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## Genetic Services Policy Project

### Cystic Fibrosis: A Policy Brief

#### **What is Cystic Fibrosis (CF)?**

- CF is an autosomal recessive genetic condition with multi-system effects.
- Clinical course is highly variable, though early mortality is a common feature.
- It is often described as the most common fatal genetic disease in Caucasians.

#### **Who is affected by CF?**

- CF affects approximately 30,000 children and adults in the U.S. and occurs in approximately 1 in 3,500 live births.
- CF most often affects people of European descent, though may be found in all racial and ethnic groups.
- 80% of patients with CF are diagnosed by age three; only 10% of patients are diagnosed after age 18. The age at diagnosis is decreasing due to increased utilization of prenatal diagnosis and newborn screening.

#### **What are the genetic and non-genetic contributions to CF?**

- CF results when an individual inherits two abnormal copies of the CFTR gene on chromosome 7, one copy from each parent. Individuals who carry one abnormal gene (CF carriers) are typically unaffected.
- The estimated carrier frequency for a CF mutation is between 1 in 25 and 1 in 29 among European-Americans.
- The  $\Delta F508$  mutation, the most common gene variant, accounts for about 70% of CF carriers.
- Since the initial discovery of the CFTR gene in 1989, researchers have identified over 1,000 mutations of the gene. Severity of illness may be related to particular mutations.
- Non-genetic modifiers, such as environmental tobacco smoke, respiratory pathogens, and socioeconomic status (SES), may affect health outcomes.

#### **What are the clinical features of CF?**

- Patients with CF produce mucus that clogs the lungs and results in lung infections and eventual pulmonary failure.
- Patients with CF have difficulty in absorbing nutrients from food because the mucus keeps digestive enzymes from reaching the intestines.
- Liver damage and hepatic failure may result from blocked bile ducts.
- Pancreatic damage may lead to diabetes.
- Median life expectancy for individuals with CF is 33.4 years (CFF, 2006 data).

#### **What are the psychosocial impacts of CF?**

- As with other chronic illnesses, CF may have significant psychosocial impacts on affected individuals and families.

- Adolescents may be at particular risk for emotional and behavioral difficulties and poor adherence to complex treatment regimens.
- Stressors may include missed school and work, financial difficulties, and challenges associated with planning for the future (e.g., vocation, intimate relationships, and family).
- Better lung function and strong social support are associated with improved psychological status in adults with CF.

### **Who provides care for CF? In what setting?**

- Multiple providers are typically involved in the identification and care of individuals with CF, including prenatal care and primary care providers, pulmonology and gastrointestinal specialists, geneticists and genetic counselors, respiratory therapists, nutritionists, social workers, and nurses.
- Given the multi-system nature of the disease, comprehensive coordinated care is recommended and has been shown to improve health outcomes.
- The Cystic Fibrosis Foundation (CFF), the leading advocacy group for CF, accredits 115 comprehensive care centers nationwide (including 94 adult programs) and is affiliated with an additional 54 programs. (CFF, 2007)

### **What are standard treatments and therapies for CF?**

- Treatment depends on the stage of disease and the organs involved. Regimens often involve multiple medications and treatment modalities, and may include investigational therapies.
- Particular treatments include:
  - Chest physical therapy (PT) or percussion, which involves clapping on the back and chest to dislodge mucus. Studies suggest high frequency oscillating therapy vests may improve compliance and outcomes over manual chest PT.
  - Antibiotic treatments like TOBI® (tobramycin) aerosolized antibiotic to help address lung infections. Azithromycin is another antibiotic used for patients who are chronically infected with *Pseudomonas aeruginosa* bacteria.
  - Mucus-thinning therapies such as Pulmozyme® (rhDNase, dornase alfa) and hypertonic saline to improve lung function
  - Enzyme replacement for pancreatic insufficiency
  - Nutritional supplements to combat nutritional deficiencies
  - Lung transplantation and lifetime use of anti-rejection medication and immunosuppressant therapies to treat patients with end-stage CF
  - Psychosocial support
- Numerous new products and services, including gene-based therapies, are in the development pipeline or in clinical trial stages.
- Treatment outcomes are monitored in a national CF registry supported by CFF.

### **What costs are associated with CF?**

- Lifetime direct costs of CF are estimated at \$200,000 to \$300,000 (1996 values, 5% discount rate).
- Annual cost of medical care in 1996 averaged \$13,300 per patient, ranging from \$6,200 among patients with mild disease to \$43,300 among patients with severe disease.
- Of total costs, 47% were from hospitalization, 18% were from DNase (Pulmozyme®), 12%

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were from clinic visits, and 10% were from outpatient antibiotics.

### **What is the role of genetic services in CF?**

- Overview
  - The primary role of genetic services in CF is in the identification of carriers and affected individuals, as well as counseling for reproductive decision-making. Genetic research plays an important role in the development of new therapies.
- Carrier screening and prenatal diagnosis:
  - Expert opinion has recommended carrier screening for CF mutations for adults with a positive family history, partners of people with CF, couples planning a pregnancy, and couples seeking prenatal care. (ACOG/ACMG, 2001)
  - Mutation panels used in carrier screening identify the most common mutations, but may miss rare mutations. Specific mutations may vary between different racial/ethnic groups (e.g., African Americans, Hispanics).
  - Prenatal diagnosis for CF (i.e., amniocentesis and DNA testing of the fetus) is offered when both the mother and father are carriers, or if the mother is a carrier and the father's status is unknown. Prenatal diagnosis may offer reassurance if the fetus is unaffected or give the couple the options of preparing for the birth of an affected child or terminating the pregnancy.
  - CF carrier screening and prenatal diagnosis costs are approximately \$150-200 per person for carrier testing, and \$1,500-2,000 for amniocentesis. Prenatal carrier screening and subsequent prenatal diagnosis for CF is cost effective assuming affected pregnancies are terminated.
  - Pre-implantation genetic diagnosis (PGD) and selection of unaffected embryos may be used by carrier couples who choose to undergo *in vitro* fertilization (IVF); however, this option is expensive (average cost \$12,400 for IVF plus an additional \$3,000 for PGD) and not widely utilized.
- Newborn screening
  - The Centers for Disease Control and Prevention has suggested and endorsed the inclusion of CF on newborn screening panels because of potential benefits from early nutritional treatment, such as improved growth, as well as potential cost savings from reduced use of health care services.
  - Guidelines for implementing CF newborn screening programs have been developed to address concerns that adequate treatment, counseling and support services are in place prior to initiation of universal screening programs. (CFF, 2007)
  - Several different protocols using combinations of immunoreactive trypsinogen (IRT), DNA analysis, and sweat testing have been developed.
  - As of September 2007, 31 states have implemented CF newborn screening programs and an additional 12 states offer optional/selective testing or are planning to implement mandatory programs. (NNSGRC, 2007)
- Diagnosis
  - Diagnostic testing to confirm an abnormal newborn screening test or to evaluate a symptomatic child (or, rarely, an adult) is conducted through the gold standard "sweat test" and/or DNA analysis.
  - Reliable sweat testing is available at CFF-accredited centers.

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- Genetic counseling
  - Genetic counseling is recommended for carrier couples and families with a child diagnosed with CF or identified as a CF carrier on newborn screening.
- Genetic treatment
  - Clinical trials with gene-based therapies (e.g., replacement of the abnormal CTFR gene with a normal copy) have been ongoing since the early 1990s with limited success to date.
- Genetic research
  - Research includes studies of genotype/phenotype correlation to predict disease severity and/or response to therapy.

**What genetic service delivery or policy issues are highlighted in this case?**

- Clinical service delivery issues
  - Implementation of guidelines
    - Studies show a significant increase in use of CF mutation testing after release of ACOG/ACMG guidelines in 2001, though there is limited data about who is actually using these services. Surveys of providers suggest the majority of prenatal care providers are offering CF screening to at least some of their patients.
    - Guidelines were withheld until adequate support and educational materials were developed to improve implementation. This approach may be useful for other conditions.
    - Carrier testing in preconception settings (e.g., family planning settings) appears to be underutilized, which may reflect the general underutilization of preconception services.
  - Availability of services/providers
    - Any provider may offer CF carrier screening, sending blood or buccal specimens to centralized labs for testing. Typically, prenatal care providers (e.g., obstetricians, midwives, family physicians), who may have additional education or informational resources, provide carrier screening.
    - Comprehensive prenatal testing (e.g., amniocentesis) and genetic counseling services are available in larger metropolitan areas, which may require travel.
    - CF care centers are available in larger metropolitan areas in all regions of the country. For families living outside these areas, care coordination between local primary care providers and the CF centers is important.
    - There is a growing need for adolescent and adult services as life expectancy continues to increase.
  - Public health services
    - Implementation of state newborn screening programs and ongoing monitoring of these programs will be a continued area of policy focus over the next several years.
    - Several state-sponsored adult CF programs (e.g., Idaho, Michigan, Texas, Virginia, and Ohio) have recently faced elimination or major cuts due to state budget deficits.

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- Financial/payer issues
  - Private and public insurers typically cover CF testing in prenatal and pediatric settings as per standards of care. Coverage of preconception and pre-implantation genetic diagnosis testing may be limited, but more data are needed.
  - Adults with CF may have difficulty in obtaining private insurance due to pre-existing condition clauses and unaffordable premiums. They may need to rely on public insurance or state high-risk pools, which are not available in all states and have variable requirements.
  - Payers may be slow to cover costs of emerging therapies. The small target population makes it challenging to build the evidence base needed to support positive coverage policies. The process of appealing coverage decisions is cumbersome and time-consuming for consumers.
  - Even if payers cover treatments, consumers may be responsible for significant co-payments (e.g., 10% of inpatient costs, and 20% of outpatient treatment costs).
  - Pharmacy and medical equipment companies have developed assistance programs to increase access to products; however, these programs typically have income qualifications and other restrictions.
  - States may use their federal Children with Special Health Care Needs funding to pay for direct services for individuals with CF; however, this is typically the “payer of last resort”.
- Legal/regulatory issues
  - States (e.g., Florida) have attempted to pass mandates for insurance coverage of CF treatment and equipment, but these have failed due to strong insurance lobby opposition.
- Industry issues
  - Industry has a key role in developing novel tests and treatments to improve detection and care for CF. Industry faces the challenges of high costs for research and development for a limited population group, the need to make services accessible for consumers, and the desire to have profitable businesses. Patenting of products limits competition and competitive pricing, but may provide incentives for companies to develop new therapies for these conditions.
  - Genentech, the maker of Pulmozyme®, has demonstrated a commitment to patient access and to continued research into new and improved treatments.
- Consumer/advocacy issues
  - The Cystic Fibrosis Foundation, founded in 1955, has been a major driving force in the development of policies and initiatives related to CF, raising awareness, funds, and political support for the cause. This includes advocacy for genetic services programs, such as newborn screening. Though the group’s influence has been a key ingredient in progress for the disease, concerns have been raised that differential power may adversely impact resource allocation to other groups/causes (e.g., sickle cell disease).
- Research issues
  - Experience with CF points to the great value of data collection tools (e.g., the national CF registry) for monitoring and improving performance and outcomes.

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