Cystic Fibrosis Foundation Patient Registry

Data Use Manual

Data release year: 2021

Contents

Commonly used acronyms and terms

Related to cystic fibrosis

- BMI: Body Mass Index
- CDC: Centers for Disease Control and Prevention
- CF: Cystic Fibrosis
- CFF: Cystic Fibrosis Foundation
- CFFPR: Cystic Fibrosis Foundation Patient Registry
- CFRD: Cystic Fibrosis-related diabetes mellitus
- CFTR: Cystic Fibrosis Transmembrane Conductance Regulator
- CRMS: CFTR-related Metabolic Syndrome
- FEV_1: Forced Expiratory Volume in 1 second
- GI: Gastrointestinal
- Guidelines: The CF Foundation provides several clinical care guidelines related to diagnosing CF
- HIPAA: Health Insurance Portability and Accountability Act of 1996, as amended by HITECH (Health Information Technology for Economic and Clinical Health Act)
- IRB: Institutional Review Bboard
- OGTT: Oral Glucose Tolerance Test
- PFT: Pulmonary Function Test, measured by spirometry
- Sweat test: measurement of concentration of salt in sweat for determining CF diagnosis
- WHO: World Health Organization

Related to data entry and analysis

- Affiliate program: Affiliate programs are typically smaller and primarily serve pediatric patients.
- CF Care Center: The CF Foundation Care Center Network, comprised of CF centers that include pediatric, adult, and affiliate programs, makes high- quality specialized care available to people with CF throughout the United States.
- CRF: Case Report Form (also referred to as “Questionnaire”) used to report data to the CF Registry.
- Data Warehouse: The physical database that houses data for the population of people with CF whose data are in the Patient Registry.
- Imputed variables: Imputed or derived variables are variables that are created from other variables but not explicitly collected in the CRFs. For example, the CRF collects date of birth, but the Registry adds an age variable that is created from the date of birth.

Introduction

The current Cystic Fibrosis Foundation Patient Registry (CFFPR) includes data reported since 1986. As of 2021, data from approximately 31,000 people with CF are included in the CFFPR. Data are entered into the Registry's secure database by care center staff CF Foundation (CFF)-accredited care centers across the United States (which encompass more than 130 adult, pediatric, and affiliate programs). Each care center obtains institutional review board (IRB) approval from its institution for enrolling individuals into the Registry and is responsible for obtaining and recording signed consent forms. The Registry is a tool for researchers who wish to pursue observational studies about persons with CF in the United States. To date, hundreds of manuscripts have been published about pulmonary, nutritional, and microbiological outcomes among persons with CF as well as research pertaining to many CF treatments and therapies. The CF Foundation serves as the coordinating center for data collection and data preparation. Confidentiality is maintained and all Health Insurance Portability and Accountability Act (HIPAA) regulations are strictly enforced.

This Data Use Manual is for investigators planning to conduct research using data from the CFFPR. The manual is intended to provide background on the evolution of the CFFPR and to guide users through the data elements that may be used in analysis. We strongly recommend researchers review this document to understand the CFFPR before submission of a data request. The full data dictionary is provided at the time of data delivery.

History of the CF Foundation Patient Registry

CFFPR data have been collected through a web-based portal (known as PortCF) since 2003. Care teams report data to CFFPR using five electronic data-capture forms (also referred to as case report forms [CRFs] or questionnaires): demographic, diagnosis, encounter, care segment episode, and annual review forms. All data are entered by staff at CF care programs from the data available in the medical record or obtained over the course of CF clinical care. Data reported via these CRFs are published in the CFFPR Annual Data Report.

- The **demographic form** captures date of birth, sex, race, Hispanic ethnicity, state of birth, and other information needed to verify that the record is for a unique individual. Information on the date and cause of death are also captured on this form.

- The **diagnosis form** is used to record the means by which a CF diagnosis was reached, describing symptoms, if any, at diagnosis, as well as the results of tests to confirm diagnosis, including pilocarpine iontophoresis sweat tests and CFTR genotype.

- The **encounter form** is used to record data from clinic visits or other encounters between the care center and the registry participant and includes data on anthropometric measures, respiratory microbiology, CF medications, pulmonary function tests (PFTs), CF-related complications, laboratory tests, and airway clearance therapies.

- The **care episode segment form** reports dates and limited details from hospitalizations and courses of home intravenous (IV) antibiotics, including the reason for hospitalization and results of PFTs conducted at the start and end of the episode.

- Each year, CF care centers are required to complete an **annual review form** for each patient seen. This form is used to collect information not included in the encounter forms, such as socioeconomic status, health insurance, and transplant information. These five CRFs are used to create the four analytical data files made available for CFFPR-based research.

Timeline of major changes to data collection

Researchers should consider how changes to CFFPR data collection may be relevant for their specific research objectives, noting that frequency of reporting has changed over time as the addition of new variables or field options. The following timeline shows major changes to the CFFPR.

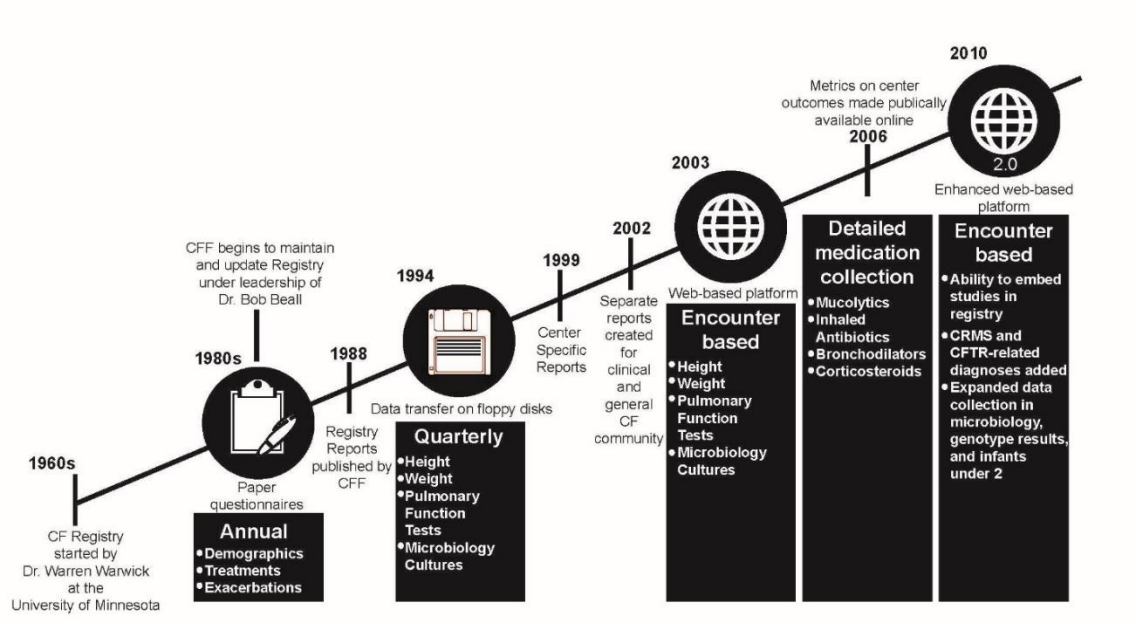


Figure credit: Knapp EA, Fink AK, Goss CH, Sewall A, Ostrenga J, Dowd C, Elbert A, Petren KM, Marshall BC. The Cystic Fibrosis Foundation Patient Registry. Design and Methods of a National Observational Disease Registry. Ann Am Thorac Soc. 2016 Jul;13(7):1173-9.

1986–1993 data

Annual data on demographics, diagnosis, clinical data, health care utilization, and comorbidities were initially collected on paper case report forms, then on floppy disks. Before 1994, this consisted of a single year-end questionnaire. Researchers should appreciate the distinction between the frequency of encounters with the CF care provider(s), which **occurred more often than once a year,** and the frequency of data reported to the CFFPR. **During this time, data were reported to CFFPR annually per registry participant.**

Clinical measurements (PFTs, height, and weight) were recorded for the first inpatient or outpatient visit in the year when all three measurements were reported. The month of the measurement was reported but not the exact date (these dates are imputed). Similarly, respiratory microbiology results were reported from the first culture obtained in the year, but the month of measurement was not recorded.

Including these data for these early years into the current encounter-level analytical data file structure required the imputation of an event date. For clinical measurements, the 15th of the month of measurement was used. For microbiology results, February 15 was used. If these two dates were the same, then a single encounter record was created. If they were different, then two encounter records were created. If a registry participant was seen at more than one center in the year, then additional encounter records were also created.

1994–2002 data

In 1994, the year-end questionnaire was expanded to allow quarterly reporting of height, weight, bacterial culture surveillance, and pulmonary function testing. For each quarterly measurement, a date was also recorded. This date may be imputed to reflect quarterly reporting, not the exact date of the measurement. From 1994 to 1998, the respiratory microbiology section was revised to allow reporting of any positive culture results obtained in the year (any vs. none), reported with an imputed date of February 15. In 1998, the form was again expanded to include up to four separate culture results, along with the date for each culture, and up to two separate lab results reported with those dates.

Researchers should appreciate the distinction between the frequency of encounters between a CF care provider(s) and their patient, which may have occurred **more often than quarterly** during this period, and the frequency of data reported to the CFFPR. **During this period, data were reported quarterly per person (for a maximum of four measures per indicator, per person [per CF care center attended] reported in a calendar year).**

2003–2009 data

In 2003, the CF Foundation transitioned Registry data collection to a clinical encounter–based system and launched PortCFv1, a web-based data entry application known as PortCF. Staff at CF care centers were no longer limited in the number of measurements per person per year that could be entered. Additional data elements were added to many of the sections as listed under "Description of data files." A Hospital/Home IV section was added to record data including begin and end dates for each hospitalization and each home-IV antibiotic course.

Researchers should appreciate that from 2003 onward, individual encounters with the CF care provider(s) could be reported to the Registry. In addition to reporting individual encounters with their specific dates and measurements obtained, an annual review form is completed for each person to document indicators that are ascertained on an annual basis such as vital status or transplant status.

2010 major updates

In 2010, the Registry expanded again when the CF Foundation upgraded to a second version of the Registry platform known as PortCFv2. From 2010 onward, CFFPR data were collected through PortCF on five electronic data-capture forms still in use today: demographic, diagnosis, encounter form, care episode, and annual review forms. Data elements in several new areas, including diagnosis of CFTR-related metabolic syndrome (CRMS) and CFTR-related disorders, and mycobacterial infections were added.

2020 – present major updates

In 2020, location field options were updated to account for telehealth (phone only or phone/video) From March to May, CF care teams were instructed to use location "Other" to indicate a telehealth visit.

CFFPR population and data management

Everyone in the Registry is assigned a unique encrypted ID (eDWID). The eDWID can link individuals across the four analytical data files. Only encrypted patient IDs are shared with researchers. A unique program-specific patient ID is assigned to each individual in the CFFPR when they consent to participate with their CF care center. The CFFPR team reviews the list for potential duplicates in the event an individual Registry participant seeks care at more than one CF center in a calendar year. The deduplicated list is then used to assign the unique patient IDs. Records of all merges are maintained by CFF. Diagnosis and demographics records reported by more than one CF center are merged. Data from all annual records for a person for a year are incorporated into the annualized record. For example, a report of oxygen therapy by any center will result in a report of oxygen therapy on the annualized record, even if the primary program did not report oxygen therapy.

Death and transplant validation

After data entry for the year is closed, the CFFPR team confirms all reported death and transplant dates with CF care centers. The process involves emailing every center with data entered and confirming all death and transplant dates that occurred in the last year as well as inquiring about any additional people not on the list who died or received a transplant. Information on transplants is reported once a year.

Lost to follow-up

The CFFPR does not define individuals as lost to follow-up (LTFU) as they may return to a CF care center in the future. Researchers should define LTFU status in a manner appropriate for their specific research question.

We highlight major changes to data entry and the addition of new variables in the specific sections that follow. The first calendar year for which data are available from each variable is reported in the Registry population as indicated in the ***CFFPR Data Dictionary****.*

Accessing CFFPR Data for Research

Researchers interested in using the CFFPR will submit a request for data via the online portal hosted at cff.org. Researchers will identify members of their research team, summarize the research objectives and analytical plan, and indicate the specific variables requested for analysis. Each data request is assigned a Patient Registry Request Number (PRR#), which should be referenced in all communications by research teams to facilitate data delivery and project tracking.

Data release by year

The CFFPR is updated an annual basis, which we refer to as a "data release year." For each data release year, we update the entire time series from 1986 to the present reporting year. Researchers should not expect historical data to go unchanged from one data release year to another. There are instances for which an individual's historical data may change, depending on the circumstance. This could include a decision to no longer participate in the Registry, changes to diagnosis details, updated genotype data, and updated death or transplant details.

External researchers should be advised that in their data request application, they will be required to specify the calendar years of data required for the project. We only release the most recent data release year, subset to the calendar years of data required to implement the proposed analysis, not for all calendar years available in the CFFPR. After a project is approved, if research teams require an updated data set for a new data release year, they can request it in writing at datarequests@cff.org.

Description of data files for researchers

There are four data files available to researchers: (1) demographics and diagnosis data, (2) encounter-level data, (3) care episode data, and (4) annualized data. A detailed list of all variables and definitions is available in the Data Dictionary.

Unless otherwise requested, files released to researchers only include individuals with a positive diagnosis of CF. Data from individuals with a diagnosis of CRMS or CFTR-related disorder can also be obtained by request.

Protected health information (PHI): dates v. ages

Variables that contain PHI require an institutional use agreement to be signed between CFF and the institution(s) where data will be held. Researchers who do not wish to request PHI variables associated with dates (encounter date, date of birth, date of death, etc.) can instead request the age of these events to the first decimal point.

Data delivery and data codes

Researchers can request data delivery in one of two formats: (1) a SAS file or (2) a .csv file. Researchers should consider the needs of their project in terms of the possible size of the data file (it may require multiple files due to size), need for labels or formats, and analysis software to determine the best format for their specific project.

The coding for the encounter file is different from the annualized data file. Data entry at the encounter level includes check boxes to report a variety of data elements. As a result, the encounter data set codes these variables as "1" for "yes" and "missing" for fields where the check box was not selected. There are a few cases where values of "0" reflect a missing response if a check box response is dependent on the responses to a prior field. Most of the answer options on the encounter case report form are check boxes.

- A checked box is a "yes" value.
- **An unchecked box is not the same as a confirmed "no."**

In the annualized data file, if a question was never answered throughout the year, but the annual form was completed, it is recorded as "no" (= 0). A specific list of data codes for each variable are provided in the CFFPR Data Dictionary.

Missing values

To better segment individuals with missing data, the Registry data files contain the following special SAS missing value codes for the annualized file:

- .W = Was not asked (for years before a variable was added)
- .T = Individual is post-lung transplant (for PFT variables)
- .M = Entire form is missing
- .N = Not applicable (for variables such as pregnancy questions for males)
- .U = Unknown

Missing value fields for .csv files are indicated as blanks.

Summary of Analytical Data Files Available

There are four data files available to researchers: (1) demographics and diagnosis data, (2) encounter-level data, (3) care episode data, and (4) annualized data. The files (and the variables within those files) a research team receives will depend on the variables requested for a given research project.

Demographics and diagnosis data file

Demographics data can be entered by any CF care center that has access to an individual's record. The demographic form captures date of birth, sex, race, Hispanic ethnicity, state of birth, and other information needed to verify that the record is for a unique person. Information on the date and cause of death are also captured on this form. The diagnosis form is used to record how a CF diagnosis was reached, describing symptoms, if any, at diagnosis, as well as the results of tests to confirm diagnosis, including pilocarpine iontophoresis sweat tests and CFTR genotype. Most of this information remains unchanged over time; however, there are some items that could have multiple entries, such as if a person had multiple sweat test values to confirm a CF diagnosis. Diagnosis date is the earliest date of diagnosis reported for the current diagnosis type. If a person is seen at more than one CF center, the CFFPR reports the date of diagnosis as reported by the primary center.

Encounter data file

Data are reported at clinical encounters with the CF care team. The encounter form is used to record data reported by the CF care team, including routine outpatient follow-up, hospital-based visits, telehealth (as of 2020), and home IVs. These data include basic anthropometric measures, respiratory microbiology, CF medications, PFTs, CF-related complications, laboratory tests, and airway clearance therapies. This includes qualitative data (was their patient seen by the dietitian, do they have any microorganisms found in a culture, etc.) as well as quantitative data (height, FEV_1, blood glucose levels, etc.).

These data may be entered as occurring at one of the following locations:

- CF care center
- Hospital
- Home IV
- Other
- Telehealth (with video) – option added May 2020
- Telehealth (phone only) – option added May 2020

An encounter at a CF care center occurs when a member of the CF care team meets with a patient. Encounters entered as location hospital or home IV can include information not collected in the care episode form (such as bacterial culture results and multiple PFT values). Encounters that occur outside of typical clinic visits, hospitalizations, or periods of home IV treatment (e.g., lab visits, visits to the PFT lab) can be recorded with a location of "other." From March 2020 to May 2020, CF care teams were instructed to use location of "other" to indicate a visit that occurred via telehealth offered during the initial months of the COVID-19 pandemic.

Before 2020, encounters reported with a location of "other" could include (but were not limited to) any use of telehealth.

Care episode data file

Researchers interested in historical hospitalization and home IV data should pay close attention to the nature of CFFPR data collection over time. For research questions specific to hospitalizations and home IVs that occurred between 1986 and 2002, researchers can access these data (reported on an annual basis) in the **annualized data file**:

- For hospitalization data between 1986 and 1993, the total number of hospitalizations and number of days hospitalized, as well as any home IV antibiotic therapy, were reported via **the annual review form**.

- In 1994, the reasons for hospitalization (acute respiratory exacerbations, GI or other reason, unknown), the number of home IV antibiotic therapy courses, and total days were added to **the annual review form**.

- Starting in 1995, the total home IV antibiotic therapy courses and total number of days on home IVs, as well as any home oxygen use, were added to **the annual review form**.

From 2003 onward, the care episode form reports periods of hospitalization and home IV treatments. Unlike encounters, which occur on a single day, episodes of care are characterized with a start and an end date (or start and end age) and cover the entire period during which a person is hospitalized or treated on a home IV antibiotic course.

Starting in 2003, specific reasons for each care episode were reported. Reasons for care episodes include the following (available since 2003):

- Pulmonary exacerbation
- Pulmonary complication other than exacerbation
- Gastrointestinal complications
- Transplant-related
- Sinus infection
- Nontransplant surgery
- Other
- Nontuberculous mycobacteria (NTM) treatment (full year available as of 2019)

CF care teams document individual hospitalizations or home IVs using the care episode segment CRF. A single care episode reported in the analytical episodes data file can consist of multiple care segments that have at least one common reason for hospitalization and back-to-back dates. Two or more care episode segments that are adjacent or overlapping (from care episodes and/or encounters, and from one or more centers) are combined into a single care episode with the largest possible date range. All reasons for hospitalization are included. For overlapping days, the location hierarchy is hospital > home IV.

These reported segments are then used to construct the episode data file shared for research purposes, which consolidates care episode segments in which individual segments represent a continuous period of care. This includes the start and end date (or start and end age), the reason for the hospitalization or home IV, and any PFT results. CF care teams can report height, weight, and pulmonary function data captured at the beginning or end of a care episode. **These measures are included in the encounter analytical data file with the corresponding start or end date of the episode and are coded as location = hospital.**

- Care episodes with a start and end date are reported in the calendar year of the end date. A person is flagged as "hospitalized" or "home IV" in both calendar years if applicable, and all days are counted through the reporting year of the end date.
- Care episodes with no end date are flagged in the year of the start date as "hospital" or "home IV" and have number of days "unknown."
- Encounters reported using the **encounter form** with a hospital location and start, and end dates are counted as hospital days with reason "unknown." If the field "pe_assessment" is marked 2,3,4, (indicating exacerbation severity), the reason for hospitalization is coded as pulmonary exacerbation.
- Encounters with reported using the **encounter form** home IV location and start and end dates are counted as home IV days, reason "unknown." If the field "pe_assessment" is marked 2,3,4, the reason for hospitalization is pulmonary exacerbation (PEx).
- Hospital and home IV "days" refer to nights of care episode. A hospitalization or home IV has zero days if the start and end dates are the same.

For example, a person may be hospitalized for a pulmonary exacerbation on January 10th and then discharged on January 17th but prescribed home IV therapy for the same exacerbation until January 24th. This would appear in the analytical data file as a single care episode from January 10th to the 24th (derived from two underlying care segments). In this example, the care episode data record would summarize the seven nights hospitalized and seven nights treated with home IVs.

Hospital and home IV events can be reported to the CFFPR via the **care episodes segment form** or via the **encounter form** with a location of hospital or home IV. **Researchers should appreciate that additional data relevant to a period of hospitalization or IV treatment can be reported by CF care teams using the encounter form and by indicating a location of hospital or home IV. We recommend investigators identify encounter dates that fall within episode start and end dates.** Any data not entered in a care episode segment form can be reported using the **encounter form**. This includes data such as prescribed medications or bacterial cultures obtained during a care episode.

Encounters with a location of hospital or home IV are concatenated (combined in a specific series) into care episodes if they are continuous (i.e., no break in days) or are reported no more than three days between each other and have at least one reason for the hospitalization or home IV, which is the same as for the previous encounter. For example, a pulmonary

exacerbation hospital stay followed immediately by home IV for pulmonary exacerbation would be combined to create a single pulmonary exacerbation care episode.

Encounter and episode segment data can be linked via the dates (or ages) associated with the reported data. Researchers should note that encounter dates and episode dates (or ages) may not permit exact matching if the encounter date recorded falls within or outside the start and end dates of an episode, and they should compare the location field reported. There are also plausible scenarios in which a care episode would be reported with no corresponding encounter record(s).

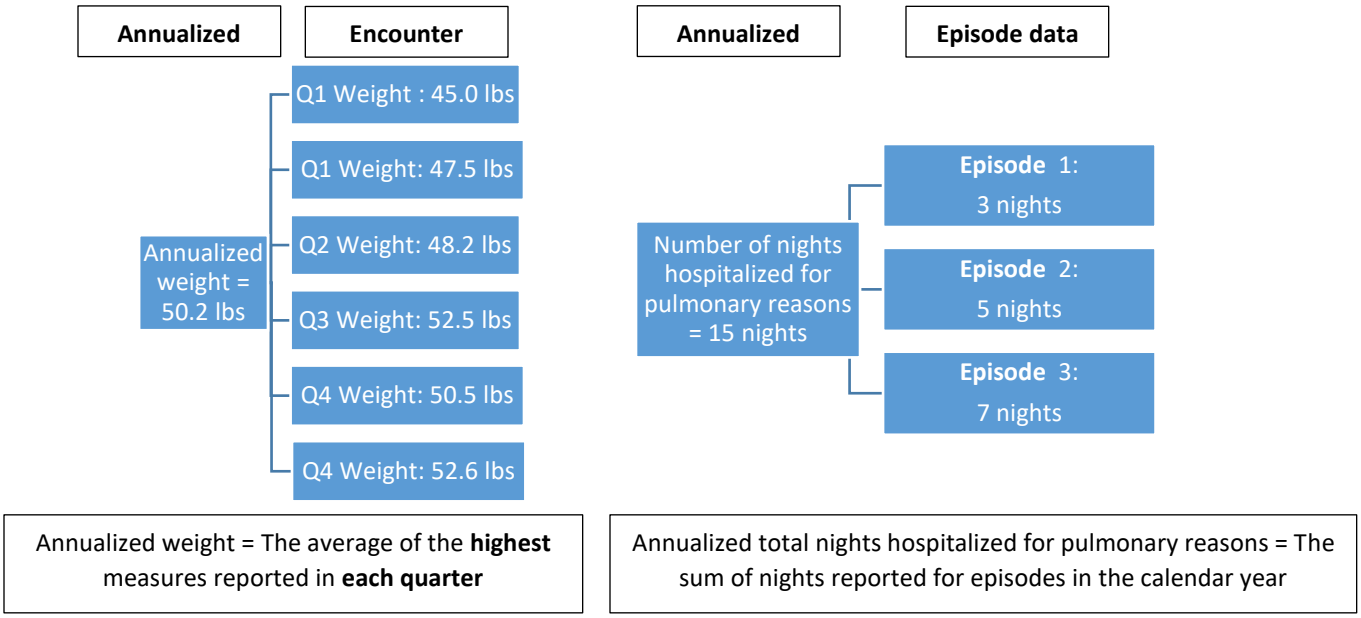
Annualized data file (summarized by calendar year)

There is a difference between data **reported on an annual basis** (ascertained as part of the annual review) and data that are **"annualized" for the purposes of summarizing encounter-level or episode data**. The CF Foundation asks CF care centers to provide an annual review for each patient. The annual review is completed once a year based on data entered throughout the year. This includes death, transplant, insurance, and socioeconomic information. This is also the only form where the response options include "unknown" for certain questions, as the care center team may have had a brief interaction with a patient or not know the answer to a question, such as secondhand smoke exposure.

The **annualized file** summarizes data for each year a person participates in the CFFPR. These data are composed of three specific data types: (1) data reported by CF care teams via the **annual review report form**, (2) data that are **derived from measures taken over the course of encounters** reported in the calendar year, and (3) data that are **derived from care episodes** reported in the calendar year. The annualized data set also derives the number of clinic visits, number of clinical measurements (FEV_1, height, etc.), and other summary count measures.

Encounter-level data are converted to the annual level for reporting purposes, such as medications prescribed, reported complications, or microbiology results. Episode-level variables are also converted to the annual level for reporting purposes, such as total number of hospitalizations and number of home IV events. Refer to the CFFPR Data Dictionary for exact definitions of annualized variables of interest.

A few examples of an annualized variable creation are illustrated below:



Calculating the denominator for major data elements

It is important to note that denominators may be different depending on the nature of the research question. While many records are complete, there are instances in which certain data elements are missing or not collected. For example, a person may provide a microbacterial culture during a clinic visit, but a mycobacterial culture (to screen for NTM) is not performed. In this case, such person would contribute to any denominator used to calculate prevalence or incidence of pathogens detected via microbacterial surveillance but would not be included in a denominator to calculate prevalence or incidence of NTM. There are variables in the analytic files that serve as indicators that correspond to whether the data were collected for a person or not (e.g., ”any annual” for annual reviews and” A_MedVars” for any medication data reported).

Description of Major Data Elements

Demographics

The demographics case report form collects all demographic and diagnosis information about a person. Examples of variables included in this section are the following:

- First year in the Registry
- Date of birth or year of birth
- All known information about the person's diagnostic history
- Genotype data

Diagnosis

Diagnosis data are collected for all individuals whose data are entered into the CFFPR. There are 24 individual diagnosis fields that can be selected for an individual to report information that may have contributed to a CF diagnosis (e.g., diagnosis suggested by newborn screening, diagnosis suggested by meconium ileus/other intestinal obstruction, etc.). Refer to the **Data Dictionary** to review the complete list. If there is a history of CF diagnosis, all diagnostic tests are recorded.

CF Care teams can report the results of multiple sweat tests (if performed). The most recent sweat test is released to the analytic file. For example, if a patient obtains a sweat test multiple times, the date of first sweat test is collected to document the date of when a CF diagnosis was attempted. Data that are released include the most recent sweat test date and value.

Researchers can access the following:

1. Date of latest sweat test
2. Year of latest sweat test
3. First reported sweat test date
4. Latest sweat test value reported
5. Highest sweat test value reported

If data regarding a person's diagnosis are entered in a free text field, this is matched or converted to the corresponding diagnosis variable. For example, if the protein name p. Arg117H is entered in a free text field, this is classified as R117h.

Diagnosis date is the CF diagnosis date as reported by the primary center. If unknown, it can be an approximation. Because centers may not be aware that a patient had been previously diagnosed by another center, it is possible for the diagnosis date to be later than reported encounter data. Also, sometimes the diagnosis type for a person changes due to new information and, thus, the diagnosis date is changed.

Genetics

Individual genotype information is documented and recorded, if available. This includes the date of genotyping and variant type(s). If a person has been genotyped multiple times, the most recent information is reflected. Researchers can request the classification of CFTR variants based on CFTR protein function. Not all CFTR variants have been given a variant class, so those not in classes I through V are referred to as not classified. Individuals are assigned to one of three variant class groupings (class I–III, class IV–V, and not classified), combining the classes of their individual variants as follows:

1. If either CFTR variant (at least one allele) is class IV or V (often referred to as residual function), then they are assigned to the class IV–V group.
2. If both variants are classified as class I, II, or III, then they are assigned to the class I–III group.
3. Otherwise, genetic variants are listed as not classified. For variant classes, values coded as .N or 0 or other variants indicate that the person was genotyped, and a variant was identified but the functional characteristics of that variant have not yet been determined, so that variant has not yet been assigned a variant class.
4. Within the CFFPR, a variant class variable is created when the final demographics and diagnosis data set is output.

An indicator variable is available to identify whether a CFFPR participant has any F508del alleles (homozygous, heterozygous, or none). Depending on certain circumstances, the poly-T tract can be CF-disease causing. The poly-T variant and poly-TG repeat options only become available if one of the following variants is selected:

- TG12/T5
- TG12
- TG10
- TG11
- R117H
- I148T
- R117C
- M470V
- I1027T
- L997F
- F1052V
- R1162L
- G622D
- 5T

Patient residence

Patient state of residence is derived from the patient's zip code. If a zip code is not reported, then the state of the primary center is used and a state edit flag is reported (st_edit). Before 2013, zip code was included on the demographic file. This created a problem in that zip code was overridden whenever a patient moved. In 2013, it was moved to the annualized file. Zip code for previous years was restored whenever possible by reviewing archive files.

Primary program

Primary program is a derived variable and is based on an algorithm that accounts for all centers reporting data for a person in a year. If a person is only seen at one center (program) in the year, then that program is classified as primary. If a person is seen at multiple centers, then selection is based on an algorithm that accounts for the completeness of the data reported and the number of visits reported in the calendar year. For annual reporting purposes, the primary program determines where the person will be counted. At the encounter level, the program variable is the program where the person was seen. At the care episode level, the site_os_id is the program reporting the care episode.

Health insurance

Patients can report to their CF care team all health insurance coverage they have received throughout the year, and multiple insurance categories can be selected per person each year. If a person has the majority of the year (at least six months) of not being insured, this is indicated as no insurance. For example, a person can have Medicaid, a private insurance policy, and no insurance selected during a single annual review.

The options reported are health insurance policy (private), Medicare, Medicaid, state special needs program (e.g., MCMH, CCS, CRS, GHPP), TriCare or other military health plan, Indian Health Service, or other.

CF care teams are asked to report whether their patients were covered under a parent's health insurance plan and whether patients received free medicine or copay/deductible insurance assistance.

Education

This is ascertained each year in the annual form. For individuals aged 18 years and older, CF care teams report the level of education: less than high school, high-school diploma or equivalent, any college, college graduate, masters- or doctoral-level degree (added in 2010), or unknown. The spouse level of education can be reported as well. Among children aged younger than 18 years, education is reported as "less than high school" and CF care teams report the mother's and father's education separately. Since 2016, CF care centers can carry forward the response values from the previous year's annual review for all education variables.

Employment, household size, income, and marital status

Employment status is ascertained on an annual basis, with the following options: employed full time, employed part time, full-time homemaker, unemployed student, disabled, retired, and unknown. This is ascertained for CFFPR participants ages 18 years and older. Household size is reported as the total number of people currently living in the person's household. Total combined household income before taxes was added in 2005 and is ascertained during the annual review.

Marital status options are as follows since 1991: single/never married, living together, married, separated, divorced, widowed, and unknown. This is ascertained for CFFPR participants ages 18 years and older. The responses from this field can be carried forward from the previous year's annual review as of 2016. Marital status was ascertained for persons aged 21 years old and older in 1991 and 1992, and then those aged 18 years old and older from 1993 onward.

The responses for employment, household size, household income and marital status can be carried forward from the previous year's annual review as of 2016.

Pregnancy

Since 1990, pregnancy has been ascertained for female CFFPR participants as yes, no, or unknown in a calendar year. If a person is reported as pregnant, CF care teams can report the outcome of the pregnancy: live birth, stillbirth, spontaneous abortion, therapeutic abortion, undelivered, unknown.

Parent height

Parental height and weight values can be entered in any unit and are stored in metric units. Parental height and weight values are not reported for individuals aged 21 years old and older.

Smoking status

Three variables are available to characterize smoking status. CF care teams can report if a person smokes cigarettes during the calendar year (added in 2006), how often the patient was exposed to secondhand smoke (added in 2006), and if the person lives in a household where someone smokes (added in 2012).

The options for person-reported cigarette use are no, occasionally, yes/regularly <1 pack per day, yes/regularly ≥1 pack per day, declined to answer, no known, and not applicable. For a person's exposure to secondhand smoke, the options are daily, several times per week, several times per month or less, never, declined to answer, and not known.

Research involvement

Since 2010, CFFPR maintains an indicator variable to report whether an individual participated in an interventional drug study during the calendar year and a second variable ascertaining

participation in an observational research study. CFFPR does not collect data on the specific research studies in which individuals may have participated.

Transplant status

Transplant status is ascertained in the CFFPR on an annual basis. Each CFFPR participant is classified according to transplant status, which includes previous years of data. The options available are not pertinent; accepted, on waiting list; evaluated, final decision pending; evaluated, rejected; and had transplantation. Transplant by organ is reported for lung (bilateral), heart/lung, lung (lobar/cadaveric), lung (lobar/living donor), liver, kidney, and other. The date of the most recent transplant is also obtained as part of the annual review form. Finally, the annual review reports on post-transplant complications as follows: bronchiolitis obliterans syndrome, lymphoproliferative disorder, and other. Only date of first lung transplant or year of first transplant is available for researchers to request. We provide year of transplant for other transplant types.

Because it is possible for a person to receive multiple transplants, to ascertain transplant status **researchers must compare data reported in both the demographic and annual file**. Individuals with a history of previous transplant could be added to a transplant waitlist in a given calendar year, which should be compared to year of first transplant. Researchers can request variables to indicate if a person has ever received a transplant as well as transplant status for a given review year.

Individuals who receive lung transplants have certain variables that are set to missing with the indication (. T in a SAS datafile, left blank in a .csv file). The CFFPR nullifies certain variables, including pulmonary medications, clinical trial participation, microbiology, PFTs, and oxygen therapy for CFFPR participants after lung transplant.

Vital status

Death information is reported via the demographics case report form. CF care teams can collect the date of death (exact or approximate) or age of death, or year extracted from death date. The primary cause of death list contains the following options (year added): cardiac/respiratory (1986), liver disease/liver failure (1986), trauma (1990), suicide (1990), transplant-related (bronchiolitis obliterans; 1992), transplant-related (other; 1992), drug overdose (2018), other (1986), and unknown (1986).

General encounter information

Encounter-level reporting in 2003, including reported encounter date. Beginning in 2006, the location of the encounter was available. This initially included clinic, hospital, and home IV with "other" added to the list of locations in 2014. Partway through 2020, phone and phone/computer video were added as options for location, and home IV was removed as an

option. Encounter locations are summarized by calendar year in the annualized file as separate variables.

The CFFPR collects data on individuals seen by multidisciplinary care team members. In 2003, data regarding patients seen by a social worker and dietitian/nutritionist were available. In 2006, the option for respiratory therapist/physical therapist was added, and, in 2016, these were split into individual fields for evaluation by respiratory or physical therapist. Also in 2016, an option became available for if a patient consulted with a pharmacist. In 2018, the Registry began collecting data on whether a patient consulted with a mental health coordinator.

Encounter age is derived from the date of birth reported and the date of the encounter reported. Encounter age is a key variable in determining height, weight, and PFT percentiles. Thus, if the encounter age changes, then these variables are recalculated.

Pulmonary exacerbation assessment

The exacerbation assessment field has been available since 2010 and became mandatory when completing the encounter form midway through 2012. Please see the Port CF data entry for guidelines on how exacerbation status is determined when a treating physician has not provided an assessment.

Pulmonary exacerbation data can be obtained for each encounter or summarized for the calendar year. In encounter-level data, the variable “pe_assessment” indicates whether a pulmonary exacerbation was assessed, ranging from absent to severe. Treatment options may be entered under the “medscurrentepisode” variable if a non-absent exacerbation is evaluated. Treatment options are increased airway clearance, oral non-quinoline antibiotics, oral quinolone antibiotic, inhaled antibiotic, inhaled antibiotic plus oral non-quinoline antibiotic, or inhaled antibiotic plus oral quinolone antibiotic. Pulmonary exacerbations specifically treated by IV antibiotics are identified through the care episodes case report form and summarized for the calendar year (since 2003).

Annualized data include fields that summarize the exacerbation history for each person over the calendar year. This includes any assessment of a pulmonary exacerbation in the year (yes/no). The total number of encounters with exacerbation assessments are summarized by absent, mild exacerbation, moderate exacerbation, and severe exacerbation. These fields have been available since 2010. The total number of encounters for which crackles were reported is also calculated for the calendar year.

Anthropometric measures

Height and weight values can be entered in any unit and are stored in metric units. The CFFPR documents height and weight as reported and corrected for implausible values. Growth charts developed by the Centers for Disease Control and Prevention (CDC) are used to calculate height, weight, weight-for-length, and BMI percentiles for individuals aged younger than 20 years. For individuals aged younger than 2 years, z-scores and percentiles based on the World Health Organization (WHO) growth charts are also available for weight-for-age, length-for-age,

and weight-for-length. Percentiles are calculated at the encounter level according to encounter age.

Body mass index (BMI)

Absolute BMI is reported for all CFFPR participants ages 20 years or older. BMI percentiles are derived using CDC reference standards and reported for individuals between ages 2 and 19 years. Encounter-level height/weight/BMI percentiles and z-scores are annualized by taking the average of the highest values for each quarter. Variables at the annualized level retain the same variable name as at the encounter level but with an "A_" prefix. calculation of annualized BMI variables is split based at age 20.

Pulmonary function testing (PFT)

The CFFPR only reports PFT data among individuals 6 years of age or older. Forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio have been reported in CFFPR since 1986, but measures of forced mid-expiratory flow (FEF)25–75% were added to the CFFPR in 2010. From 1986 to 1993, CF care centers reported measurements from pulmonary function testing at the first inpatient or outpatient visit recorded in the year.

From 1994 to 2003, measures were reported quarterly. CF care centers were instructed to enter the best PFTs for each quarter (in liters) and to enter height and weight measurements taken on the same day as the highest PFT.

After 2003, care centers were able to enter PFT results for each clinical encounter. Beginning in 2012, the Registry switched to Global Lung Initiative (GLI) reference equations to calculate percent predicted values based on the Registry-reported absolute volume (in liters), age, sex, race, and height. All historical PFT data from 1986 onwards have been transformed to percent predicted values according to the GLI equations. To account for the increased utilization of home spirometry, a field confirming pulmonary function testing was performed in a laboratory setting adhering to ATS standards was added in 2021 (options: Yes; No; Unknown).

Data entry requires CF care centers to report the absolute measures (in liters) obtained through spirometry, and percent predicted values are calculated for the Registry using the methods detailed by Quanjer *et al.* CF care centers can report instances for which a PFT was not obtained during an encounter if a person was unable to perform the test.

Pulmonary function data are summarized for the calendar year. An indicator variable (yes/no) identifies subjects for whom results for at least one PFT was reported. The total number of measures for FEV_1, FVC, FEF25–75%, and FEV_1/FVC ratio are also calculated per person per calendar year. Annualized PFT measures are calculated as the average of the best spirometry results for each quarter in the year. Lung function measures are also summarized for posttransplant subjects based on GLI equations in separate PFT variables.

Lab values

Lab variables have been collected since 1997 beginning with serum creatinine. Glucose testing data have been reported on an annual-level basis since 1998 and an encounter-level basis since 2003. The variables available are random blood glucose, fasting blood glucose, OGTT fasting glucose level, 1-hour blood glucose, and 2-hour blood glucose. Starting in 2003, hemoglobin A1C values began to be collected, and, in 2010, liver function tests and fecal elastase began to be collected at the encounter level.

Supplemental feeding

Supplemental feeding has been reported since 1989. This includes tube feeding (nasogastric, gastrostomy, and jejunal) since 1989, total parenteral nutrition since 1991, and oral supplementation since 2000.

Infant feeding data have been reported at each encounter since 2010. The type of feeding can be reported as breast milk, breast milk plus formula, formula exclusively, other food, and unknown. Formula type can be reported as cow milk, soy milk, predigested, and other. Data summarized by the calendar year dichotomizes these fields (any reported vs. none).

Screening tests

Screening variables document whether screening tests were performed in a calendar year. In some cases, the results of those screening tests are also reported in CFFPR via the annual review. Examples are summarized in the table below.

Screening test	**Year added to CFFPR**	**CFFPR reports results of screening test?**
Chest x-ray	2006	No
IgE screening	2010	No
Liver function tests performed	2015	Yes – refer to lab results
Fat-soluble vitamin levels measured	2005	No
Screening for anxiety disorder	2015	No
Screening for depression	2015	No
DEXA scan performed	2010	Yes
Colonoscopy performed*	2018	Yes
Eye exam to check for cataracts performed	2020	No

*Required field for all individuals > 30 years of age.

The annual review form collects data on whether individuals have been screened using recommended or other valid depression and anxiety screening tools. These screening variables were added in 2015. From 2016 onward, a response on these fields is required to complete annual form data entry.

Microbiology

Microbiology data have been collected since 1986; results are from the first culture collected during the year. Beginning in 1994, all positive culture results obtained anytime during the year were recorded. In 1998, up to four separate bacterial culture dates and any positive cultures that were collected could be recorded. After 2003, all cultures taken during the year could be recorded, and the bacterial culture date is not uniformly reported as the same date as the encounter. Bacterial culture dates documented in the CFFPR are as reported by CF care teams. In 2010, the Registry began collecting mycobacterial culture dates. The annual file collects the number of cultures performed and whether a species was cultured positive or not during the year. Data summarized for each calendar year also report the total number of cultures each participant provided.

Microbiology species collected since 1986 are Staphylococcus aureus (MRSA added in 1996), *Pseudomonas aeruginosa* (PA), *Haemophilus influenzae*, *Burkholderia cepacia*, Aspergillus, Candida, other, and unknown. In 1991, the Registry began collecting *Klebsiella pneumoniae*/other and Xanthomonas, and Achromobacter was added in 1996. In 2010, the number of microbacterial and mycobacterial species expanded to include more individual species (see CFFPR Data Dictionary). Detection of aspergillus (any species), candida (any species), and scedosporium species are reported according to the date of microbacterial culture.

Susceptibility testing

The results of susceptibility testing are reported for PA only. When entering data on a person infected with PA, options will appear on the case report form to list the type of PA (mucoid/non-mucoid) and any antibiotic resistance detected. There is variation in the number of people with a mucoid PA phenotype due to differences in reporting PA colony phenotypes among microbiology labs.

Antibiotic resistance has been collected in the CFFPR since 1998 for aminoglycosides, quinolones, and beta lactam classes. Multiple drug-resistant PA (variable name: A_MDR_PA) is defined when antibiotic resistance is to two or more antibiotic classes is reported for a single encounter and is available in the annualized data file. Multiple drug resistance is not applicable if resistance to two or more antibiotic classes is reported across separate encounters.

Mycobacterial cultures

The CFFPR reports the date of mycobacterial cultures and type of culture performed (sputum, induced sputum or bronchoscopy). Acid-fast bacilli (AFB) details were not collected in the CFFPR until 2010 and are recorded in the Registry under the encounter form and are also summarized for inclusion on the annualized file. Researchers using the mycobacterial data should note that not all registry participants provide mycobacterial cultures at all encounters.

Burkholderia cepacia *complex*

The Registry listed *Burkholderia cepacia* (*B. cepacia*) as *Pseudomonas cepacia* until 1997. We maintain a variable on the year *B. cepacia* was first reported and year confirmed. Other *Burkholderia cepacia* complex species variables were added to the Registry in 2010.

Treatments (excluding CFTR modulator therapies)

Medications are recorded during encounters and reflect the date the medication may have been prescribed. The CFFPR is not designed to ascertain adherence to medication. Therapies collected by the CFFPR include antibiotics, CFTR modulators, pancreatic enzymes, and other therapies including dornase alfa and hypertonic saline. The Registry also has collected drug intolerances and allergies since 2006 for select therapies. The Registry provides data on whether the care team has reported any medications or not, which is used to accurately determine the denominator in a cohort. Medication data can be carried forward by data entry personnel—prescriptions can be auto populated from the previous encounter.

Inhaled/oral antibiotics reported at the encounter level

The CFFPR collects data on inhaled/oral antibiotics prescribed for tobramycin solution, TOBI pod haler, Bethkis, other inhaled aminoglycoside, colistin, aztreonam, other chronic inhaled antibiotics, azithromycin, clarithromycin, quinolone, cephalosporin, sulfa, amoxicillin, and tetracycline.

Other pulmonary medications

The CFFPR started capturing prescription of pulmonary medications in 1994 beginning with dornase alfa and high-dose ibuprofen (1995) and hypertonic saline in 2005. Acetylcysteine was added in 2006. Bronchodilators, corticosteroids, and acid blockers also began collection in 2005. Bronchitol (Mannitol®) was added in 2021.

Acid blockers and other GI treatments

Daily use acid blocker can be reported at individual encounters, with options for H2 blocker (e.g., Zantac, Pepcid), proton pump inhibitor (e.g., Prilosec, Nexium) or unknown. Multiple options can be selected. Ursodeoxycholic acid can also be reported.

PERT (pancreatic enzyme replacement therapy)

The variable indicating a person is receiving PERT (variable name: isoenzymes) was first reported in the CFFPR in 1990. The data are represented as a yes/no answer for specific PERT dosages. Lipase units per largest meal and lipase units per day (available since 2010) are derived from the underlying enzyme prescription details reported to care teams on an encounter-level basis, which requires care teams to identify the specific enzyme dose in terms of capsules per day. Researchers should appreciate that these data reflect prescribed quantities of PERT, not adherence to that prescribed amount.

Airway clearance

Researchers can request data on primary airway clearance technique (ACT) reported by CF care teams on an encounter-level basis. The CFFPR does not track adherence to ACT use. The options available are positive expiratory pressure (PEP), postural drainage with clapping (CPT), forced expiratory techniques, oscillating PEP, high-frequency chest wall oscillation (e.g., Vest), exercise, none, or other. Only one option is permitted.

Noninvasive ventilation and oxygen therapy

Use of noninvasive ventilation during the calendar year is reported on an annual basis (since 2006), as well as use of oxygen therapy (since 1989). The options for oxygen therapy are yes, continuously; yes, nocturnal; yes, with exertion; yes, prn (as needed); no; or unknown.

Flu vaccine

Ascertainment of flu vaccine is reported on an annual basis, specifically if a person received their vaccination between September and January. This field has been available since 2006.

COVID-19 vaccine

Ascertainment of COVID-19 vaccine status is reported on an annual basis. This field was added to the Registry in 2021.

NTM treatment initiation

NTM treatment initiation is ascertained on an annual basis since 2010. The CFFPR does not collect specific details on the type of treatments used for NTM nor the exact dates of initiation or cessation.

Palivizumab (Synagis®)

Among subjects aged younger than 2 years, CF care teams can report whether the person was given palivizumab in the calendar year according to respiratory syncytial virus (RSV) season (September through January). This field has been available since 2008.

Growth hormone

Growth hormone use is reported annually since 2005.

CFTR modulator therapy

CFTR modulator therapies have been introduced according to the following timeline. Note that eligibility for a CFTR modulator depends on calendar year, age, and CFTR variant(s).

Ivacaftor (Kalydeco®)

- 2012: Age 6 years or older (only G551D for on-label)
- 2014: Age 6 years or older (R117H + other variants)
- 2015: Ages 2–5 years included

- 2017: Label expansion to additional variants
- 2018: Age 1 year or older
- 2019: Age 6 months or older
- 2020: Age 4 months or older, label expansion to additional variants

Lumacaftor/ivacaftor (Orkambi®)

- 2015: Age 12 years or older (homozygous F508del)
- 2016: Age 6 years or older
- 2018: Age 2 years or older

Tezacaftor/ivacaftor (Symdeko®)

- 2018: Age 12 years or older (homozygous F508del or F508del + additional variants)
- 2019: Age 6 years or older

Elexacaftor/tezacaftor/ivacaftor (Trikafta®)

- 2019: Age 12 years or older and at least one F508del variant
- 2021: Age 6 years or older and at least one F508del variant, additional label expansion

CF care teams report prescriptions for CFTR modulator therapy; this does not necessarily indicate that the person-initiated use of the therapy at the date of the prescription. In encounter records, the following options for prescriptions for the four US Food and Drug Administration (FDA)-approved CFTR modulators are as follows:

CFTR modulator	Year field added	Frequency options
Ivacaftor monotherapy	2011	50 mg BID 75 mg BID 150 mg BID Other regimen (dose/frequency)
Lumacaftor/ivacaftor combination therapy	2015	Full dose BID Half dose BID Other regimen (dose/frequency)
Tezacaftor/ivacaftor combination therapy	2017	Full dose BID Half dose BID Other regimen (dose/frequency)
Elexacaftor/tezacaftor/ivacaftor triple combination therapy	2019	Full dose BID Half dose BID Other regimen (dose/frequency)

Drug intolerance for CFTR modulator therapies is documented in the encounter form as a yes/no option.

CF-related complications

Complications are comorbid conditions for persons with CF. Before 2003, complications were reported by CF care teams on the **annual form (as part of an annual review)**. In 2003, they were moved to the **encounter form**. Complications may be uploaded (e.g., "carried forward") from data entered for previous clinical encounters. Before July 2015, the "Upload Complications" option in the PortCF data entry interface could be used to upload all complications reported from the previous encounter. As of July 2015, this functionality was changed to only include complications that are considered chronic, such as CF-related diabetes (CFRD), arthritis, osteoporosis, asthma, and GERD. Care centers may also report that a person does not have any complications by reporting the "no complications" variable in PortCF.

Diabetes status

Diabetes status has been reported on an annual basis in the CFFPR from 1986 to 2003. From 2003 onward, CFRD status can be reported using the **encounter case report form** as a complication, and diabetes status is also reported using the **annual form**. Data on diabetes management is only reported using the **annual form**.

Beginning in 2003, CFRD status is reported for each encounter and is also recorded in the **annual form** completed by CF care teams. The current options for CFRD status on the **encounter-level form** are impaired glucose tolerance (fasting blood glucose [FBG] < 126; 2-h postprandial glucose [PG] 140–199), CRFD with or without fasting hyperglycemia, type 1 diabetes, and type 2 diabetes. Individuals with no diabetes or impaired glucose tolerance are identified as such in the **annual form.**

In the annual review, CF care teams report diabetes status as one of the following: normal glucose metabolism, impaired glucose tolerance (FBG < 126; 2-h PG 140–199), CRFD with or without fasting hyperglycemia, type 1 diabetes, and type 2 diabetes. Data on chronic insulin are available in the CFFPR dating back to 1986. Data on intermittent insulin are available dating back to 1997. Data on oral hypoglycemic agents are available dating back to 2002. Secondary complications of diabetes are also reported on an encounter-level basis as of 2003. Variables introduced before 2003 were previously reported on an annual basis. The options are retinopathy (added in 1998), microalbuminuria (1998), chronic renal insufficiency (2010), chronic renal failure requiring dialysis (2010), and peripheral neuropathy (2010). These complications are not mutually exclusive. Additional variables related to diabetes and management are summarized in the table on the next page.

Please refer to the Data Dictionary for specific variables and definitions.

Variable	**Year introduced**	**Current frequency of reporting**
CFRD status (annual form)	1986	Annual
Retinal eye exam performed by ophthalmologist	2010	Annual
Spot urine sent for albumin/creatinine ratio	2010	Annual
Was patient prescribed treatment for CFRD?	1986	Annual
Dietary change	2003	Annual
Oral hypoglycemic agents	2002	Annual
Intermittent insulin	1997	Annual
Chronic insulin	1986	Annual
Any episodes of severe hypoglycemia	2010	Annual
Retinopathy	1998	Encounter
Microalbuminuria	1998	Encounter
Chronic renal insufficiency	2010	Encounter
Chronic renal failure requiring dialysis	2010	Encounter
Peripheral neuropathy	2010	Encounter

Hepatobiliary complications (liver disease)

Complications related to liver disease have been reported in the CFFPR as early as 1989. The first variable used for this purpose was "Liver disease, cirrhosis." A summary of when variables related to liver disease have been added to the CFFPR is presented in the table below.

Variable	Year introduced
Gallstones	2010
Gallstones requiring surgery/procedure	2010
Liver disease, cirrhosis	1989
Esophageal varices	2010
Gastric varices	2010
GI bleed related to varices	2003
Splenomegaly	2010
Hypersplenism	2010
Ascites	2010
Encephalopathy	2015
Acute hepatitis	2015
Acute hepatitis - infectious	2015
Acute hepatitis - non-infectious	2015
Acute hepatitis - unknown	2015
Liver disease, non-cirrhosis	1993
Hepatic steatosis	2010
Liver disease, other	2010
Acute liver failure	2015
Liver enzymes elevated (for 2003–2009)	2010

From 2003 onward, CFFPR data report liver-related complications at the encounter level only. The complications data reported via encounters is annualized to create indicator variables summarizing whether the specific complication was reported (yes/no). Before 2003, quarterly or annual reports of complications were used to derive liver disease status for a calendar year.

As of 2015, the following liver-related complications require data entry personnel to indicate if they exist for each encounter (there is not mechanism to auto populate data from a previous encounter): gall stones; gall stones (requiring surgery/procedure); liver disease, non-cirrhosis; acute liver failure (no underlying disease); hepatic steatosis; liver disease (other); and all hepatitis-related fields.

Bone and joint complications

Since 2003, the following complications related to bone or joint health are reported via encounters: arthritis/arthropathy, bone fracture, osteopenia, and osteoporosis. Researchers interested in osteopenia and osteoporosis should be aware that variables reporting DEXA scan results may not be concordant with what is reported as a complication.

Pulmonary complications

The CFFPR collects data on the following pulmonary-related complications: allergic Bronchopulmonary aspergillosis (ABPA), asthma, hemoptysis, and pneumothorax requiring a chest tube.

Gastrointestinal (GI) complications

CFFPR collects complications pertaining to GI conditions for the following: chronic constipation, distal intestinal obstruction syndrome (DIOS), fibrosing colonopathy/colonic stricture, GERD, GI bleed requiring hospitalization (non-variceal), history of intestinal or colon surgery, pancreatitis, peptic ulcer disease, rectal prolapse, and *C. diff*. colitis. Encounter-level reports of chronic constipation, GERD, and history of intestinal or colon surgery indicate prevalent complications. All other GI fields should be reported for the encounter for which they are incident.

Other complications

The CFFPR enables reporting of a range of other complications, including anxiety, depression, cancer, and sinus disease. A full list is summarized in the table below.

Variable	**Year introduced**
Absence of vas deferens	2005
Anxiety disorder	2010
Cancer confirmed by histology	1992
Depression	2000
Hearing loss	1997
Hypertension	2006
Kidney stones	2006
Nasal polyps requiring surgery	1991
Renal failure requiring dialysis (cause other than CFRD)	1996
Sinus disease (symptomatic)	2005

Cancer, kidney stones, and nasal polyps requiring surgery are reported as incident events. All other fields listed in the table above should be interpreted as prevalent comorbidities.

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