

Online supplement

Cystic fibrosis registries diagnosis inclusion Criteria

Patients captured on the Canadian Cystic Fibrosis (Registry (CCFR) and the South African CF Registry (SACFR) for the calendar year 2018 were included according to the diagnostic criteria below. For both countries 1) patients consented to have their data collected by the registries and 2) were alive in the year 2018.

Diagnostic Inclusion Criteria:

Canadian Registry:

For a diagnosis of CF, the patient must meet the standard guidelines for having CF (based on clinical symptoms, sweat testing, genotyping; J Pediatr 2008).

SACFR:

Two sweat tests value > 60 mmol/L chloride: CF diagnosis accepted

One sweat test value > 60 mmol/L chloride or sweat conductivity > 90 mmol/L and DNA Analysis/Genotyping – two identified disease-causing CF mutations as reported in CFTR2 database: CF diagnosis accepted; or

Sweat value less than or equal to 60 mmol/L chloride then both these should be fulfilled:

- a. DNA Analysis/Genotyping – two identified disease-causing CF mutations; and
- b. Clinical Presentation consistent with typical or atypical CF.

Sweat conductivity without DNA confirmation of two disease causing CFTR mutations as reported in CFTR2 database will be accepted for SA registry only if both following criteria are met:

- a. clinical presentation consistent with typical CF
- b. at least two separate sweat conductivity measurements ≥ 90 mmol/l

Table S1. Explanation of data variables extracted from the Canadian and South African Cystic Fibrosis Registries

Variable	Description	
Demographic Data		
Age	Calculated as age in years from Date Of Birth (DOB) to 31 December 2018. DOB was set to the 15 th of the month in both registries to protect confidentiality.	
Sex	Male or Female	
Ancestry/Ethnicity	<i>South Africa</i> Caucasian Black African Other: mixed Race, Asian, Indian Unknown	<i>Canada</i> Caucasian Black Other: Asian, South Asian, First Nations People, Hispanic, two or more races

		Unknown
Diagnosis		
Diagnosed by Newborn screening	Yes, No Not available in SA	
Meconium Ileus	Yes, No or Unknown	
Age of Diagnosis	Calculated from DOB to Date of Diagnosis in months.	
Genotype categorised	Categorised as: p.Phe508del homozygous (Yes/No) p.Phe508del heterozygous (Yes/No) Other /Not p.Phe508del Unknown	
CFTR mutation class	Categorised as: Class I-III (minimal function) Class IV-VI (residual function)	
Mutation Allele Frequency	Frequency of 10 most frequently occurring Allele mutations Includes category for unknown mutation	
Sweat Test	Chloride value in mmol/L If two chloride values are recorded the first sweat test value should be calculated for that patient for analysis.	
Sweat Conductivity (SACFR only)	Conductivity value in mmol/L If two conductivity values are recorded the first value should be calculated for that patient for analysis.	
Lung Function		
FEV ₁ Litres	The best pre-bronchodilator FEV ₁ value (litres) for the 2018 calendar year is selected. Includes children 6 years and older at date of lung function Excludes lung function measurements taken after lung transplant Date of this measurement collected for nutrition and GLI calculations	
FEV ₁ percentage predicted value (%)	Calculated according to Global Lung Index (GLI) using the best pre-bronchodilator FEV ₁ value (litres) for the 2018 calendar year.	
Nutrition		
Pancreatic Status in 2018	Determined by fecal elastase measurements and/or prescription of pancreatic enzyme replacement therapy. Pancreatic Sufficient Pancreatic Insufficient Unknown	
Weight (Kg)	Weight at the time of best pre-bronchodilator FEV ₁ value for 2018 is selected. If no FEV ₁ recorded for the year, the last weight measurement of the year is selected. Date of this measurement collected for nutrition calculations	

Length/height (cm)	Height at the time of best pre-bronchodilator FEV ₁ value for 2018 is selected. If no FEV ₁ recorded for the year, the last height measurement of the year is selected. Date of this measurement collected for nutrition calculations.
Nutrition classification	Weight in kg Length in cm BMI – kg/m ² for patients >18 years BMI z-score (BMIz) parameters calculated according to World Health Organisation references equation children 0-19 years.
Microbiology	
Any Isolates in 2018	Any Pseudomonas isolated in 2018 Any MRSA isolated in 2018 Any NTM isolates in 2018 Recorded as: Yes, No or Unknown *Other infections and chronic infection status of specific infections could not be sufficiently harmonized between countries to permit meaningful comparisons.
Complications	
Cystic Fibrosis Related Diabetes in 2018	Yes, No or Unknown Diagnosis of CF related diabetes requiring insulin. This includes people who have impaired glucose tolerance in Canada but not South Africa. If someone has Type 1 diabetes or juvenile diabetes, this can be included under the category of 'CF-related' diabetes.
Liver cirrhosis/portal hypertension	Yes, No, or Unknown Includes clinical (hepatosplenomegaly), radiologic (U/S, CT scan that shows enlarged spleen or nodular liver), pathologic (liver biopsy) evidence of cirrhosis and splenomegaly which implies portal hypertension or if there is endoscopic evidence of oesophageal or gastric varices in the reporting year. If a patient only has elevated liver enzyme tests with no evidence of cirrhosis or portal hypertension, do NOT check this complication. In Canada cirrhosis was recorded between 2015-2018 ensuring the most recent estimate.
ABPA	Yes, No or Unknown in 2018. ABPA is defined as anyone diagnosed with ABPA by a physician based on clinical judgment, biochemistry or other laboratory testing in the reporting year.
Therapies	
Pulmonary	
hypertonic saline	Yes, No or Unknown

	minimum of 3 months of therapy in the reporting year
rhDNase	Yes, No or Unknown minimum of 3 months of therapy in the reporting year
macrolides	Yes, No or Unknown minimum of 3 months of therapy in the reporting year
Inhaled antibiotics	Yes, No or Unknown minimum of 3 months of therapy in the reporting year Yes, includes any inhaled treatment preparation from the SA and Canadian registries including: gentamycin, amikacin, aztreonam, tobramycin, colistin, levofloxacin, vancomycin, or any other inhaled antibiotic
Number of IVI courses per year	Yes, No or Unknown If Yes – 1/2/3/4/5 or more Canadian Registry: Combining variable for pulmonary admission and Home IV events
GIT	
Pancreatic Enzyme Replacement Therapy	Yes, No or Unknown
Transplant in 2018	
Received Liver Transplant in 2018	Yes, No
Received Liver Transplant prior to 2018	Yes, No
Received Lung Transplant in 2018	Yes, No
Received Lung Transplant prior to 2018	Yes, No
Modulators	
CFTR Modulators (any)	Yes , No
Deaths	
Number of Deaths in 2018	
Age of death	Calculated in years from DOB to Date of Death