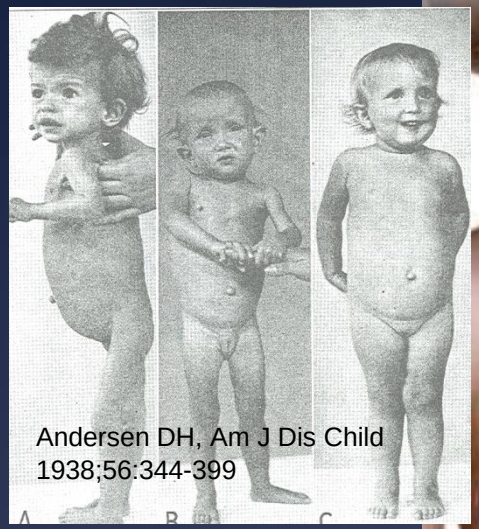
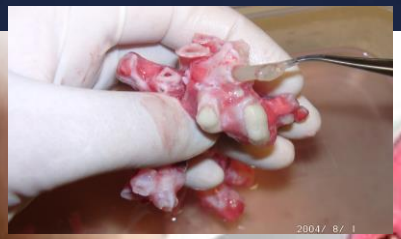
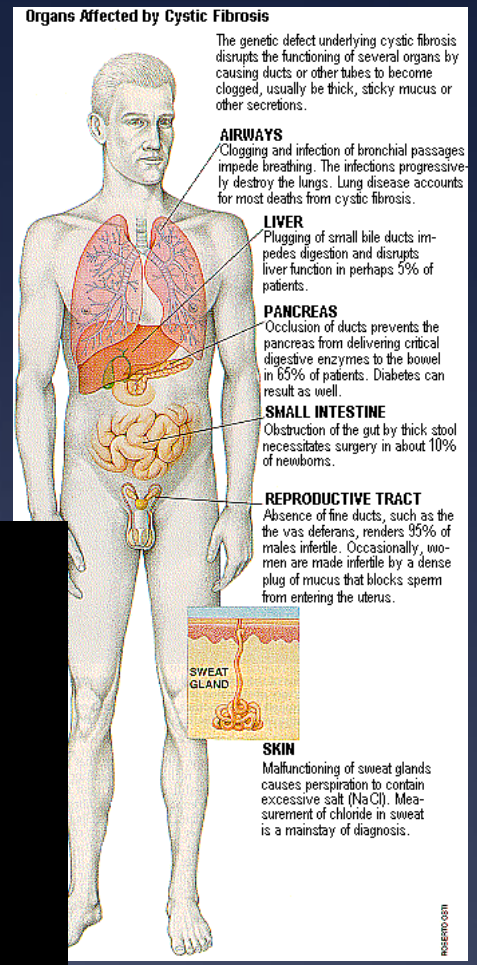
Cystic Fibrosis

What do you think of when someone says Cystic Fibrosis?



Andersen DH, Am J Dis Child 1938;56:344-399



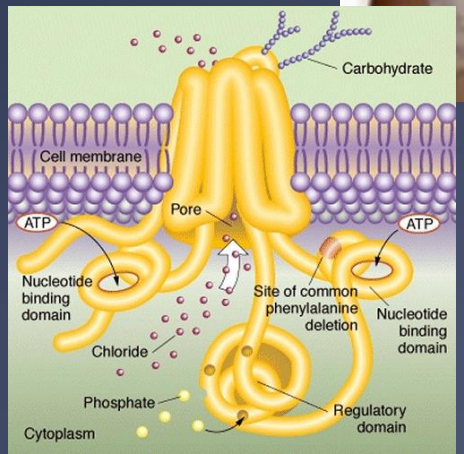


Cystic Fibrosis (CF) is an autosomal recessive disease affecting pulmonary, gastrointestinal, and exocrine gland function .

CF is the most common life shortening genetic disease in the Caucasian population.

Mutations in the gene that encodes for the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein cause CF

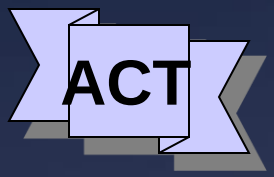
CFTR



Daily Schedule of a Child with CF

* Get up in the morning and before breakfast

Inhaled bronchodilator (5-10 minutes)



Inhaled mucus modulator (pulmozyme or hypertonic saline) (10-20 minutes)

Airway clearance (20-30 minutes)

Inhaled antibiotic (TOBI/Cayston) (7-20 minutes)

Breakfast (Vitamins and enzymes (possible acid blockade))

Lunch (enzymes)

ACT (before lunch or after school)

Dinner (enzymes/ acid blockade)

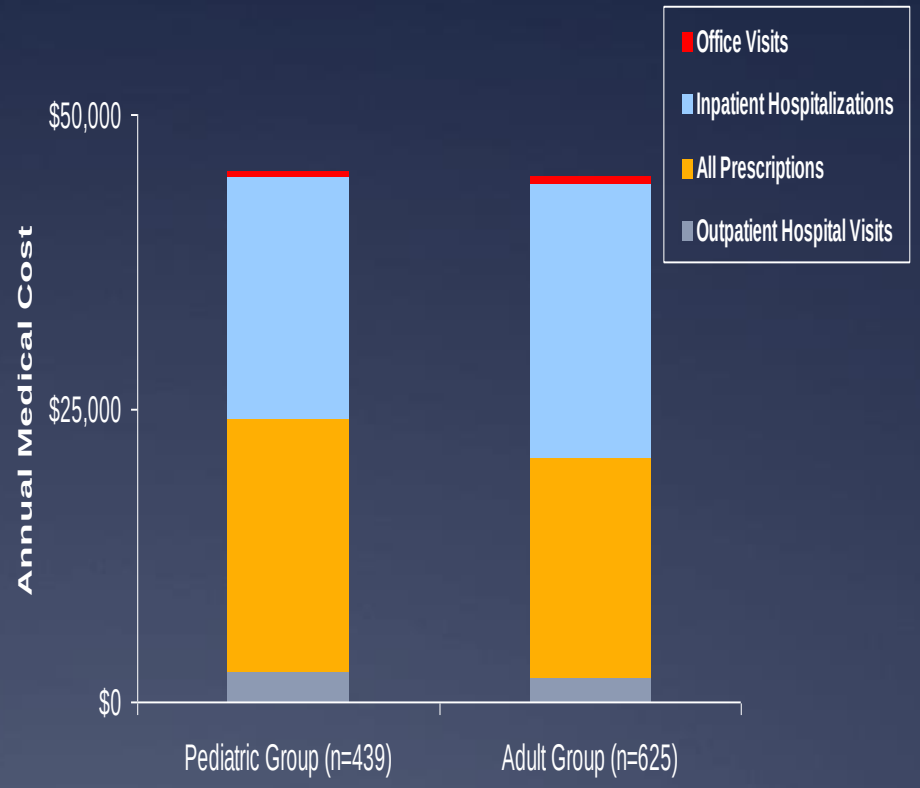
After dinner ACT

2.5 to 4.5 hours at a minimum of daily therapy

+ Liver disease, ++++Diabetes, +Anxiety/Depression

Daily Costs of Cystic Fibrosis

- Monetary
- Time (patient and family)
- Resources
- Quality of life



What does a new parent think of when the doctor says Cystic Fibrosis?

Initially they only feel:

Fear

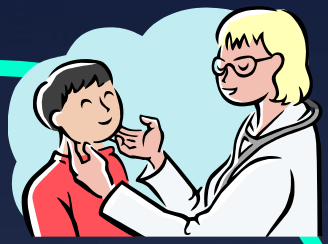
Anxiety

Dread

Panic

Sadness

Rage



BEDSIDE

CF clinic care

Comprehensive Multidisciplinary Care

Quality Improvement Program

Community Advocacy/Education

CF clinical research

Clinical Trial Network : Therapeutic Development Network (TDN)

Industry and PI initiated studies

QI Program

Community and patient education and advocacy

BENCH

CF basic science research

Small molecules that activate and correct CFTR

Gene editing / Stem cells/repairing the damage

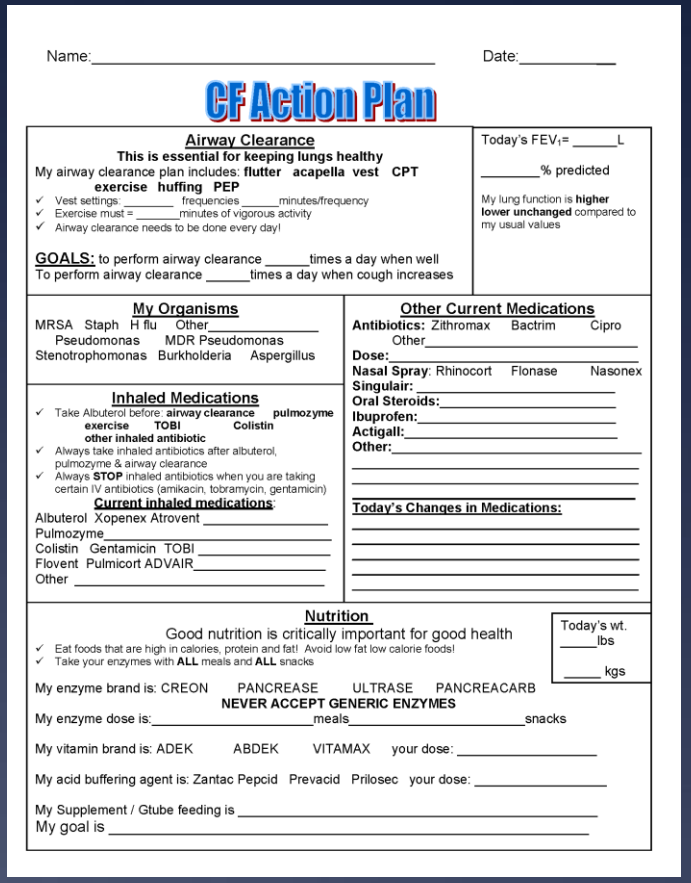
Calming the inflammatory response

Examining Pseudomonas aeruginosa

Examining the microbiome

Comprehensive Practice Guidelines

- Quarterly visits (at a minimum) monitoring growth, pulmonary function, liver function, screening for CFRD, Anxiety and depression
- Multidisciplinary approach (nutrition, social work, nursing, respiratory therapy, physical therapy, psychology, pharmacology, research coordination, medical treatment, patient and family advisory board)
- Treatment Guidelines: developed by multidisciplinary teams of experts and are based on a nationwide data that is collected from all accredited CF Centers The guidelines are evidence based (Inpatient and Outpatient practice guidelines and age specific) Annual Labs and Routine Microbiology Surveillance
- Education: families, patients, schools, communities, work places, coaches….



Name:_____ Date:_____

CF Action Plan

Airway Clearance
This is essential for keeping lungs healthy
My airway clearance plan includes: **flutter acapella vest CPT exercise huffing PEP**
- ✓ Vest settings: _____ frequencies _____minutes/frequency
- ✓ Exercise must = _____minutes of vigorous activity
- ✓ Airway clearance needs to be done every day!

GOALS: to perform airway clearance _____times a day when well
To perform airway clearance _____times a day when cough increases

Today's FEV_1= _____L
_____% predicted
My lung function is **higher lower unchanged** compared to my usual values

My Organisms
MRSA Staph H flu Other_____
Pseudomonas MDR Pseudomonas
Stenotrophomonas Burkholderia Aspergillus

Inhaled Medications
- ✓ Take Albuterol before: **airway clearance pulmozyme exercise TOBI Colistin other inhaled antibiotic**
- ✓ Always take inhaled antibiotics after albuterol, pulmozyme & airway clearance
- ✓ Always **STOP** inhaled antibiotics when you are taking certain IV antibiotics (amikacin, tobramycin, gentamicin)

Current inhaled medications:
Albuterol Xopenex Atrovent _____
Pulmozyme_____
Colistin Gentamicin TOBI _____
Flovent Pulmicort ADVAIR_____
Other _____

Other Current Medications
Antibiotics: Zithromax Bactrim Cipro
Other_____
Dose:_____
Nasal Spray: Rhinocort Flonase Nasonex
Singulair:_____
Oral Steroids:_____
Ibuprofen:_____
Actigall:_____
Other:_____

Today's Changes in Medications:

Nutrition
Good nutrition is critically important for good health
- ✓ Eat foods that are high in calories, protein and fat! Avoid low fat low calorie foods!
- ✓ Take your enzymes with **ALL** meals and **ALL** snacks

Today's wt.
_____lbs
_____ kgs

My enzyme brand is: CREON PANCREASE ULTRASE PANCREACARB
NEVER ACCEPT GENERIC ENZYMES
My enzyme dose is:_____meals_____snacks

My vitamin brand is: ADEK ABDEK VITAMAX your dose: _____

My acid buffering agent is: Zantac Pepcid Prevacid Prilosec your dose: _____

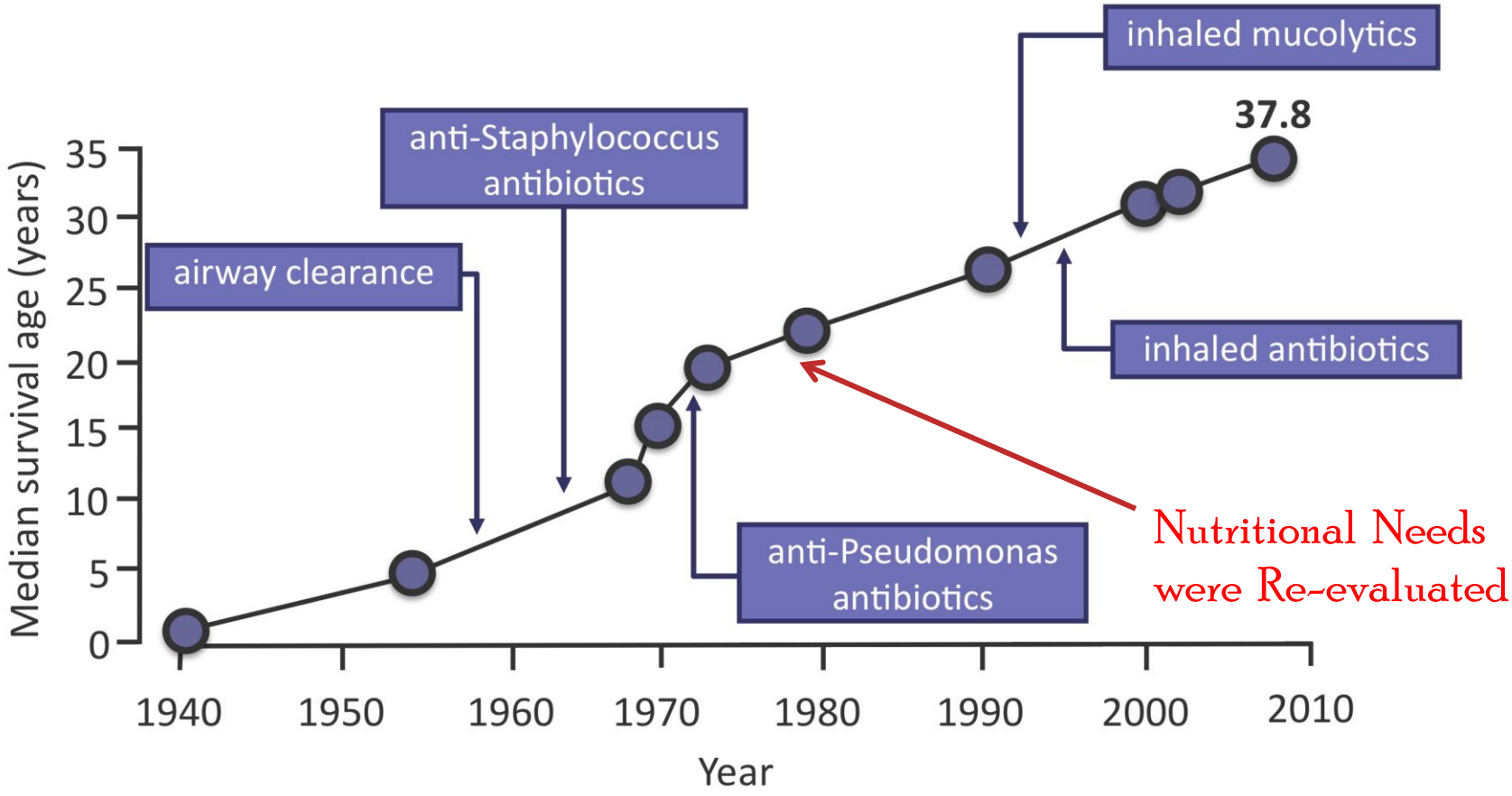
My Supplement / Gtube feeding is _____
My goal is _____

Model of care

- Weekly meetings: Review and discuss patients
- Biweekly Center meetings: Review age specific treatment/care guidelines
- Patient reviews: Review problems since last visit, goals from last visit
- Biweekly QI meetings
- Monthly Patient and Family Advisory Boards
- Quarterly educational meetings
- Annual Retreats

Cystic fibrosis: median survival age, 1940-2007

In 2016 > 40 yrs

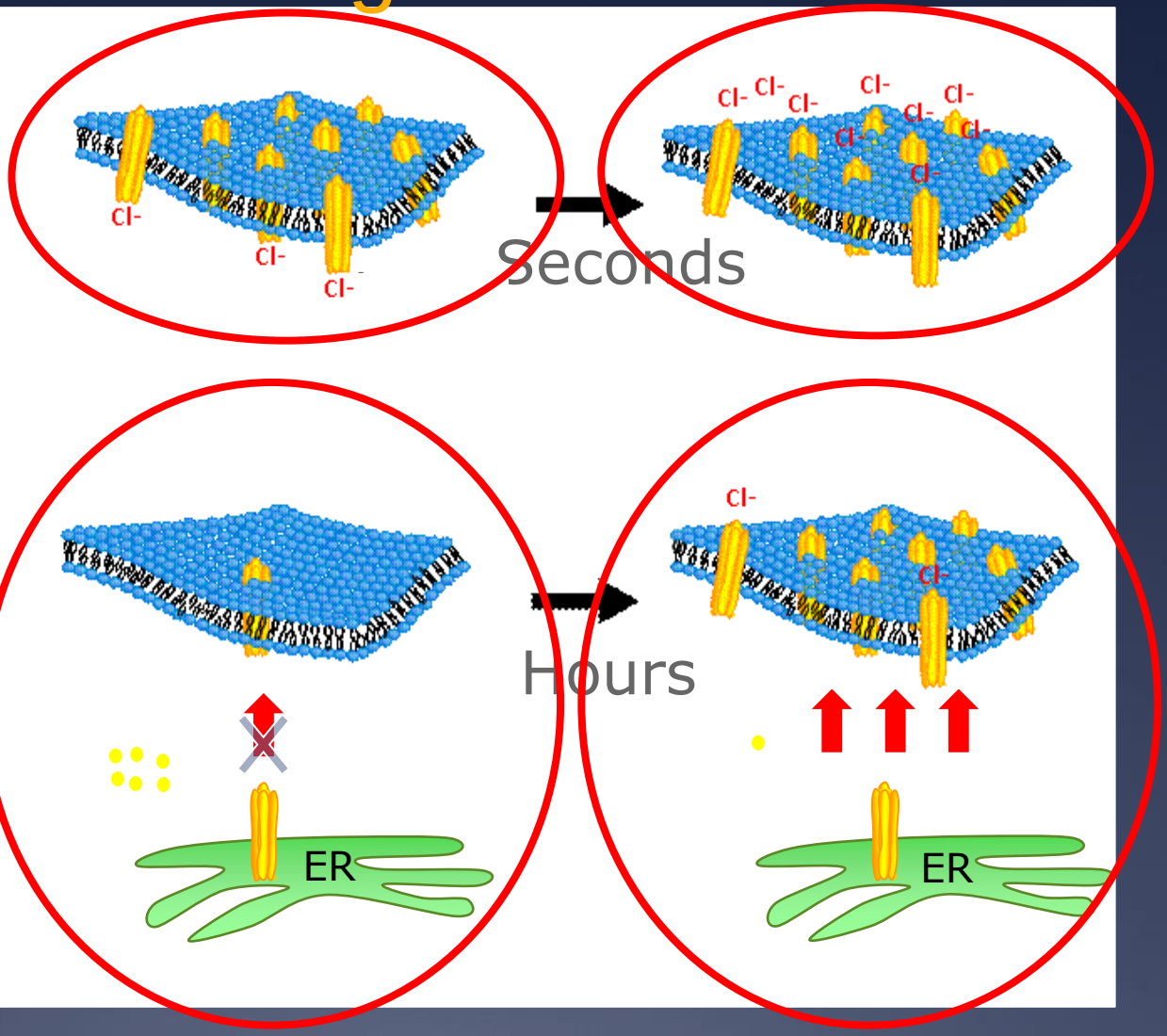


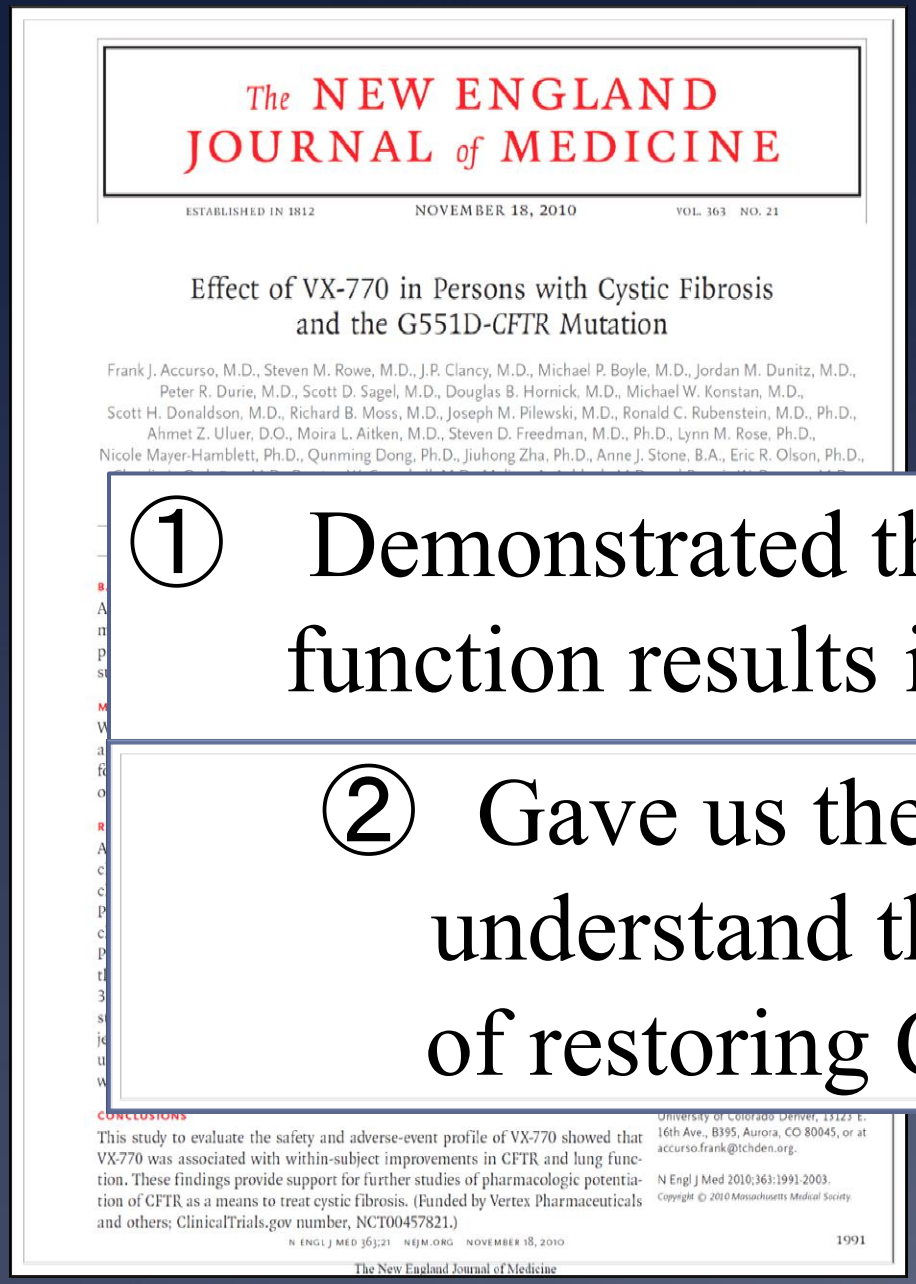
Cystic Fibrosis Foundation Registry, 2007.

Drug Devlopment: Approach to Restoring CFTR Function

Potentiators:
Increase the flow of ions through CFTR present
at the cell surface

Correctors:
Increase the cellular processing and delivery of CFTR proteins to the cell surface





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 18, 2010 VOL. 363 NO. 21

Effect of VX-770 in Persons with Cystic Fibrosis and the G551D-*CFTR* Mutation

Frank J. Accurso, M.D., Steven M. Rowe, M.D., J.P. Clancy, M.D., Michael P. Boyle, M.D., Jordan M. Dunitz, M.D., Peter R. Durie, M.D., Scott D. Sagel, M.D., Douglas B. Hornick, M.D., Michael W. Konstan, M.D., Scott H. Donaldson, M.D., Richard B. Moss, M.D., Joseph M. Pilewski, M.D., Ronald C. Rubenstein, M.D., Ph.D., Ahmet Z. Uluer, D.O., Moira L. Aitken, M.D., Steven D. Freedman, M.D., Ph.D., Lynn M. Rose, Ph.D., Nicole Mayer-Hamblett, Ph.D., Qunming Dong, Ph.D., Jiuhong Zha, Ph.D., Anne J. Stone, B.A., Eric R. Olson, Ph.D.,

CONCLUSIONS

This study to evaluate the safety and adverse-event profile of VX-770 showed that VX-770 was associated with within-subject improvements in CFTR and lung function. These findings provide support for further studies of pharmacologic potentiation of CFTR as a means to treat cystic fibrosis. (Funded by Vertex Pharmaceuticals and others; ClinicalTrials.gov number, NCT00457821.)

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N Engl J Med 2010;363:1991-2003.

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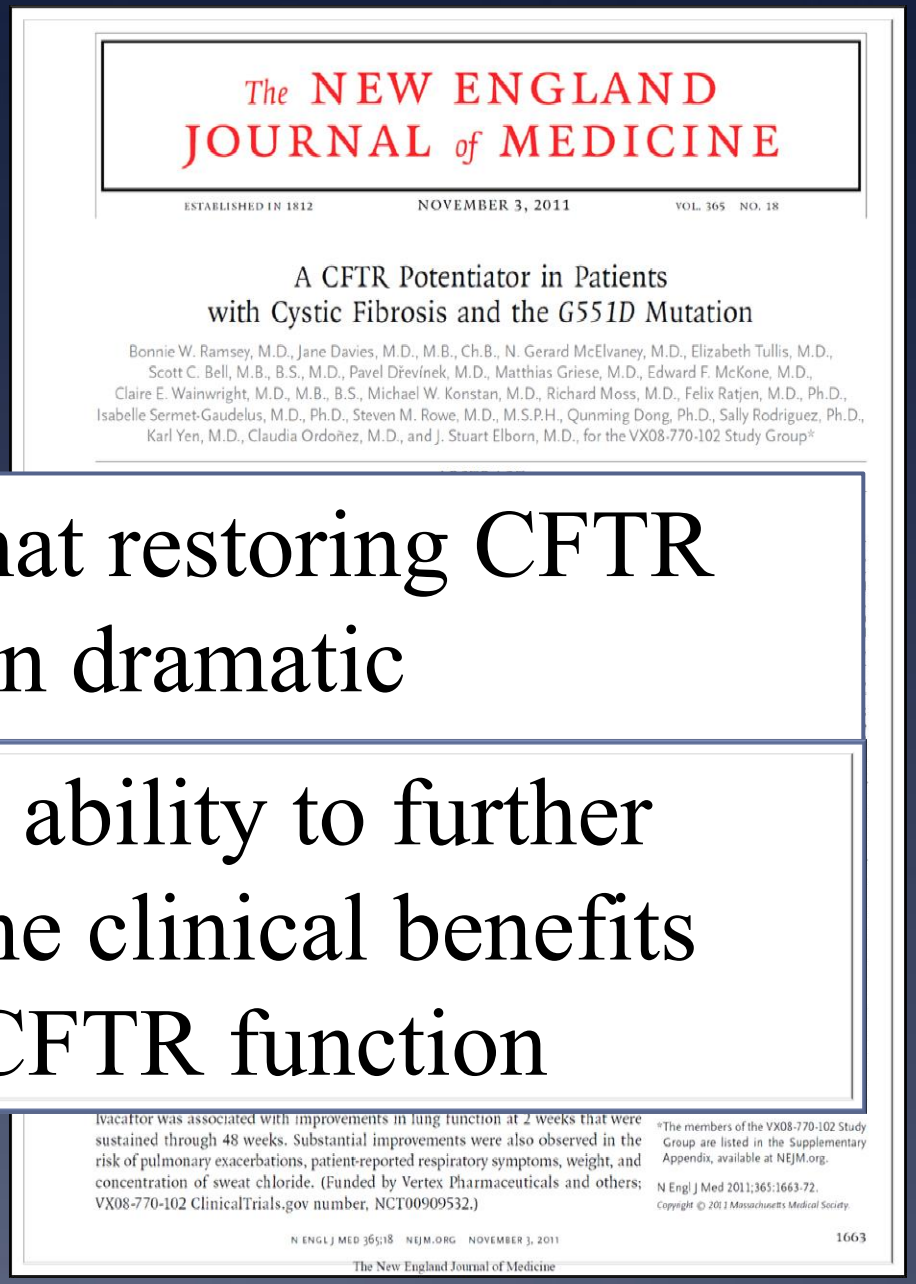
N ENGL J MED 363;21 NEJM.ORG NOVEMBER 18, 2010

1991

The New England Journal of Medicine



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 3, 2011 VOL. 365 NO. 18

A CFTR Potentiator in Patients with Cystic Fibrosis and the *G551D* Mutation

Bonnie W. Ramsey, M.D., Jane Davies, M.D., M.B., Ch.B., N. Gerard McElvaney, M.D., Elizabeth Tullis, M.D., Scott C. Bell, M.B., B.S., M.D., Pavel Dřevínek, M.D., Matthias Griese, M.D., Edward F. McKone, M.D., Claire E. Wainwright, M.D., M.B., B.S., Michael W. Konstan, M.D., Richard Moss, M.D., Felix Ratjen, M.D., Ph.D., Isabelle Sermet-Gaudelus, M.D., Ph.D., Steven M. Rowe, M.D., M.S.P.H., Qunming Dong, Ph.D., Sally Rodriguez, Ph.D., Karl Yen, M.D., Claudia Ordoñez, M.D., and J. Stuart Elborn, M.D., for the VX08-770-102 Study Group*

Ivacaftor was associated with improvements in lung function at 2 weeks that were sustained through 48 weeks. Substantial improvements were also observed in the risk of pulmonary exacerbations, patient-reported respiratory symptoms, weight, and concentration of sweat chloride. (Funded by Vertex Pharmaceuticals and others; VX08-770-102 ClinicalTrials.gov number, NCT00909532.)

*The members of the VX08-770-102 Study Group are listed in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2011;365:1663-72.

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N ENGL J MED 365;18 NEJM.ORG NOVEMBER 3, 2011

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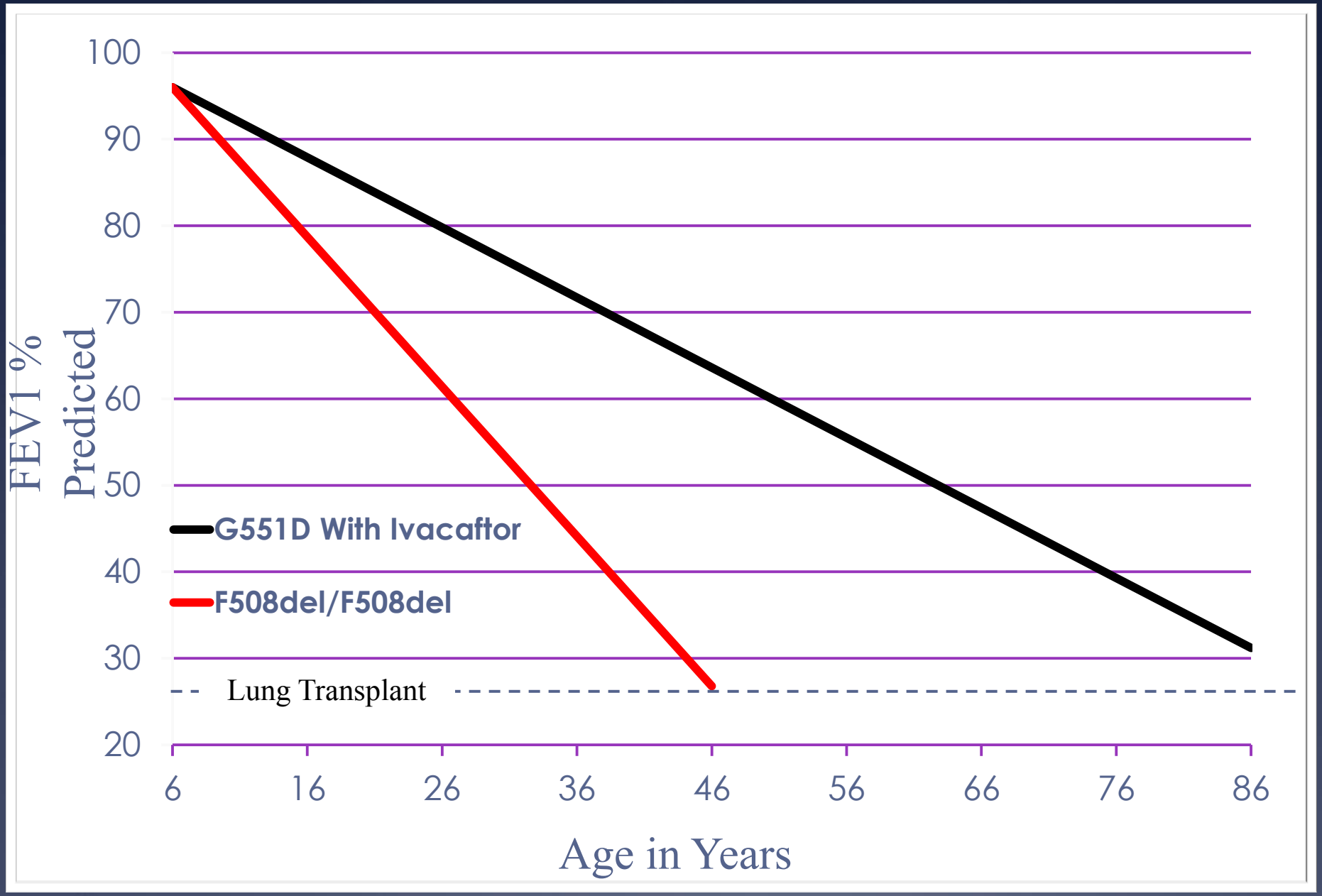
The New England Journal of Medicine

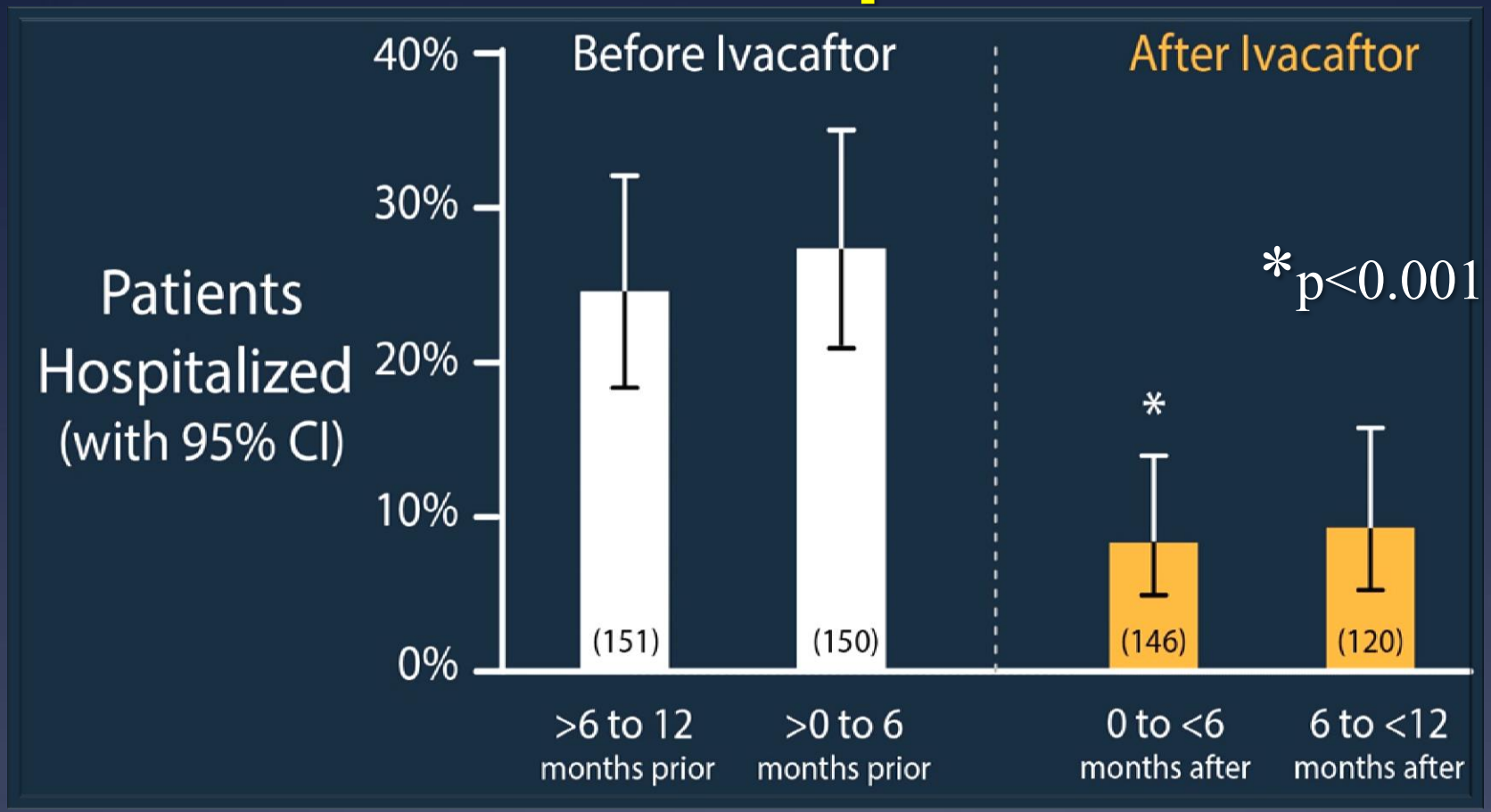
① Demonstrated that restoring CFTR function results in dramatic

② Gave us the ability to further understand the clinical benefits of restoring CFTR function

Effect of Decreased Rate of Decline in FEV_1



Restoring CFTR Function Reduces Hospitalizations

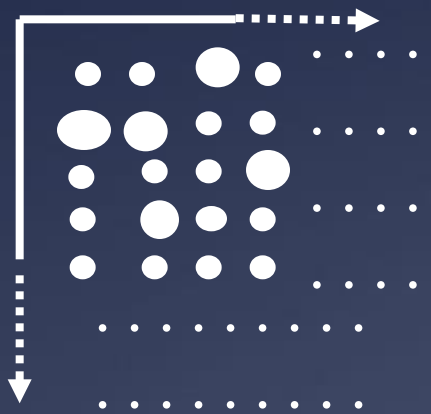


- ✓ **Improvement in weight/BMI**
- ✓ **Altered the microbiology**

Rowe, Heltshe,…Ramsey et al. AJRCCM 2014

~~Towards~~ "Personalized" CF Care: Genomics and Proteomics

- Genomics
  - Microarrays



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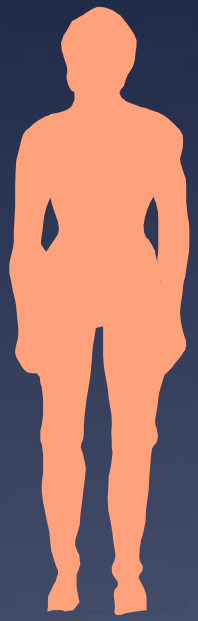

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- Modifier Genes
- Pathways of Injury
- Individual Variation
- New Treatments
- Individual Treatment Approaches

- Proteomics

Areas of Need

- **Transition from Pediatric to Adult Care**
- **Insurance needs (underinsured) for medications, hospitalizations, and medical devices**
- **Genetic counseling support for newborn screening programs**
- **Advocacy for job security for patients and for families**
- **Ability to be seen at an accredited CF Center**
- **Mental Health Providers skilled in Chronic Illness**

Questions