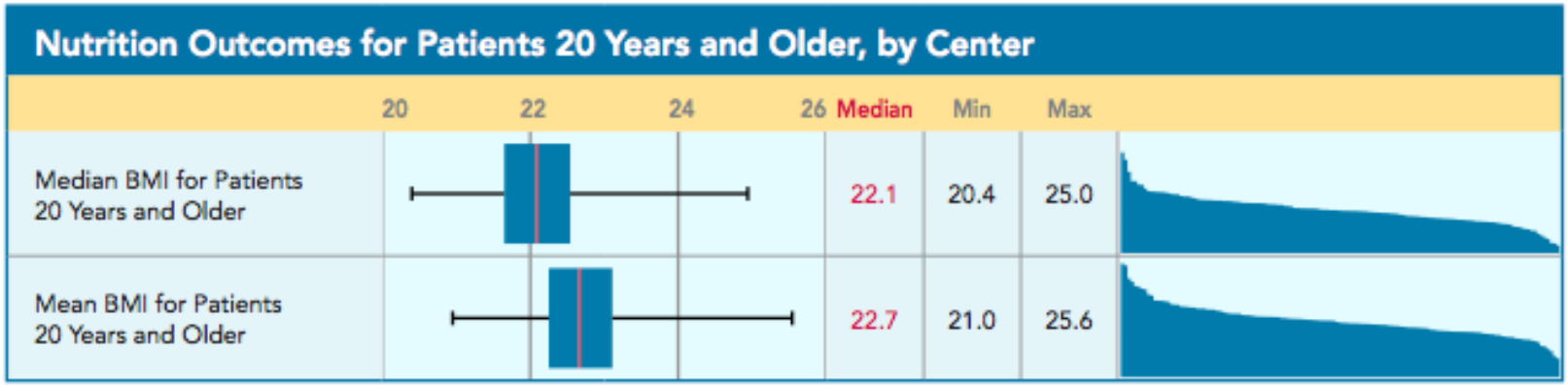


ECFSPR Software System Status - June 2013

How else can we use the CF Registry to Care for Patients?

Improving Care with CF Registries
Feedback to Centre Directors

- US CFF developed a quality improvement program throughout CF centers in the US
- Key center-based performance indicators set
  - Visits, lung and nutritional measures, microbiology.
- Published annually with feedback given to centre directors
- Information on center available online to registered users



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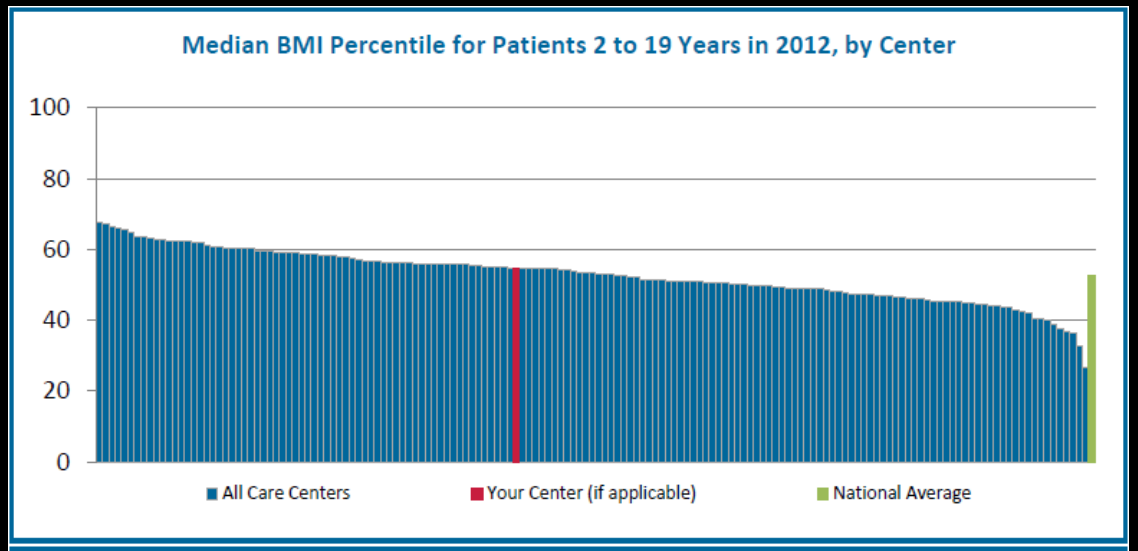
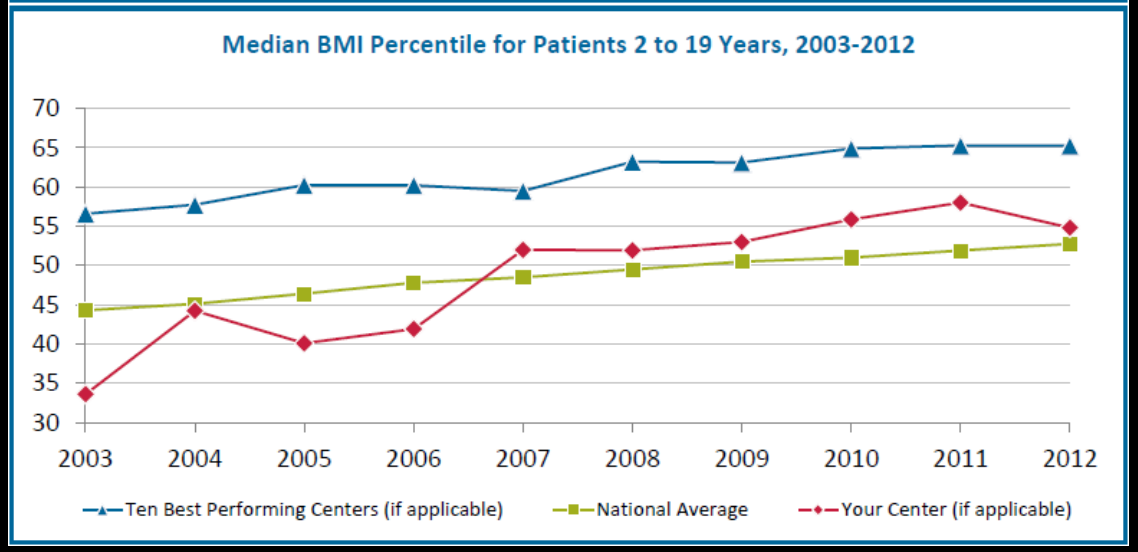
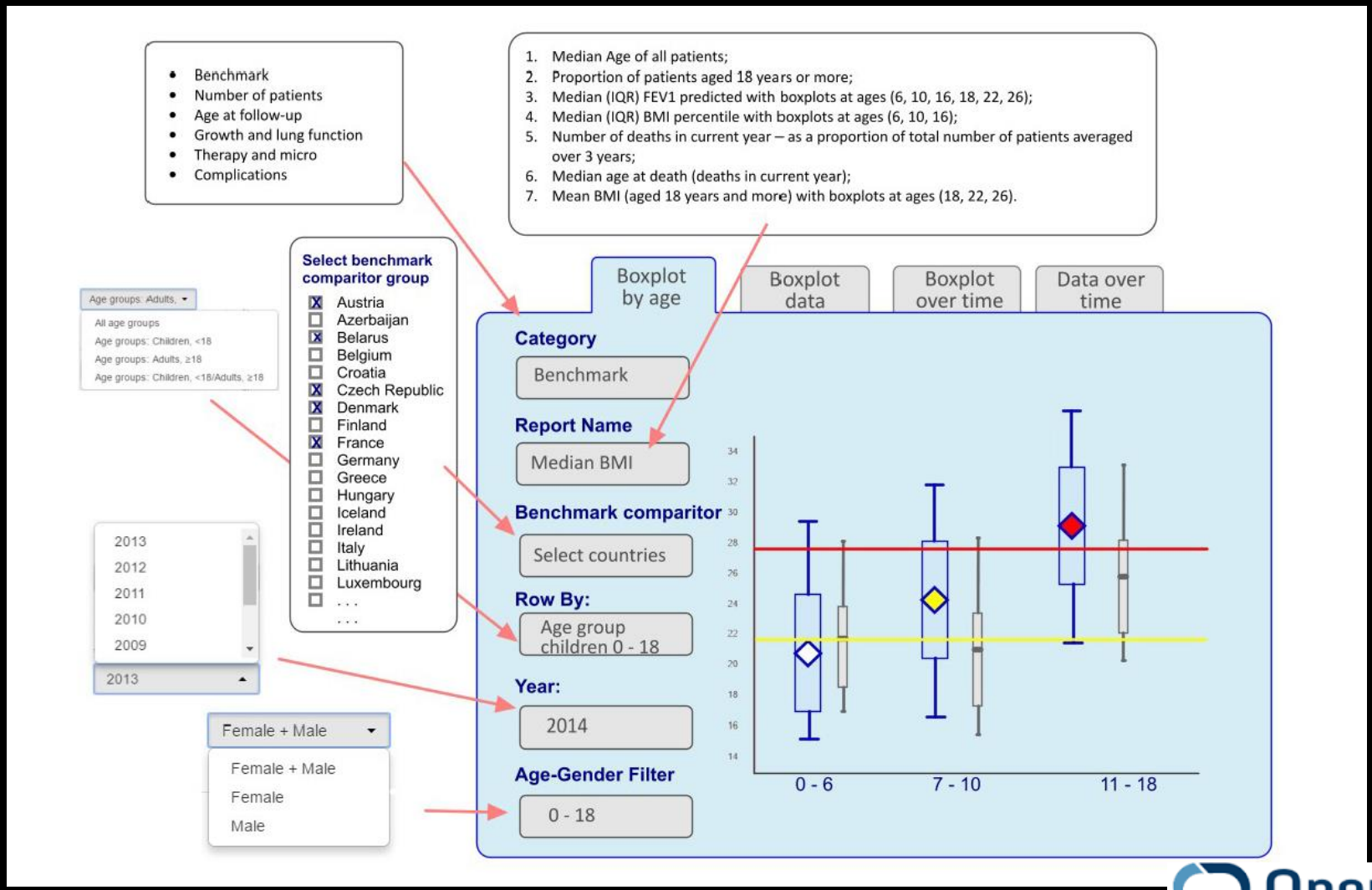
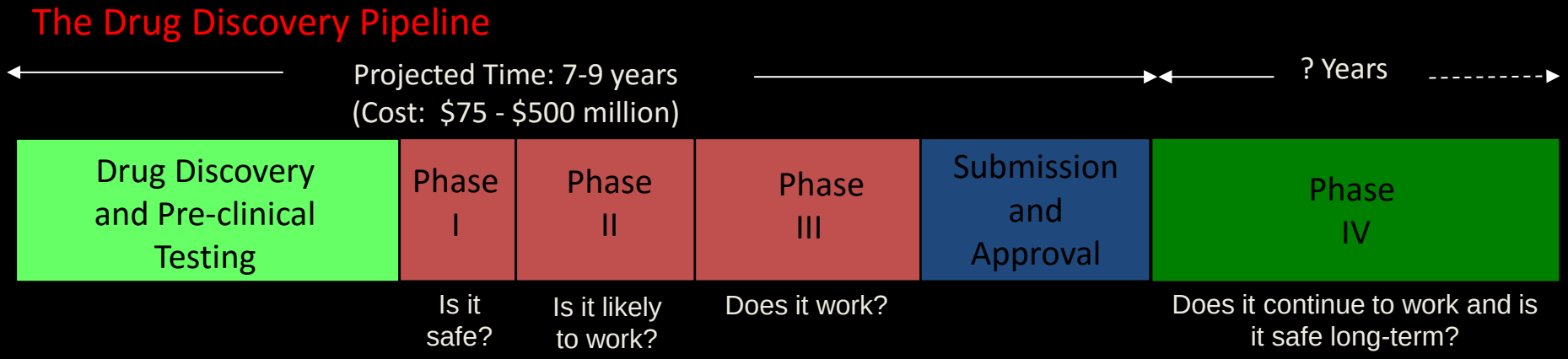




Benchmarking in Europe Using ECFS Tracker



What about New Therapies?
Do they work and are they safe?



- EU and FDA require that long term safety and effectiveness studies are carried out with newly approved therapies
- Aims to increase benefits and reduces risk of new drugs therapies
- Emphasis on “Real world” monitoring

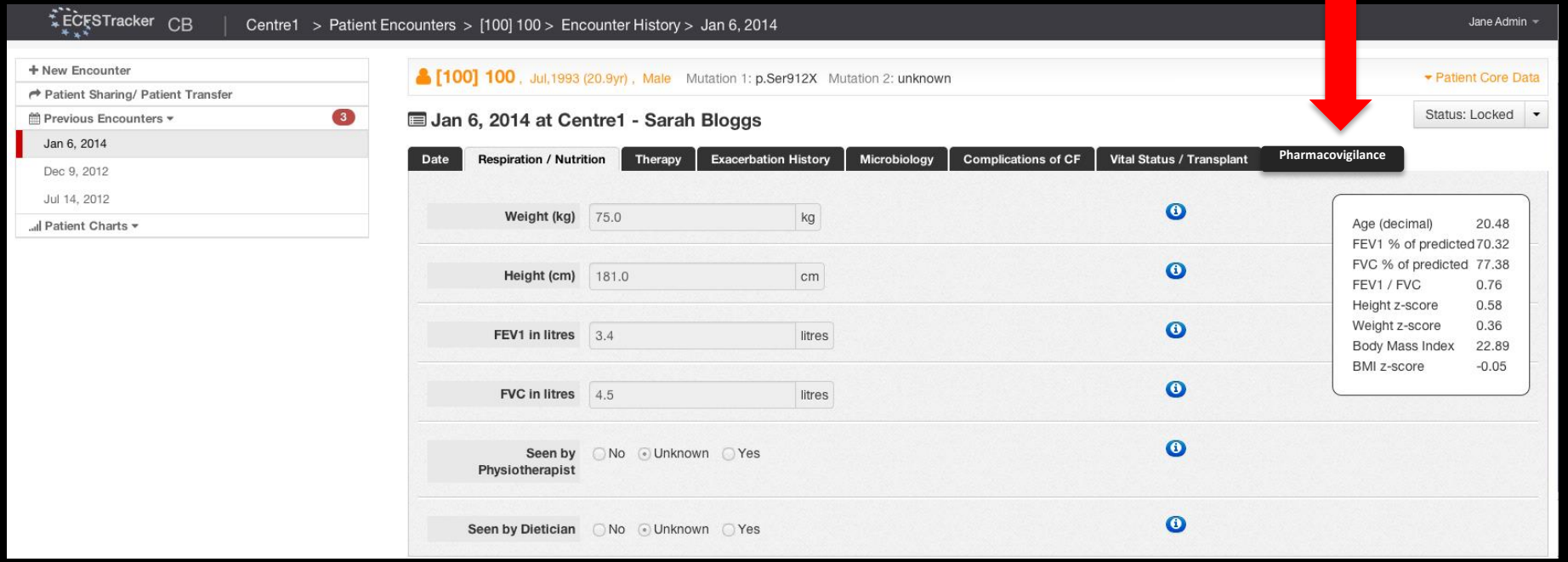
Monitoring Drug Safety/Efficacy Post Approval – Phase IV Trials

OPTIONS

1. Extension studies to RCT - “Open label study”
2. New Drug Safety/Efficacy Phase IV Registry developed and maintained by Pharma Industry
3. Use of Existing Clinical Registries

Monitoring Drug Safety/Efficacy post Approval – Phase IV Trials

- Existing CF Registries can be adapted to include modules suitable for monitoring new drugs
  - Contains PRO, specific ADRs (ECG/LFTs etc.)



Registries Can be Used to Conduct Clinical Trials

Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE trial). A multicenter, prospective, randomized, controlled clinical registry trial based on the Swedish angiography and angioplasty registry (SCAAR) platform. Study design and rationale

Ole Fröbert, MD, PhD,[a] Bo Lagerqvist, MD, PhD,[b] Thórarinn Gudnason, MD, PhD, FESC,[c] Leif Thuesen, MD, PhD,[d] Roger Svensson, MSci,[e] Göran K. Olivecrona, MD, PhD,[f] and Stefan K. James, MD, PhD[b] *Örebro, Uppsala and Lund, Sweden; Reykjavik, Iceland; and Aarhus, Denmark*

The NEW ENGLAND JOURNAL of MEDICINE

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Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Fröbert, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D., Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Angerås, M.D., Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D., Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D., Amra Kåregren, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D., Lennart Sandhall, M.D., Iwar Sjögren, M.D., Ollie Östlund, Ph.D., Jan Harnek, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D'Agostino, Sr., Ph.D.

Related article, p. 1587

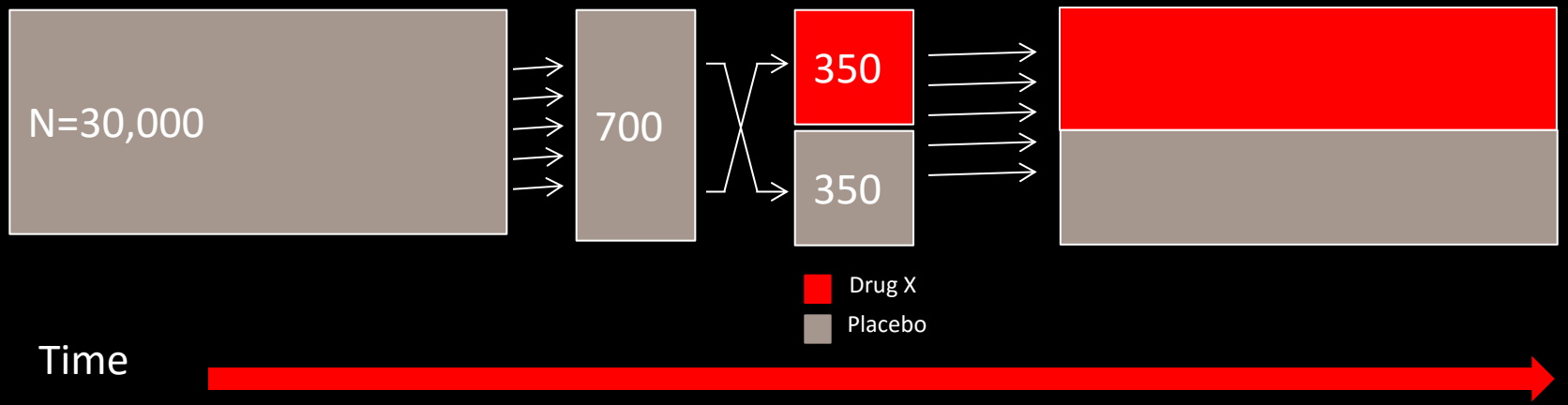
Frobert et al. Am H J 2010
Frobert et al. NEJM 2014
Laeur & D'Agostini NEJM 2014

The Multicenter, Prospective, Randomised, Controlled Clinical Registry Trial

Clinical registry with measures of patient baseline characteristics

Patient Subgroup Selection & Randomization

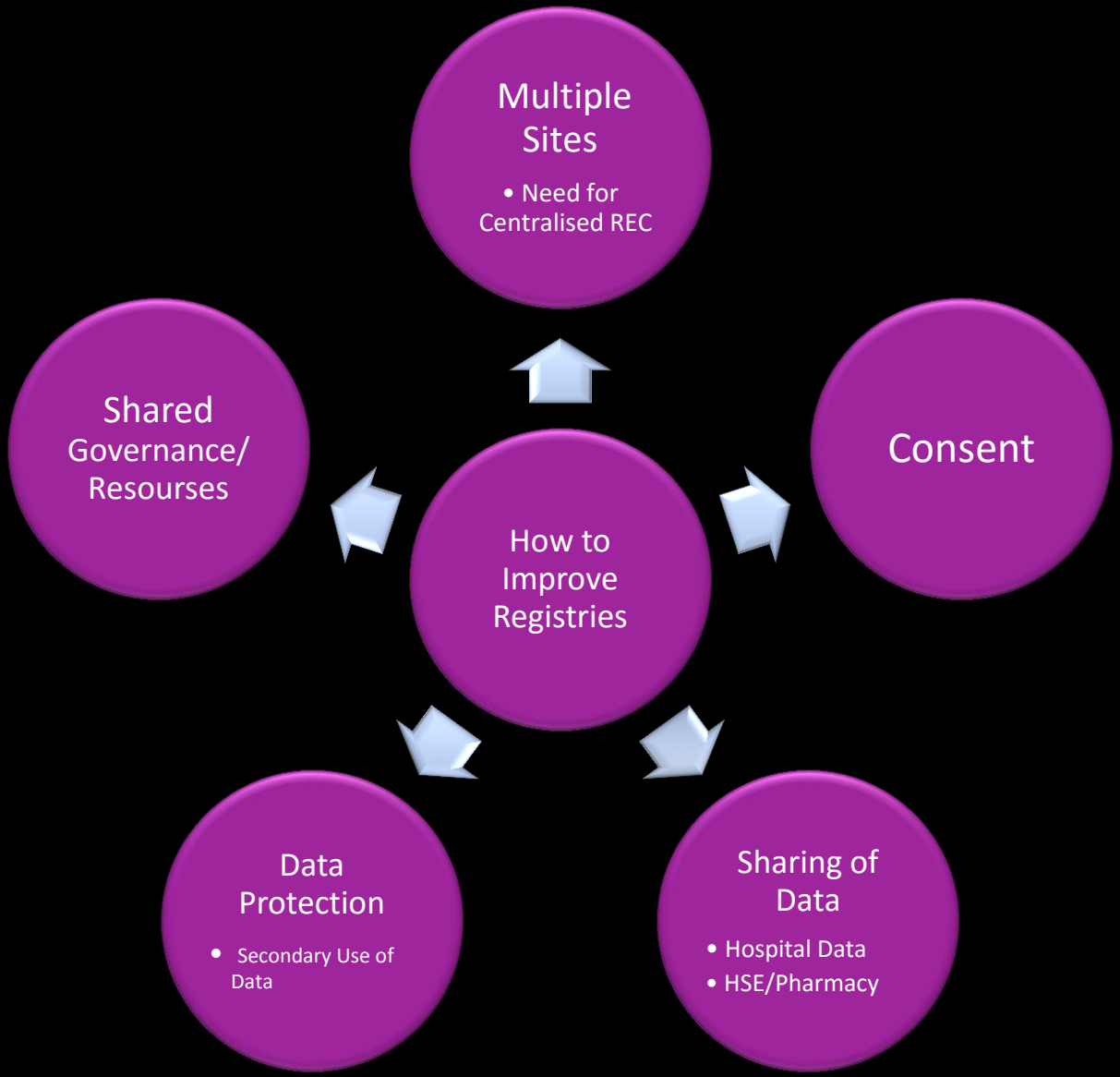
Follow-up of Patient Outcomes using Patient Registry



Conclusions

- Registries have led to a greater understanding of CF to date, largely through epidemiology research.
- Registries are now being used to directly impact patient care through
  - Encounter based data entry and use
  - Quality Improvement/Benchmarking
  - Better understanding of new drugs and different combinations of drugs through pharmacovigilance and comparative efficacy studies

How to Improve Registries



Questions?

"These new regulations will fundamentally change the way we get around them."

New Yorker, March 2009