Meeting Summary: Building the European CF Registry

Meeting of the board of the European CF Registry.
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Present board members: E Kerem – Il, C Koch – D, Anil Mehta – UK, Hanne Olesen – D, Oluf Schiotz – D.

Background

The clinical management of Cystic Fibrosis (CF) is constantly evolving. The continuous improvement in survival of CF patients is a result of changes in the understanding of the pathogenesis of the disease and the development of new methods and therapies to improve nutrition, mucociliary clearance and antimicrobial therapy. The comparison of CF populations is therefore essential for the development of standards for clinical practice. The attempt to develop a European CF Registry started around 1995 in the Paris meeting sponsored by the ICF(M)A and hosted by the French CF Association. Afterwards, it was felt that the attempt to construct a large and complex database was too ambitious at that time. Furthermore, several countries wanted to go in their own direction. Subsequently there was the Roche database that produced important and valuable information. However, it was very expensive to run the database. When Roche's funding ended, Dr. Margaret Hodson tried to get funding to continue the database from EU sources. For various reasons, the EU decided not to support the CF database. Since than, there were several applications made to the EU, and all were declined.

Several countries have established their own National CF Registry. Each country collected different sets of data utilizing different definitions and methodologies.

The aims of the European CF Registry

1. Providing essential information for the ECFS which in the initial stages will be confined to answer the following questions:
    a. How many CF patients are there in Europe?
    b. What is their clinical status, hence their needs?
    c. What are the annual trends of survival?

This information will facilitate long-term planning in terms of health expenditure allocations and developing pan European support systems. There are also a number of subsidiary aims:

2. Introducing standardization of data collection for the national registries.
3. Building an infrastructure for data collection for countries that do not yet have national registries (most of the European countries).
4. Promoting standardization of care. For example: criteria for the diagnosis of CFRD.
5. Comparing clinical data from different centers and different countries in order to improve the care of the patients.

    a. Providing data resources so that center directors can compare their own center to other European centers.
    b. Providing an audit instrument that will enable the identification of centers requiring support by the ECFS.
    c. Responding to the patients' right to know if they are receiving the standard of care treatment.
6. Facilitating research on rare CF presentations and uncommon complications.
7. Enabling identification of patients or centers that are suitable for clinical studies on new therapies or genetic research.
8. Enabling the design of studies with strict inclusion criteria that require the participation of multiple centers.
9. Providing tools to identify topics that need to be discussed in the ECFS conferences.
10. Providing tools to identify areas that need further research.
11. Providing annual report about the status of CF in Europe.

Can we build the European CF Registry?

It has been generally agreed that the database should be simple, usable and manageable.
Its data structures/repository of information should be compatible with the already existing national registries.
A simple tool to export data from the national registries to the European Registry needs to be developed.
It should be expandable so that more data can be added in the future.

It has been agreed to act on 2 levels:

1. Merging data from the already existing registries.

Two examples of national registries were presented: The UK CF Database and the Danish/Scandinavian CF Database.

The UK CF Database was built on the Microsoft Access 97 platform. It contains data collected since 2000 from 41 specialist CF centers and 12 CF clinics. It consists of biographical and clinical data including information on anthropometric measurements, pulmonary function, sputum bacteriology, current therapies, complications and social status. It consists of over 150 different fields. The data filled on paper forms for each patient is mailed to the central registry annually by each center. The CF Trust supports the UK CF Database, and centers are funded to fill the forms. Each CF Center has dedicated software within their clinic to facilitate comparison of their data against the annual national picture. See www.cystic-fibrosis.org.uk. The estimated costs are around £30-40 per patient per year. The database is funded in part by the Scottish Government but mainly by a core grant from the UK CF Trust which is a patient organization.

The Danish CF Database was developed using the Microsoft Access 2000 platform. It serves as a national database and has also served as the platform of a prospective multi-center, multinational Scandinavian P.

aeruginosa research project. The database has been adopted by at least one Norwegian CF center as a patient database. The Danish CF care is fully centralized with all patients attending one of the 2 centers in Jutland and Copenhagen. The other Nordic countries have a slightly higher number of centers. The Danish database consists of demographic data, anthropometric measurements, pulmonary function, and sputum bacteriology. The total number of data collected is significantly smaller as compared to the UK CF Database. Individual data is downloaded during the patient visit to the clinic in each participating center and sent by the Internet to the central registry located in Denmark. To be able to download the data to the Danish system all Scandinavian centers were provided with the Danish basic system - and that is how they report the data for the project. Combining these two databases requires the development of tools to export the data of interest and creating a platform that will accept it. It is felt that this is a simple technical task.

2. *Building registries in centers that are not associated with national registries*.

This is an extremely important task of the ECFS. It requires building a database in each center and country, and a method to transfer the data. It is proposed that the European CF Database could be created by merging core anonymous data from the different National databases. This model will serve as a template for the rest of the centers. We identified several difficulties that need to be addressed: Ethical committee approval for trans-national data transfer, language barriers, different operating platforms or database software, and lack of time, personnel or funding to fill the local data.
Different methods submit data from the local centers to the central registry (mailing filled forms or sending by the internet computer generated files) were discussed. Development of a computerized CF patient file might be an interesting solution that need to be explored, though it might not be easy to perform and may be very expensive.

The first step: Standardization of data collection

The national registries differ in the way some parameters are presented. In addition, databases were developed using different programs or different versions of Microsoft Access. Some differences also resulted from different definitions, different units, and variations in the use of the equations or percentiles for normal population. This makes comparisons between centers or countries difficult. There are also differences between the European registries and the American, Canadian and Australian registries. **There is an urgent need to develop an International CF Standard for data collection**, and it has been suggested that ECFS should initiate such activity.

The second step: What data should be collected?

The board discussed a large list of relevant variables. The suggested variables that were found to be included in the European CF Database are presented in Appendix 1.

Constitution and ethical issue

The already existing national registries obtained consent for collecting data for their own national registries. However, in most countries this consent is formulated in a manner that allows for using the database for research purposes, and the ECFS database can be regarded as such.
Since there are European patients registries for heart disease and cancer, it was felt that there are already available guidelines made by the commission of the EU that we should follow. It has been agreed that this issue should be discussed with the EU committee in Brussels. Dr. Anil Mehta will speak to Prof. Stacey who is an ethics expert from the UK and is involved in the EU medical research ethics committee.

Appendix 1

Suggested variables for the European CF Registry

Basic data

Country telephone code number + patient's original code
Month and year of birth (mm/yyyy)
Gender (1=male; 2= female)
Genotype 1
Genotype 2

Diagnosis

Age at diagnosis (decimals)
Sweat chloride mEq/L [highest test], positive, not done

Mode of presentation

Gastrointestinal/FTT/malnutrition
Respiratory infections symptoms
Anemia, hypoproteinemia
Meconium ileus
Family history
Neonatal screening
Electrolyte imbalance
Male infertility
Recurrent pancreatitis
Other

Current report

Patient alive 1=yes, 2=no
Pancreatic sufficiency (PS)=1; Pancreatic insufficiency (PI)= 2
Height (cm) [last test]
Height (%tile) [last test]
Weight (kg) [last test]
Weight (%tile) [last test]
BMI [last test]
BMI (%tile) [last test]
FVC liter [last test]
FEV1 liter [last test]

Bacteriology

Chronic Pseudomonas aeruginosa
Multi-resistant Chronic Pseudomonas aeruginosa
Pseudomonas aeruginosa not chronic
Staph aureus
Staph aureus (MRSA)
Nontuberculous mycobacteria –
Stenotrophomonas maltiphilia
Alcaligenes xylosoxidans
Burkholderia cepacia coplex
Hemophilus influenzae

Complications
Hemoptysis – major over 250 ml (1=no; 2=once; 3=recurrent)
Pneumothorax requiring chest drain (1=no; 2=yes)
ABPA ***(1=no; 2=yes)***
Nasal polyps (1=no; 2=yes)
Pancreatitis ***(1=no; 2=yes)***
DIOS (1=no; 2=yes)
Gastroesophageal reflux requiring treatment (1=no; 2=yes)
Fibrosing colonopathy (1=no; 2=yes)
CFRD (1= no; 2= IGGT; 3= insulin treated)
Late complications of diabetes
Elevated liver enzymes (1.5 times the upper limit)
Biliary cirrhosis \ Portal hypertension 1=no; 2=yes
Bleeding varices
CF related bone disease
Urinary incontinence (1=no; 2=yes)
Kidney stones (1=no; 2=yes)
CF related vasculitis, arthropathy
Renal failure requiring dialysis / transplant
Malignancy (1=no; 2=yes)
Liver transplant 1=no; 2=yes
Lung transplant /lung+heart (1=no; 2=yes)

Routine Therapy
Inhaled bronchodilators
Inhaled steroids
Inhaled antibiotic (1=none; 2=intermittent; 3= continuous)
Pulmozyme
Inhaled hypertonic NaCl
Continuous Oral antibiotics
Ursolit
Antacid (H2 antagonists. PPI
Systemic steroids
Oxygen therapy
Taurine

Total CF clinic visits in last year
Hospitalizations, 'in hospital'-number per year
Hospitalizations, 'in hospital'- total days/year
Total number of days on IV antibiotics
Total CF clinic visits in last year
Hospitalizations, 'in hospital'-number per year

Marital status (if over 18yrs) (1=single; 2=living together;)
Employment (if > 18yrs) (1 =yes; 2=student; 3=unable to work; 4 = unemployed)
Children – number
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Employment (if > 18yrs) (1 =yes; 2=student; 3=unable to work; 4 = unemployed)
Children – number