Cystic Fibrosis Foundation: Achieving the Mission

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The Cystic Fibrosis Foundation is a voluntary, nonprofit, health organization whose mission is "*to assure the development of the means to cure and control cystic fibrosis and to improve the quality of life for those with the disease.*" While substantial progress has been made, as evidenced by a marked increase in the median predicted age of survival, much work remains to be done. Ongoing medical programs and activities of the Cystic Fibrosis Foundation, which span basic science, drug discovery, drug development, clinical care, patient education, and advocacy, will be described in this article. The key role of respiratory therapists in the cystic fibrosis community will be highlighted. *Key words: cystic fibrosis, drug discovery, clinical trials, quality of health care, registries, health services accessibility, respiratory therapy*. [Respir Care 2009;54(6):788–795. © 2009 Daedalus Enterprises]

Introduction

The mission of the Cystic Fibrosis (CF) Foundation is "*to assure the development of the means to cure and control cystic fibrosis and to improve the quality of life for those with the disease.*" Guided by an unwavering commitment to this mission, the CF Foundation has grown from a grassroots organization founded in 1955 by families affected by the disease, into a 600-employee, 250,000-volunteer, and $250 million per year enterprise that supports basic science, drug discovery, drug development, clinical care, patient education and advocacy. Some key milestones accomplished by the CF Foundation since its inception are shown in Table 1. While substantial progress has been made, as evidenced by a marked increase in the median predicted age of survival (Fig. 1),[1] much work remains to be done. The CF Foundation's ongoing medical programs and activities, some of which will be described in more detail below, are summarized in Figure 2. In addition, this article will highlight the key role of respiratory therapists (RTs) in the CF community.

Basic Research

The framework of the CF Foundation's investment in basic science lies in the academic scientists who are funded via investigator-initiated grants and through programmatic initiatives, exemplified by the Research Development Program. Two underlying principles guide all of the CF Foun-

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Table 1. Cystic Fibrosis Foundation: Important Milestones

1955 Establishment of Cystic Fibrosis Foundation
1961 Establishment of Care Center Network
1966 Establishment of Patient Registry
1980 Formation of Research Development Program
1988 Establishment of CF Services Pharmacy
1989 Identification of CF Gene
1997 Establishment of Therapeutics Development Program
1998 Establishment of Therapeutics Development Network
2002 Launch of Quality Improvement Initiative
2003 Launch of Volunteer Leadership Initiative
2008 Establishment of Patient-Assistance Foundation

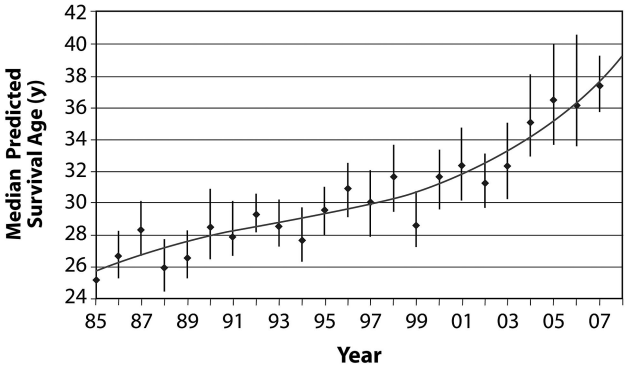

Fig. 1. The median predicted survival age by life table analysis is 37.4 years for 2007. This represents the age to which half of the current cystic fibrosis (CF) registry population would be expected to survive, given the ages of the CF patients in the registry and the age distribution of the deaths in 2007. 95% confidence bounds for the survival estimates are shown, indicating the 2007 median predicted survival is between 35.7 years and 39.3 years. (Data from Reference 1.)

dation's investments in basic research: incubation of new ideas; and support for projects that are deemed critical to accomplishing the mission of the organization. Studies funded entirely or in part by the CF Foundation have led to identification of the CF transmembrane regulator (CFTR) gene; delineating the effect of mutations on the function of CFTR; understanding of the multi-organ pathophysiology of the disease; development of animal models of CF; sequencing of the *Pseudomonas aeruginosa* genome; and establishment of assays suitable for screening of chemical compounds to support the drug-discovery efforts described below.

Established in the early 1980s, the Research Development Program brings a concentrated, multidisciplinary focus on the basic defect and pathophysiology of CF. The 11 Research Development Programs have matured into research centers of excellence, each with their own areas of expertise. Many have leveraged their support from the CF Foundation into programmatic awards from the National Institutes of Health.

The CF Foundation recently expanded its basic science program by adopting an additional research paradigm (ie, inviting selected members of the academic community from various institutions to participate in a research consortium). The goal of this approach is to organize and facilitate the efforts of multiple scientists with a common research interest to work collaboratively on a challenging problem directly relevant to achieving the CF Foundation's mission. The participants are granted latitude to pursue their own individual research interests, but are expected to provide feedback, know-how, and assistance to others within the consortium so that all members are successful in achieving their individual and collective goals. Pooling the talent and energy of multiple scientists will hopefully expedite the pace of scientific discovery. Trust and communication among consortium members are important elements in moving this research paradigm forward.

The CF Foundation also fosters collaboration and communication among researchers by sponsoring conferences where scientists can share their findings. The annual North American CF Conference is an important venue for this purpose. The CF Foundation's Williamsburg Conference is another, bringing together highly respected CF scientists from around the world to share their latest data in a relaxed and collegial atmosphere. The Williamsburg Conference has led to many new scientific collaborations.

Drug Discovery and Drug Development

Recognizing the need for new therapies, the CF Foundation established the Therapeutics Development Program to entice the pharmaceutical industry to apply their unique resources to CF. The program is designed to lower the risk for industry partners to enter an orphan disease area like CF by providing milestone-driven funding for late preclinical and early-phase clinical development of promising therapies. Much of this work is funded via Cystic Fibrosis Foundation Therapeutics Inc, a nonprofit drug discovery and development affiliate of the CF Foundation. Cystic Fibrosis Foundation Therapeutics Inc has also put several key support services in place to facilitate the drug discovery and development work, including a specimen bank, a third-party testing laboratory for CFTR assays, and a toolkit with chemical and antibody reagents. Other voluntary, nonprofit health-care organizations are now pursuing this novel and highly successful strategy—an approach that has been termed "venture philanthropy."[2]

Although the Therapeutics Development Program addresses many aspects of CF disease pathogenesis, the recent focus has been on developing therapies aimed at correcting the basic defect in CF. The successful collaboration with Vertex Pharmaceuticals (formerly Aurora Biosciences) is one example of how the program facilitates

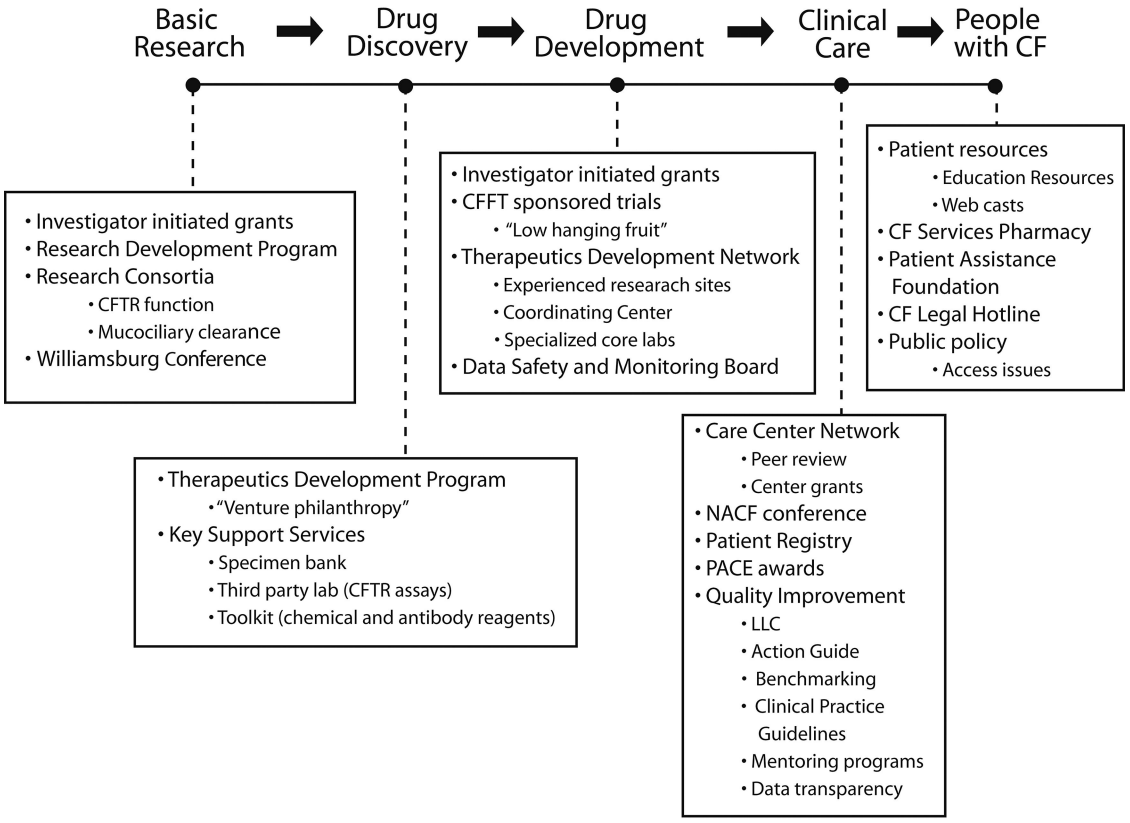

Fig. 2. The Cystic Fibrosis Foundation's ongoing medical programs and activities categorized into basic research, drug discovery, drug development, clinical care, and people with cystic fibrosis are summarized in this figure. CFTR = CF transmembrane regulator. CFFT = CF Foundation Therapeutics Inc. NACF = Annual North American Cystic Fibrosis. PACE = Program for Adult Care Excellence. LLC = Learning and Leadership Collaborative.

the development and testing of new drug candidates. This ongoing collaboration started with the screening of hundreds of thousands of chemical compounds (ie, high-throughput screening) to find those that restore function to the defective CFTR protein. "Hit" compounds in the screening assay were confirmed in secondary assays, and then the compounds were optimized via medicinal chemistry. The most promising compounds were moved into clinical development, including a "corrector" and a "potentiator," VX-809 and VX-770, respectively. Correctors increase the number of CFTR chloride channels at the cell surface, and potentiators improve the function of the CFTR protein as a chloride channel at the cell surface.

VX-809, aimed at patients with the most common mutation, delta-F508, is in phase-1 clinical trials; thus, efficacy data are not yet available. VX-770 is further along in development, with completion of a phase-2a trial, which showed a remarkable clinical response in patients with the G551D mutation.[3] While this particular drug may impact only a small percentage of CF patients who already have some CFTR protein at the cell surface, it is an important proof of concept for this scientific approach to drug development for CF. Other potential CFTR modulators in various stages of development are also showing promise. For example, PTC124, a compound developed by PTC Therapeutics, appears to be effective in the treatment of CF caused by nonsense mutations.[4] With the growing number of potential new therapies aimed at treating the basic defect, there is a palpable excitement among people with CF, families, health-care providers, and scientists.

An alternative, "low-hanging fruit" approach for developing new CF therapies examines the effect of therapies already approved by the Food and Drug Administration (FDA) and marketed for other indications. Azithromycin is a successful example of this approach. The chronic use of macrolide antibiotics has proven benefit in diffuse panbronchiolitis,[5] a disease similar to CF, seen primarily in the Asian population. Early reports suggested that macrolides might also benefit people with CF. Responding to these findings, the CF Foundation organized and sponsored a large randomized controlled trial to test the safety and efficacy of this therapy. The results showed that chronic azithromycin therapy over a 6-month period was well tolerated, improved pulmonary function, and reduced the number of pulmonary exacerbations in patients chronically infected with *P. aeruginosa*.[6] This therapy, endorsed by the

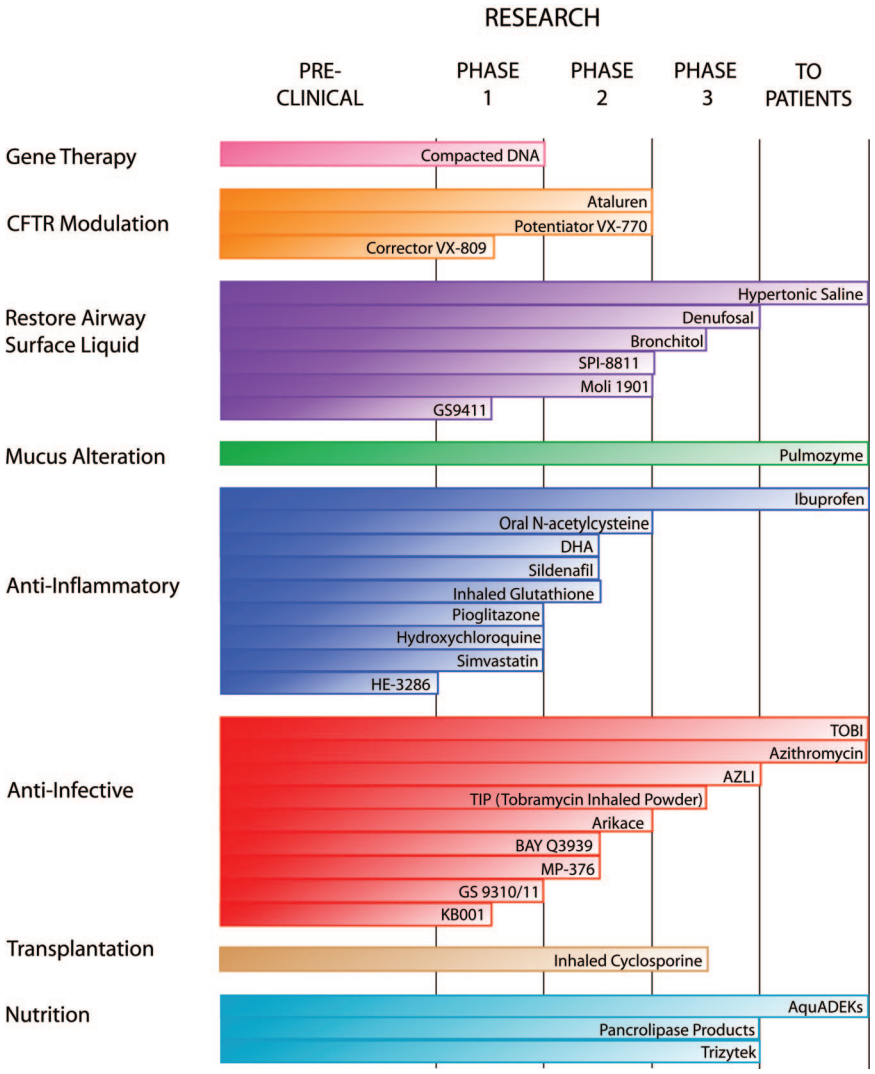

Fig. 3. The Cystic Fibrosis Foundation's drug development pipeline (go to http://www.cff.org and click on Drug Development Pipeline in Quick Links to see the most up-to-date version of the pipeline). CFTR = cystic fibrosis (CF) transmembrane regulator. DHA = docosahexaenoic acid. TOBI = tobramycin solution for inhalation. AZLI = aztreonam lysinate for inhalation. BAY Q3939 = ciprofloxacin for inhalation. MP 376 = levofloxacin for inhalation. GS 9310/11 = fosfomycin/tobramycin for inhalation. KB001 is a type of monoclonal antibody. AquADEKs is a multivitamin supplement.

CF Foundation's Pulmonary Guidelines Committee,[7] is now widely prescribed at care centers across the United States.

A key milestone in the CF Foundation's drug development work is the creation of the Therapeutics Development Network. This nationwide clinical trials network was formed to facilitate safe, rapid, and coordinated evaluation of new treatments for CF. The network consists of highly experienced clinical research sites, a coordinating center, and specialized core laboratories. Researchers participating in the Therapeutics Development Network have conducted over 50 clinical trials in a wide range of therapeutic areas; they have developed and standardized CF outcome measures, and assisted investigators and industry partners in design, implementation, and analysis of CF clinical trials. To ensure the safety of participants in the Therapeutics Development Network trials, the CF Foundation established an independent data safety and monitoring board. The resounding success of the Therapeutics Development Program and the Therapeutics Development Network is evidenced by the growing number of potential therapies in the CF Foundation's drug development pipeline (Fig. 3).

Advancing therapies through this pipeline requires many clinical trials, and the recruitment of hundreds of patients to participate in those trials. As the number and size of clinical trials have increased, the need for experienced clinical research centers has also increased. In response, the CF Foundation is expanding the clinical research in-

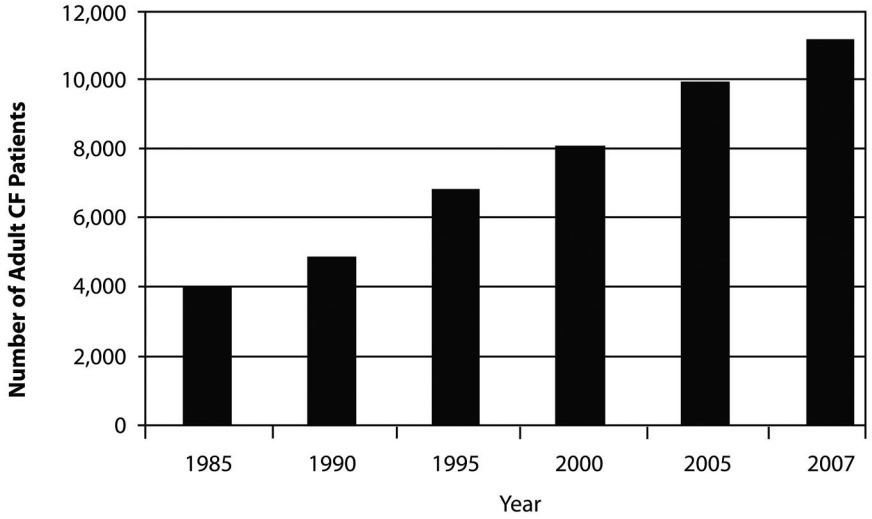

Fig. 4. The Cystic Fibrosis Foundation is working to meet the needs of the burgeoning population of adults with cystic fibrosis (CF) shown in this figure. (Data from Reference 1.)

frastructure by adding centers to the research network, providing training in Good Clinical Practice to newly recruited investigators and research coordinators, and developing a research-coordinators mentoring program. A public-awareness campaign encouraging people with CF to participate in clinical trials has also been launched. The CF Foundation hopes to foster a culture in which exemplary clinical care and fully informed participation in clinical trials are the standard of practice experienced by all people with CF at every care center.

Clinical Care

The CF Foundation's system of clinical care is a model for the care of individuals with a complex, chronic disease. The CF Foundation's Center Committee provides peer review and oversight of the Care Center Network, which includes over 110 care centers and over 50 affiliate programs. Accreditation by the CF Foundation is based on clear standards, which include credentialed and experienced physician leadership, an adequately staffed multidisciplinary care team, and participation in the CF Foundation's Patient Registry. Center grants are awarded to accredited centers by the CF Foundation to partially support their clinical activities and to cover travel expenses for the multidisciplinary teams to attend the annual North American CF Conference.

The Patient Registry was developed over 20 years ago to track national trends in survival and other key medical outcomes. Striking improvement in medical outcomes has led to a burgeoning population of adults with CF (Fig. 4).[1] Anticipating this demographic trend, the CF Foundation mandated the development of adult care programs early on, with the intent of requiring centers to deliver clinical care in an age-appropriate setting, by physicians trained in the care of adults. There are now over 90 accredited adult care programs in the Care Center Network; however, many are struggling to cope with the growing number of adults with CF. In response to this challenge, the CF Foundation has created the Program for Adult Care Excellence, to recruit additional physicians to care for this expanding adult CF population.

The Patient Registry has proven to be an invaluable tool, not only to track survival and outcomes, but also to improve them. Variability in practice patterns and outcomes among CF care centers uncovered by analyses of registry data led the CF Foundation to develop the Quality Improvement Initiative. In 2002 the CF Foundation brought together national experts in quality improvement and leaders from the clinical community to develop a strategic plan to accelerate the rate of improvement in CF care. The group asserted that years of life expectancy could be added by the consistent implementation of currently available therapies and approaches.

The vision, key strategies, and worthy goals of the Quality Improvement Initiative are shown in Table 2. Implementation of the strategic plan has included the following activities: state-of-the-art, action-oriented quality-improvement training via Learning and Leadership Collaboratives; production of a step-by-step manual on implementing quality improvement at a CF care center, entitled "Action Guide: Accelerating Improvement in CF Care"; a benchmarking initiative aimed at identifying and disseminating "best practices"; development of evidence-based clinical practice guidelines; emphasis on engaging people with CF and their families in the improvement work; development of mentoring programs for the various CF clinical disciplines; launch of a Web-enabled, encounter-based version of the

Table 2. Vision, Key Strategies, and Worthy Goals of the Quality Improvement Initiative

Vision
The delivery of exemplary care at all centers to further extend the quality and length of life for those with the disease.
Strategic Plan for Accelerating Improvement in Cystic Fibrosis Care
1. Build a shared vision of exemplary care at all care centers.
2. Develop leadership for quality-improvement work.
3. Incorporate people with cystic fibrosis (CF) and their families into the improvement work.
4. Identify and enable "potentially better practices."
5. Provide key information at the point of care.
Worthy Goals
1. People with CF and their families are full partners in their care.
2. Children and adolescents will have normal growth and nutrition, and adults will maintain nutritional status as near normal as possible.
3. People with CF will receive appropriate therapies for maintaining lung function and preventing exacerbations. Exacerbations will be detected early and treated aggressively.
4. Clinicians and people with CF and their families will be well informed partners in reducing the acquisition of bacterial pathogens.
5. People with CF will be screened for complications and treated aggressively when they are detected (eg, CF-related diabetes).
6. People with CF and their families will be well supported in their decisions about lung transplantation and end-of-life care.
7. People with CF will have access to appropriate therapies, treatments, and supports, regardless of race, age, education, or ability to pay.

Patient Registry, with a powerful query tool, and patient and center-level reports; and public reporting of center outcomes, on http://www.cff.org (click on Care Center Network in Quick Links).

The CF Foundation's Care Center Network has embraced quality improvement. Well over half of CF care centers have participated in one the CF Foundation's Learning and Leadership Collaboratives. Many centers have set "high bar" goals, have standardized their approach to care processes (eg, implementation of a treatment tracking form to ensure adherence with guidelines recommendations for chronic pulmonary therapies), and have sought new ideas for improvement from other centers. Many care centers have formed patient and family advisory boards, and others have made people with CF and parents full members of their lead quality-improvement teams.

Capitalizing on the momentum of the quality-improvement initiative, the Center Committee incorporated an assessment of quality-improvement activities into the care center accreditation process. The committee also instituted a Quality Care Award to recognize centers with a sustained commitment to quality improvement resulting in improved outcomes for their patients. Participation in improvement work is now an expectation in the CF community. Registry analyses show an increased rate of improvement in key pulmonary and nutritional outcomes, suggesting that the investment in quality improvement is having an impact.

People With Cystic Fibrosis and Families

The CF Foundation works to provide people with CF and their families with information about various aspects of the disease, and to ensure that they have full access to care and appropriate therapies. The Education Committee, composed of multidisciplinary members of the CF care team, including people with CF and parents, identifies and fills gaps in educational materials. They also review materials from other sources and sanction appropriate resources with a CF Foundation Education Committee logo, signifying that they meet the committee's rigorous standards. Key educational materials cover infection control, nutrition, and pulmonary care, and other information for people and families who are newly diagnosed with CF. All of the material is tailored to the lay public, including adjustment to the standard reading level. Many of the resources are translated into Spanish to serve the growing Latino CF population in the United States.

Over the last few years the CF Foundation has also broadcast a popular series of live Web-casts on a variety of topics. Archived versions of the Web-casts serve as an ongoing resource to the CF community. All of these resources are available on the CF Foundation's Web site (http://www.cff.org).

The CF Services Pharmacy, a wholly owned subsidiary of the CF Foundation, serves nearly 8,000 patients and fills approximately 150,000 prescriptions per year. It also plays an important support and advocacy role for the CF community. Although nearly all people with CF have some insurance, many of them are underinsured. They are facing increasing insurance premiums, higher deductibles and copays, and reaching annual and lifetime benefit caps. The pharmacy maximizes reimbursement for customers by fully coordinating insurance benefits and identifying alternative sources of coverage whenever possible, including referrals to manufacturer's assistance programs as well as providing direct assistance to families with financial hardship. The pharmacy also sponsors family education days at CF care centers and supports various research projects of interest to the CF community.

Research commissioned by CF Services Pharmacy and conducted by Milliman (Seattle, Washington) suggests that people with CF and families are increasingly forgoing clinic visits or skipping essential medications due to financial constraints. To directly address some of these financial challenges, the CF Foundation recently launched the Cystic Fibrosis Patient Assistance Foundation. This program is funded exclusively by donations from the pharmaceuti-

cal industry, while all administrative costs are covered by the CF Foundation. This arrangement ensures that 100% of these donated dollars are used for direct patient assistance. The Cystic Fibrosis Patient Assistance Foundation helps people with CF and families with co-pays and co-insurance for FDA-approved inhaled medications and paired inhalation devices. The foundation also provides reimbursement counseling to maximize insurance benefits and makes referrals to alternative funding sources when appropriate. In addition, the CF Foundation continues to sponsor the CF Legal Hotline, which provides advice to people with CF and families dealing with insurance, benefits, and disability-related legal issues.

Recognizing that access-related issues pose an important threat to the quality of care and the availability of disease-modifying therapies to people with CF, the CF Foundation has developed a robust public-policy initiative aimed at influencing anticipated reforms in health care. The goals are to raise awareness among policy makers of the challenges faced by the underinsured, and to advance basic principles of health-care reform that, if implemented, would help to ensure that those with CF benefit from the advances in care and therapies. The data from the Patient Registry and the CF Services Pharmacy illustrate the tangible benefits of providing quality care for CF and the challenges facing people with CF and families in accessing necessary care and medications.

Role of Respiratory Therapists

RTs have made enormous contributions to the CF community. Many provide direct clinical care at the bedside in the in-patient setting and/or in the out-patient clinic setting. The great majority of this clinical care is delivered at CF-Foundation-accredited care centers. Accreditation by the CF Foundation requires a multidisciplinary care team, which includes RTs.

RTs are critical members of CF care teams and often play a leadership role. Nearly all patients are prescribed some form of airway clearance and/or exercise, and the majority are on one or more inhaled medications. The core responsibilities of RTs typically include: administering and teaching about the proper use of inhaled medications; teaching how to maintain and disinfect nebulizers and compressors; teaching airway-clearance techniques; assessing adherence to the airway-clearance regimen and inhaled medications; and promoting exercise. They must remain up to date on and practice within the constraints of current infection-control guidelines, to minimize the risk of spreading organisms. They often spend a great deal of time with patients and families and thus gain valuable insights into the psychosocial context. Such information is often important in developing an effective care plan. Some RTs contribute in other ways at the care centers, at times functioning as care center clinic coordinators, research coordinators, and/or quality-improvement team leaders.

RTs have also emerged as leaders in CF at the national and international levels. They serve on a variety of CF Foundation committees, including the North American CF Conference Planning Committee, the Pulmonary Guidelines Committee, and the Education Committee. They are prominently featured at the North American CF Conference as moderators and speakers at a variety of sessions. They not only play an active role in quality-improvement work at their own centers, but have also served as members of the CF Foundation's core benchmarking teams aimed at identifying "best practices." RTs have developed a CF-Foundation-sponsored, discipline-specific mentoring program to teach RTs new to CF about the nuances of CF care. A number of experienced RTs across the country have stepped forward to serve as mentors in this program. This peer-to-peer model of sharing knowledge cross-pollinates ideas and practices across care centers and benefits both the mentors and apprentices.

Given the many contributions of RTs to the CF community, the partnership between the American Association for Respiratory Care and the CF Foundation is logical and mutually beneficial. With the growth of the CF patient population and the increased number of inhaled medications either FDA approved or in clinical development for CF, we anticipate this partnership will grow stronger over time. One tangible example of the partnership between the 2 organizations is the recent publication of the CF Foundation's clinical practice guidelines on airway clearance and exercise, which were published in RESPIRATORY CARE.[8]

Summary

The CF Foundation is tackling this devastating disease with a comprehensive, state-of-the-art approach on the research and clinical fronts. The progress to date reflects contributions from many people working together as a team to accomplish our shared mission. Important members of Team CF include people with CF and families, health-care professionals at CF care centers, including RTs, scientists in academia and industry, donors, volunteers, and CF Foundation employees. The advances in research and clinical care are heartening, and the promising therapies that target the basic defect are exciting, but much work remains to be done. RTs will continue to play a vital role as we move forward.

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Discussion

Volsko: As educators of new and up-and-coming RTs we're molding the new professionals, and we would be remiss in teaching RTs if we did not instill the value of professional stewardship and volunteerism. I'd like to encourage other educators to take on that task, and to build into their programs volunteering for organizations such as the CF Foundation, and directing some of their student activities toward support of their activities.

Marshall: Thank you.

O'Malley: Why do you think more people don't take advantage of the CF Foundation Services Pharmacy?

Marshall: A lot of people are "locked in" to a particular pharmacy by their insurance, or they have a local pharmacy where they've developed a relationship. I don't know all the reasons, but I think choosing the CF Foundation Services Pharmacy is a "no-brainer." It's a for-profit subsidiary, but whatever profit they make is invested back into medical and research programs. So why it's not more heavily used, I don't fully understand.