Children's Hospital of Richmond at VCU

LGS RESEARCH MEETING OF THE MINDS

Leveraging the Resources of a Clinical Network to Optimize Care

The Cystic Fibrosis Experience

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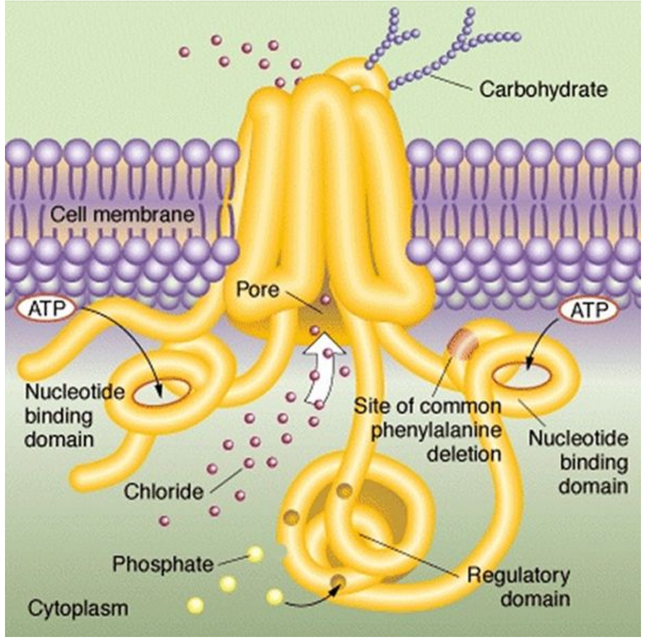
LGS FOUNDATION®
LENNOX-GASTAUT SYNDROME

Disclosures

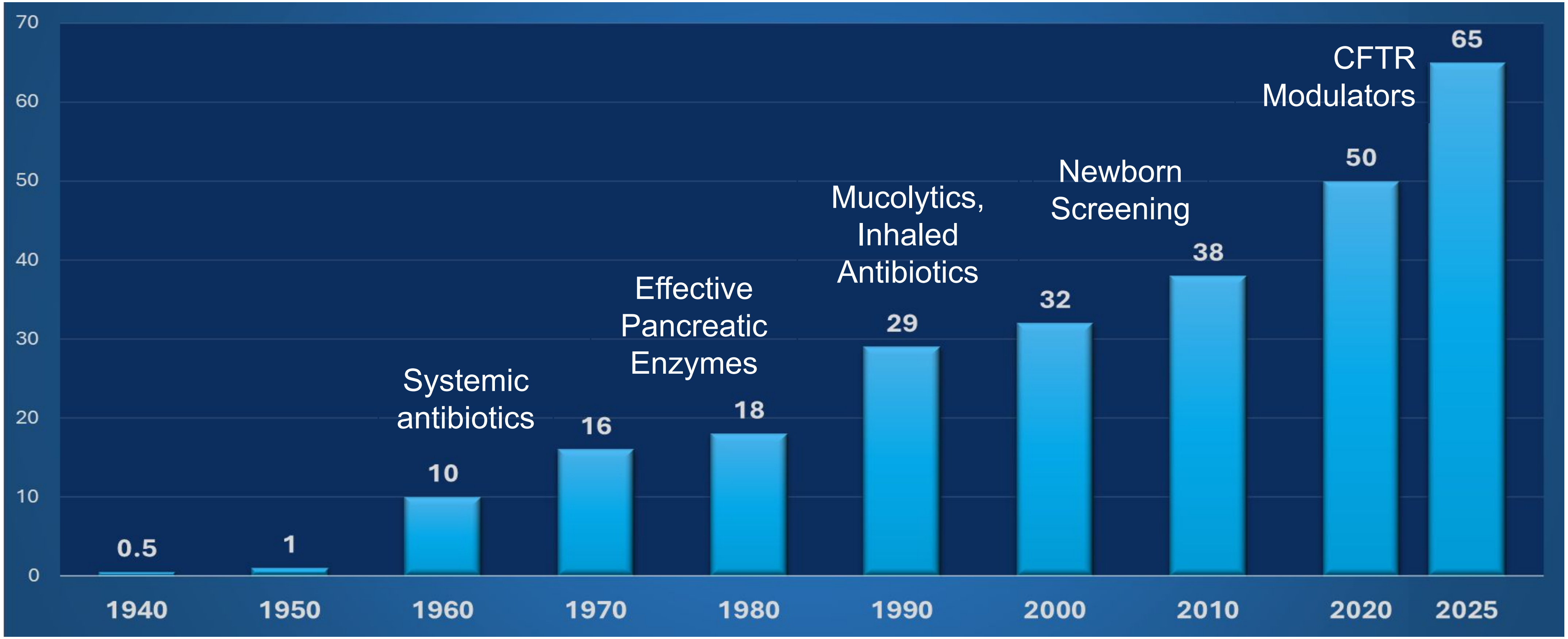
- Research Funding from Vertex Pharmaceuticals
- Consulting fees from Astra-Zeneca, Abbott Labs
- Consulting fees and research funding from the Cystic Fibrosis Foundation

Cystic Fibrosis (CF)

- CF is an autosomal recessive disease associated with an abnormality in the ion transporter protein called *cystic fibrosis transmembrane conductance regulator*
- Resulting abnormal secretions impact the
  - **Lungs:**
    - **chronic infection → bronchiectasis → respiratory failure**
  - **Digestive Tract:**
    - **exocrine pancreatic insufficiency → malabsorption → malnutrition**
    - pancreatic fibrosis → diabetes mellitus
    - biliary obstruction, ileal obstruction
  - Sweat glands:
    - salty sweat → electrolyte disturbances (and our diagnostic test)
  - Other:
    - Congenital bilateral absence of the vas deferens
    - Nasal polyps, chronic sinus disease



Median Predicted Survival (years)



Most importantly:

Clinicians learning how to better manage airway infection and nutrition by using all available therapies in a consistent and proactive way

Cystic Fibrosis Foundation (CFF)

- Founded in 1955 by a consortium of parents, physicians, and scientists.

- *Current Mission: 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.*
  - Aggressively raises money
  - Promotes and funds new research
  - Accredits the structure of CF care centers and helps to fund that structure
  - Encourages state of the art approaches to care
  - Maintains a national patient registry
  - Partners with patients and families

The CFF promotes and funds new research

- Works with NIH and supplements its granting process
- Funds new start-up companies to develop promising treatments *(venture philanthropy)*
- Funds and helps guide academic investigator-initiated research
- Provides funding to support early development of academic scientists
- Supports and facilitates clinical research
  - Therapeutic Development Network
    - Eighty CF centers collaborate on clinical trials of new therapies, with a subgroup of National Resource Centers with special expertise in developing and measuring CF clinical trial outcomes
  - Data safety monitoring board of CF experts provides oversight for all clinical trials
  - Success with Therapies Research Consortium
    - Fifteen CF centers collaborate on research promoting adherence and disease self-management
- Maintains its own research facility to advance development of cutting edge therapeutics
- Sponsors several regular and ad hoc research conferences every year

The CFF accredits the structure of CF care centers and helps to fund that structure

- CF care centers must have adequate support staff
  - Pulmonary and other subspecialty physicians
    - Grant programs to support involvement by GI, Endocrine and Adult Pulmonary
  - Respiratory Therapy, Nutrition, Social Work, Nursing (clinical coordinator)
  - Mental Health, Pharmacy, and Physical Therapy are not required but are supported by special grants
  - Adult CF care program to which all patients are transitioned by age 21
- CF care centers must have adequate lab capabilities
  - Special microbiology techniques to isolate important CF organisms
  - Reliable sweat test capabilities
- Care centers provide annual "periodic status reports" and are visited by CF physician site visitors every 3–5 years.
- The CFF provides grant funding to ensure that the resources are available.

The CFF spreads of state-of-the-art approaches to care

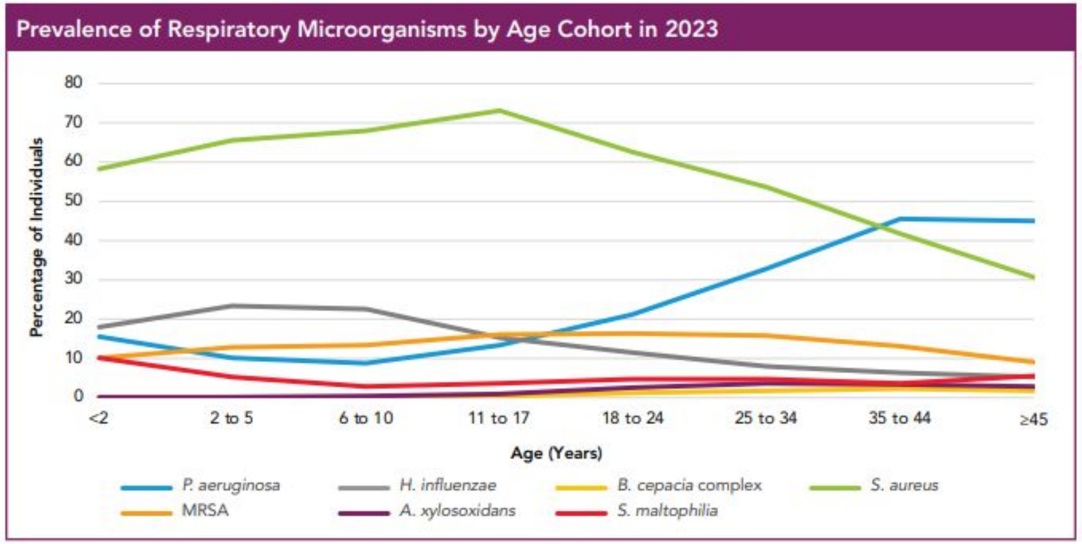
- Annual North American CF meeting consists of short courses, symposia, workshops, poster sessions, and committee meetings
  - Reports of basic science and clinical research, quality improvement, and clinical updates
  - Multidisciplinary and multispecialty
  - Networking is promoted and accomplishments are celebrated
- Discipline-specific mentoring programs
  - Gastroenterology, endocrinology
  - Nursing, nutrition, social work, respiratory therapy, pharmacy, physical therapy
- Generation of consensus statements and guidelines (often in collaboration with the European CF Society)
- Quality Improvement training to support care centers' efforts to put care recommendations into practice

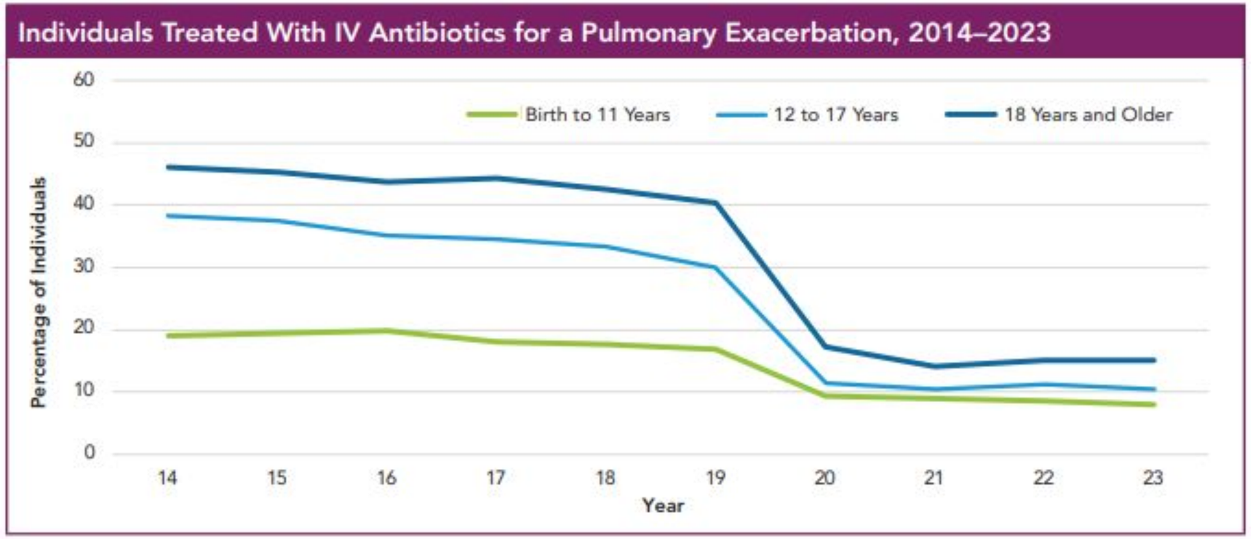
Clinical Care Guidelines (36)

- **Models of care**
  - The care model
  - The CF care team
  - Post transplant care
  - CF palliative care
- **Age specific monitoring guidelines**
  - Newborn screening
  - Infant care
  - Preschool-aged care
  - Adult care
  - Management of CRMS
- **Diagnosis**
  - Sweat testing
  - CF diagnosis
- **Infection Prevention and Control**
  - Infection prevention and control
  - Allergic bronchopulmonary aspergillosis
  - Eradication of Pseudomonas aeruginosa
  - Non-tuberculous mycobacteria
- **Respiratory Care**
  - CFTR modulator therapy
  - Care of individuals with advanced lung disease
  - CF airway clearance therapies
  - Chronic medications to maintain lung health
  - Pulmonary exacerbations
  - Lung transplant referral guidelines
  - Pneumothorax and hemoptysis
- **Nutrition and GI Care**
  - Colorectal cancer screening
  - Enteral tube feeding.
  - Nutrition in pediatrics
  - Nutrition in children and adults
  - Pancreatic enzymes
  - Vitamin D deficiency
  - Management of GI aspects of CF
- **CF Related Conditions**
  - Pain
  - CF-related diabetes
  - Bone disease
  - Liver disease
  - Screening and treating depression and anxiety
  - Endocrinology
  - ENT care

The CFF National Patient Registry (CFFNPR)

- Contains demographic and clinical data on >98% of all patients attending accredited care centers
  - Care Center funding is proportional to data entry which is therefore maximized
  - The CFFNPR has been duplicated (more or less) by countries around the world
- Its content and use have evolved over the last 50 years.
  - Initially used to offer a snapshot of the CF population


Prevalence of Respiratory Microorganisms by Age Cohort in 2023

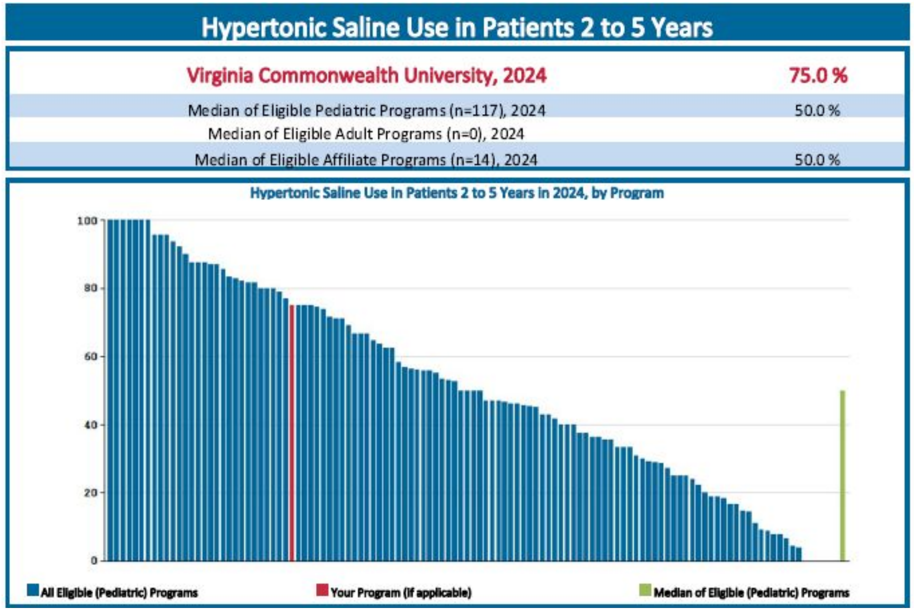

Individuals Treated With IV Antibiotics for a Pulmonary Exacerbation, 2014–2023

The CFF National Patient Registry (CFFNPR)

- Over the last 30 years it has taken on an essential role for hypothesis-driven investigations of disease associations
  - Relationship of airway microbiology to pulmonary outcomes and mortality
  - Relationships of socioeconomic status and race/ethnicity to disease outcomes
  - Real-world effectiveness of therapies (comparative effectiveness research)
  - Linkages with other registries
    - US Census data (by zip code of residence)
    - United Network for Organ Sharing (UNOS) database
    - Children’s Hospital Association Pediatric Health Information System (PHIS)
    - Other international CF databases
- CFFNPR analyses are often the entry point for new CF investigators and the starting point for generating new hypotheses regarding novel disease-altering therapies

The CFF National Patient Registry (CFFNPR)

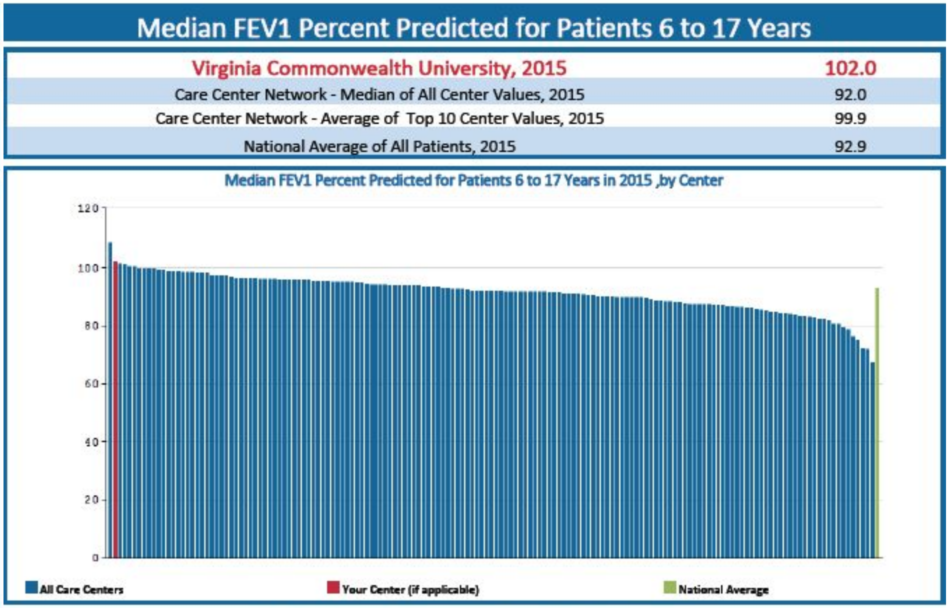
- Over the last 20 years, it has been used to compare processes and outcomes among care centers
  - Variation in disease outcome leads to discoveries regarding how best to provide care



Hypertonic Saline Use in Patients 2 to 5 Years

Virginia Commonwealth University, 2024	**75.0 %**
Median of Eligible Pediatric Programs (n=117), 2024	50.0 %
Median of Eligible Adult Programs (n=0), 2024	
Median of Eligible Affiliate Programs (n=14), 2024	50.0 %

Hypertonic Saline Use in Patients 2 to 5 Years in 2024, by Program



Median FEV1 Percent Predicted for Patients 6 to 17 Years

Virginia Commonwealth University, 2015	**102.0**
Care Center Network - Median of All Center Values, 2015	92.0
Care Center Network - Average of Top 10 Center Values, 2015	99.9
National Average of All Patients, 2015	92.9

Median FEV1 Percent Predicted for Patients 6 to 17 Years in 2015 ,by Center

The CFF National Patient Registry (CFFNPR)

- Over the last 20 years, it has been used to compare processes and outcomes among care centers as a tool for quality improvement
  - Variation in disease outcome leads to discoveries regarding how best to provide care
  - Variations in outcomes and processes show opportunities for improvement and allow programs to track the effect of their own internal attempts to improve.

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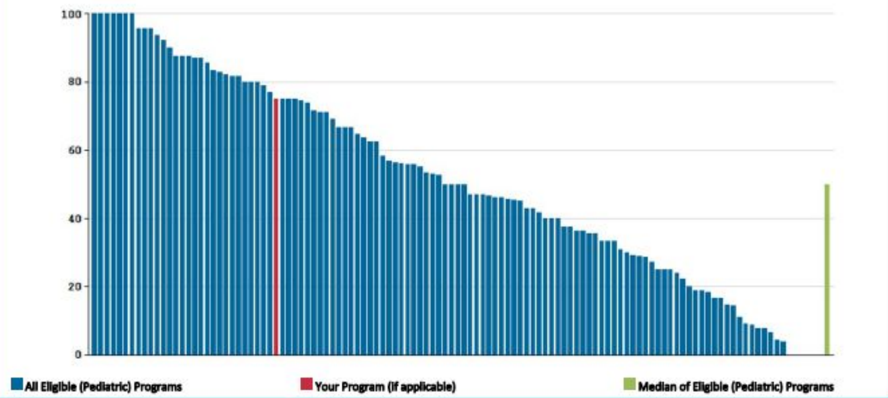
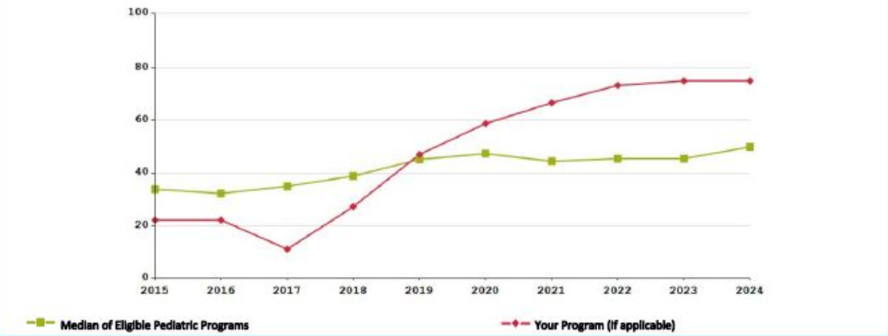


Hypertonic Saline Use in Patients 2 to 5 Years, 2015-2024



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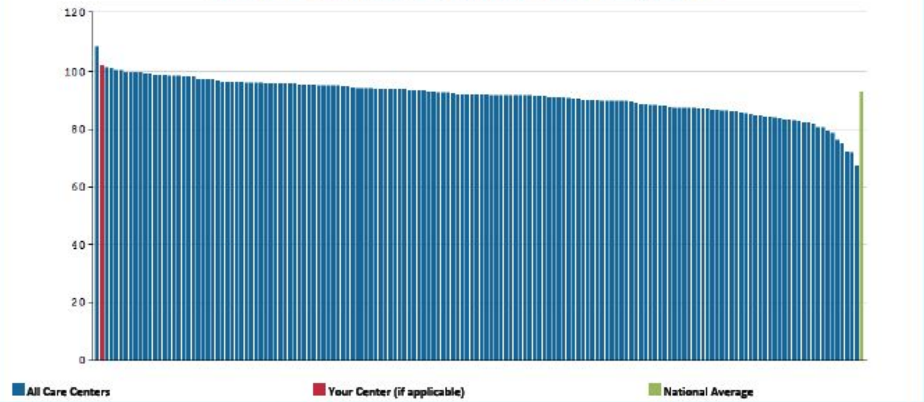
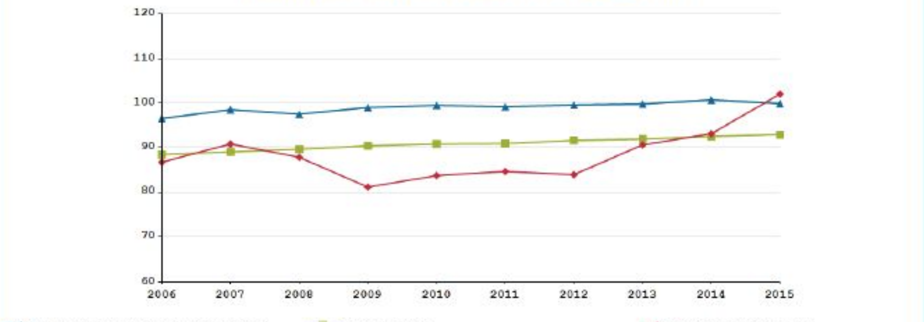


Median FEV1 Percent Predicted for Patients 6 to 17 Years,2006-2015



The CFF National Patient Registry (CFFNPR)

- The CFFNPR is also used to assist at clinic encounters

Patient Summary Report for : [redacted] Age 6.7 Years Date of Birth [redacted] CFF ID: 1646031

Diagnosis Information

Diagnosis Date : 10/26/2018

Diagnosis : Cystic Fibrosis

Mutation 1 : F508del

Poly T Tract : Poly TG Repeat :

Mutation 2 : F508del

Poly T Tract : Poly TG Repeat :

Sweat Test Date : 01/02/2019 Sweat Test Value : 103

Recent Clinical Dates and Values

Clinic Visit : 04/02/2025

Hospitalization From : 05/23/2023 To : 06/06/2023

Reason : Pulmonary Exacerbation

Home IV From : To :

Nutritionist/Dietician : 04/02/2025 Pharmacist: 12/11/2024

RT: 12/11/2024 PT: 04/02/2025

Social Worker : 09/04/2024

	% Predicted	Date	Raw Value
FEV1 % Predicted :	92.18	04/02/2025	0.95
FVC % Predicted :	112.66	04/02/2025	1.26
FEF25-75 % Predicted :			

Primary ACT : HF Chest wall Oscillation

Weight (kgs) : 19.10 Height (cm) : 107.80

Weight For Length : BMI Percentile : 74.77

BMI Value :

Chest X-ray (year) : 2024 Pregnancy (year) :

Dexa Scan (year) : IgE Screening (year) : 2024

Depression Screening (year) : 2024

Anxiety Screening (year) : 2024

Transplants : None

CFF QI Efforts to improve outcomes

- Patient registry providing data support with patient and center-level reports
- Transparency of center-specific processes and outcomes
- Benchmarking
- Teach quality improvement to the care teams
  - “Learning and Leadership Collaboratives”
  - “CF Learning Network”

Why Quality Improvement? Care guidelines are not enough

- Konstan MW et al. *Pediatr Pulmonol.* 1999;28:242-247 showed that adherence to basic CF guidelines was poor:

CFF guidelines recommended, at minimum	% of patients receiving this
– Quarterly visits to the CF center	58%
– Biannual pulmonary function testing	76%
– Annual airway cultures	79%
– Annual chest x-ray	68%

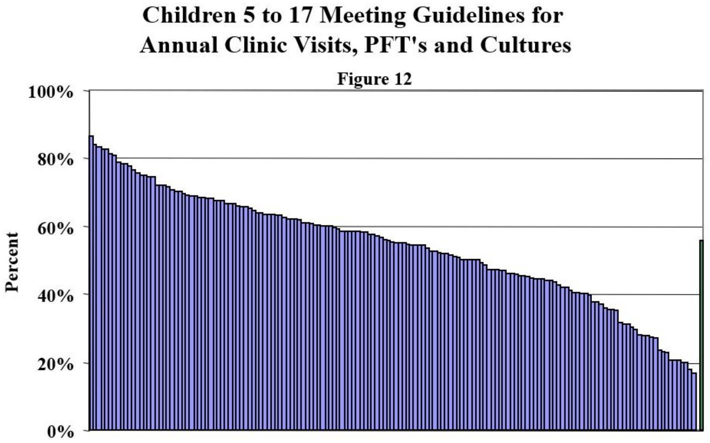

Children 5 to 17 Meeting Guidelines for Annual Clinic Visits, PFT's and Cultures

Figure 12

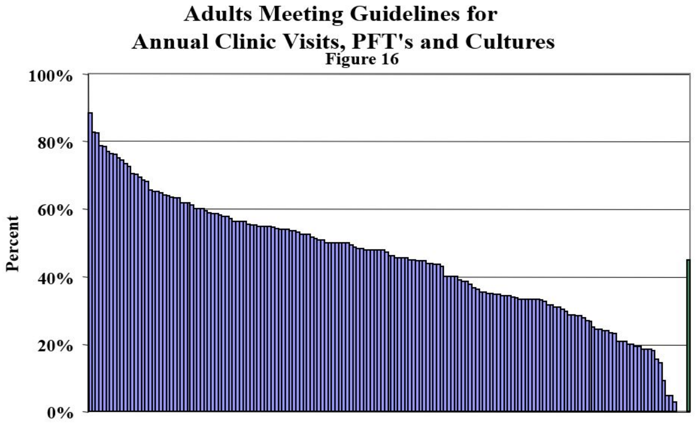
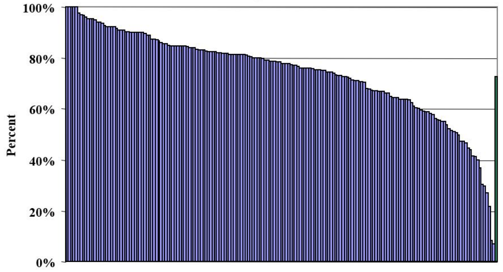

Adults Meeting Guidelines for Annual Clinic Visits, PFT's and Cultures

Figure 16

Care guidelines are not enough

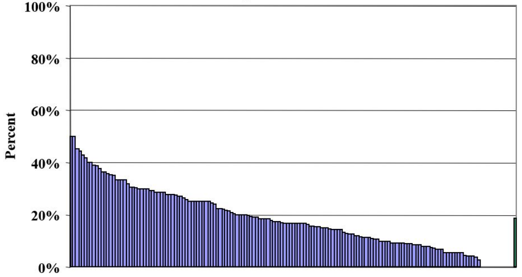
- Use of other evidence-based screening and treatments (2003):



Glucose Screening in Non-Diabetics >13 Years, by Center

(Random, Fasting, or OGTT)

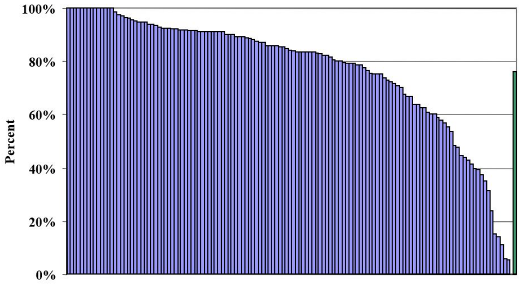
Figure 35



Home Supplemental Feeding Rates in Children in Nutritional Failure, by Center

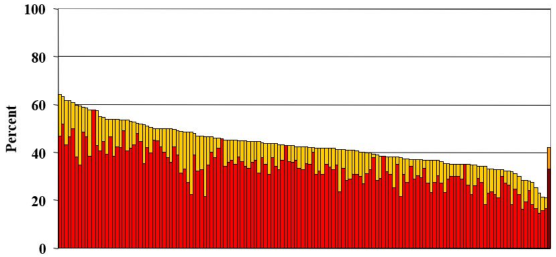
(gastrostomy, nasogastric, parenteral, jejunostomy)

Figure 22



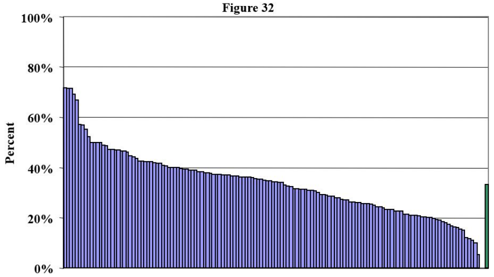
Children in Nutritional Failure who saw a Nutritionist in 2003

Figure 23



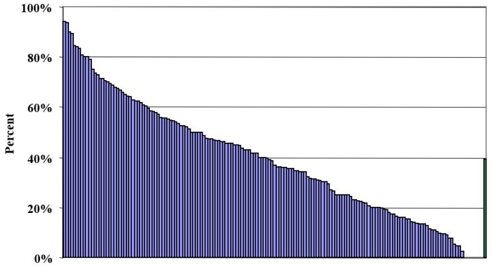
Children in Nutritional Failure or at Risk of Failure, by Center

Figure 21



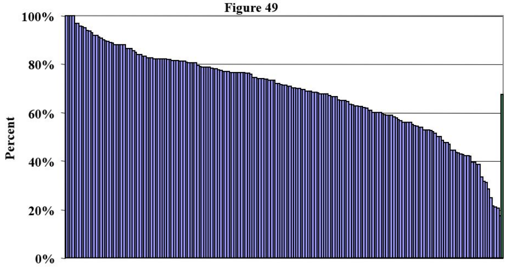
Acute Exacerbations in Children 5 to 17, by Center

Figure 32



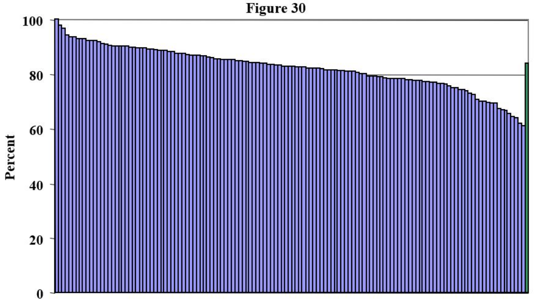
Chronic Macrolide Use in "Eligible" Patients 6 to 30, by Center

Figure 47



Pulmozyme Use in Patients >5 Years with FEV1<90% Predicted, by Center

Figure 49



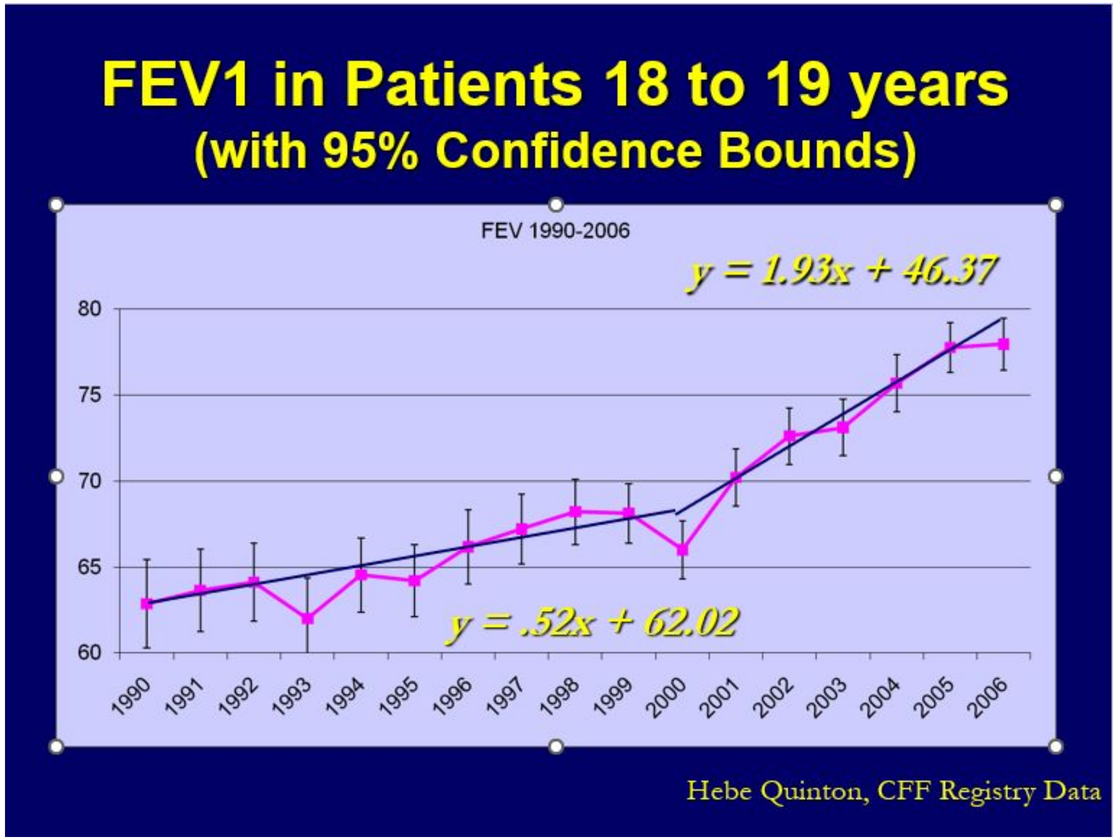
Median FEV_1 Percent Predicted for Patients 13 to 17, by Center

Figure 30

Variation in processes and outcomes

- The CFFNPR showed that better adherence to guidelines and better outcomes are not correlated with
  - Reputation
  - Research activity
  - Experience (center size)
  - Variation in risk factors (Social determinants, intrinsic disease severity)
- Beginning in the early 2000's, the CFF embraced an aggressive QI program
  - Tapped external expertise from Institute for Healthcare Improvement, National Initiative for Children's Healthcare Quality, and The Dartmouth Institute
  - Began a series of "Learning and Leadership Collaboratives" to train CF care teams on QI methods
  - Established the CF Learning Network, initially supported by the Cincinnati Children's Center for Healthcare Quality and now run internally to coordinate QI activities across the CF care network
    - A major theme is "co-production", ie, collaboration with parents and patients

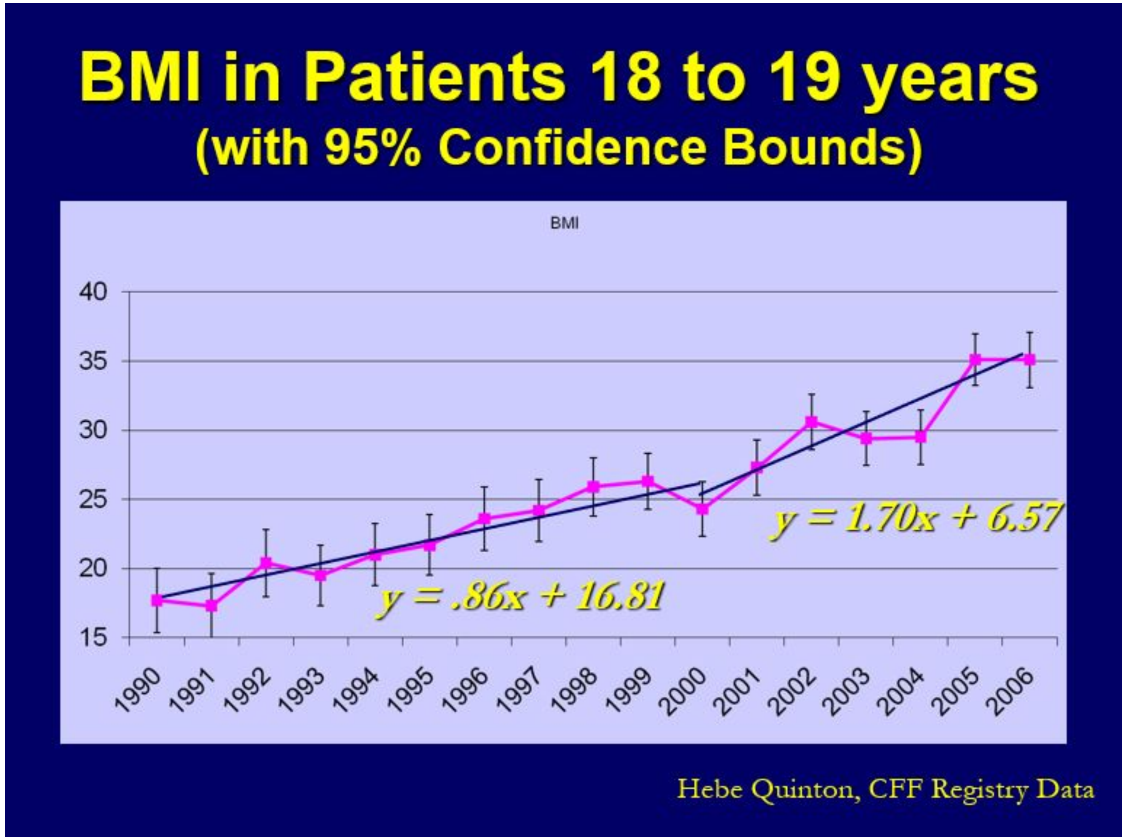
Impact of CF QI



FEV1 in Patients 18 to 19 years

(with 95% Confidence Bounds)

Hebe Quinton, CFF Registry Data



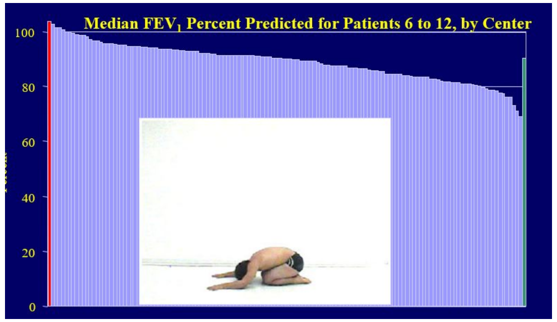
BMI in Patients 18 to 19 years

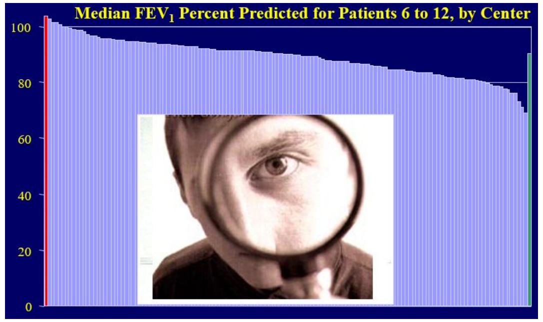
(with 95% Confidence Bounds)

Hebe Quinton, CFF Registry Data

Benchmarking

- Randomized clinical trials represent the gold standard approach to determining efficacy of treatments
  - However, in rare diseases we cannot do large clinical trials to test every possible question
  - Furthermore, effective chronic disease healthcare delivery is a complex undertaking, and requires more than just knowing what to prescribe
- The benchmarking project used CF Registry data to find the best performing care programs regarding pulmonary and nutritional outcomes and sent a complete multidisciplinary care team to visit them and examine their approach.
  - This was done separately for adult and pediatric programs





Benchmarking – recurring themes

- High-functioning team ensures consistent care
  - Strong leadership
  - “Intentional consensus” regarding care approaches
  - Good communication and cooperation among team members
  - Pre-clinic planning meetings
- High expectations for outcomes among providers and families
- Early and aggressive management
  - Little reliance on “rescues”
- Patients/families are engaged, empowered, and participate on the team
  - Well informed on disease management and its rationale
  - Their expectations provides additional assurance that they will receive the right treatment at the right time

The keys to our success in CF care

- Strong and flexible leadership from the CF Foundation
  - Fundraising
  - Collaboration with partners (patients and families, industry, NIH, international)
  - Adaptation to new ideas (registry, QI, parent/patient involvement, industry partnerships, mental health, disparities
- The CFF National Patient Registry
  - Research, clinical care and QI
- Clinical care guidelines and their active dissemination
  - With tracking and support from the CF registry
- Multidisciplinary team building
  - NA CF Conference

Thank you for your attention

Questions?