Background and Epidemiology

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KEYWORDS

• Cystic fibrosis • Newborn screening • FEV_1 • BMI • *Pseudomonas aeruginosa* • MRSA • Mortality

KEY POINTS

- Survival for people with CF has improved greatly and for the first time adults with CF outnumber children with CF.
- The introduction of newborn screening has changed how CF is recognized; today, most people with CF are diagnosed in the neonatal period.
- Changes in CF therapies, disease measures, and outcomes can be tracked longitudinally using large registries, such as the CF Foundation Patient Registry.
- Progressive lung disease can be detected in early life via sensitive measures, such as chest CT scans and the lung clearance index.
- CF is a multisystem disease with complications that include pancreatic insufficiency, sinusitis, CF-related diabetes, infertility, and depression and anxiety.

INTRODUCTION

Cystic fibrosis (CF) is the most common autosomal-recessive cause of early mortality in caucasians worldwide.[1] However, significant advances in therapies and outcomes for people with CF over the past 30 years have brought hope and optimism to clinicians, researchers, and most importantly, individuals and families with CF. In just the past few years, therapies that directly correct errors caused by mutations of the Cystic Fibrosis Transmembrane Conductance Regulator (*CFTR*) gene have received regulatory approval,[2,3] the current median predicted survival is approaching 40 years (and even longer in Canada and some other countries),[4,5] and the number of adults with CF outnumber the number of children with CF in the United States for the first time.[6]

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These recent successes illustrate the great strides that have occurred since "cystic fibrosis of the pancreas" was first described by Dorothy Anderson in 1938.[7] At that time, few children with CF lived beyond 5 years, and it was not until the introduction of airway clearance, pancreatic enzyme replacement therapy, nutritional supplements, and anti-*Staphylococcus* antibiotics in the 1960s to 1970s that life expectancy began to extend into adolescence.[1]

CYSTIC FIBROSIS FOUNDATION PATIENT REGISTRY

Many of the developments in CF have occurred at care centers accredited by the CF Foundation (CFF). Modeled on the first successful therapeutic program developed in the 1950s,[8] CF care centers follow CFF Care Guidelines, deliver multidisciplinary care, and have appropriate inpatient and outpatient medical, diagnostic, and laboratory facilities.[9] They are part of a network that includes pediatric, adult, and affiliate programs. As of 2014, there were 121 CF care centers geographically dispersed within the United States. All accredited care centers must contribute data to the CFF Patient Registry (CFFPR).[10] The CFFPR is an ongoing, observational study that is the primary tool for monitoring the health of individuals with CF in the United States. Starting in the 1960s, the CFFPR has evolved to expand the quantity and frequency of the information collected from individuals with CF. Data entered into the CFFPR include demographic and diagnostic information, anthropometric values, pulmonary function test (PFT) results, cultures of respiratory secretions, CF complications, comorbidities, and prescribed CF medications. Thus, the CFFPR is a valuable resource used extensively to inform clinical care, support quality improvement initiatives, and conduct research. Outside of the United States, CF registries exist in Canada, the United Kingdom, Europe, and Oceania, all of which are used to better the understanding of individuals with CF and the course of the disease.[11]

INCIDENCE

Among white persons, CF occurs in approximately 1 in 3000 to 4000 live births.[12] Approximately 1 in 25 to 30 white persons are carriers of a pathogenic mutation of the *CFTR* gene. In other races and ethnicities CF occurs less commonly, including approximately 1 in 4000 to 10,000 Latin Americans, 1 in 15,000 to 20,000 African Americans, and even less commonly in Asian Americans.[12] In the United States, approximately 1000 individuals are diagnosed with CF each year (**Fig. 1**).[6]

Before the widespread use of newborn screening (NBS), individuals with CF were diagnosed either after presenting symptomatically, or via family history. The list of presenting signs and symptoms indicates the multiorgan system nature of the disease (**Box 1**). In 2004, the Centers for Disease Control and Prevention recommended that all states consider NBS for CF.[13] Since then, the proportion of individuals diagnosed via NBS has risen to account for nearly two-thirds of all diagnoses.[6] The early diagnosis of CF after NBS is associated with improved nutritional outcomes and may improve later pulmonary function.[14–16] Similar to NBS, prenatal screening is also widely available, although it accounts for only a minority of diagnoses (4% in 2014).[6] Overall, reports are inconsistent regarding the impact prenatal screening and NBS have had on incidence rates; some reported differences may be in part caused by changes in racial and ethnic distributions over time.[17–19]

The introduction of NBS for CF has also led to the recognition of patients who have abnormal NBS results, but do not meet the diagnostic criteria for CF. The terms "CFTR metabolic syndrome" in the United States and "CF screened positive, inconclusive diagnosis" in Europe have been introduced to characterize the symptoms of these