CF Testing: Why we do the things we do

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University of Florida
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Menu of tests

- Bloodwork
  - Complete metabolic panel
  - CBC
  - GGT
  - PT/PTT
  - IgE
  - Vitamins A, D, E, K
  - Glucose tolerance test
- Respiratory cultures
  - Culture and sensitivity
  - AFB for atypical mycobacteria
- Chest xray
- Chest CT
- Abdominal Ultrasound
- Bone scans
- Plethysmography
- PFT's
- Bronchoscopy

Back in the day…

In 1938 Dorothy Andersen, MD, identified “CF of the pancreas; Median age of survival was barely six months.

In 1940’s Pancreatic replacement enzymes were developed

Ann Kates, 52 and her mother Doris Tulcin, one of the CF Foundation founders.

52 years ago, helped establish the CF Foundation

1989 Discovery of the CF Gene
CFF Fundraising
Age of survival 25 years

1993 Pulmozyme® approved

1997 Therapeutics Development Program
TOBI is approved

2009 Newborn Screening in All 50 states

2010 Over thirty+ therapies in progress
Age of survival 37+ years
Cayston approved by FDA

2012 Kalydeco approved by FDA

CFF Care Center Network

Accredited Care Centers

Minimum Criteria
For
CFF Center Accreditation

To be accredited…

- Initial application
  - Site visit
  - Reviewed by a center committee
  - Approval as center or affiliate center
  - Some funding
- To remain accredited
  - Annual application
  - Data entry “earns” most of the funding
  - IRB approval for CF registry
  - Successful site visits every 5 years at minimum

Cystic Fibrosis Foundation
26th Annual North American
Cystic Fibrosis Conference
October 11-13, 2012 · Orange County Convention Center · Orlando, Florida

University of Florida

Accredited for both Pediatric and Adult Centers

1966

CF patient registry

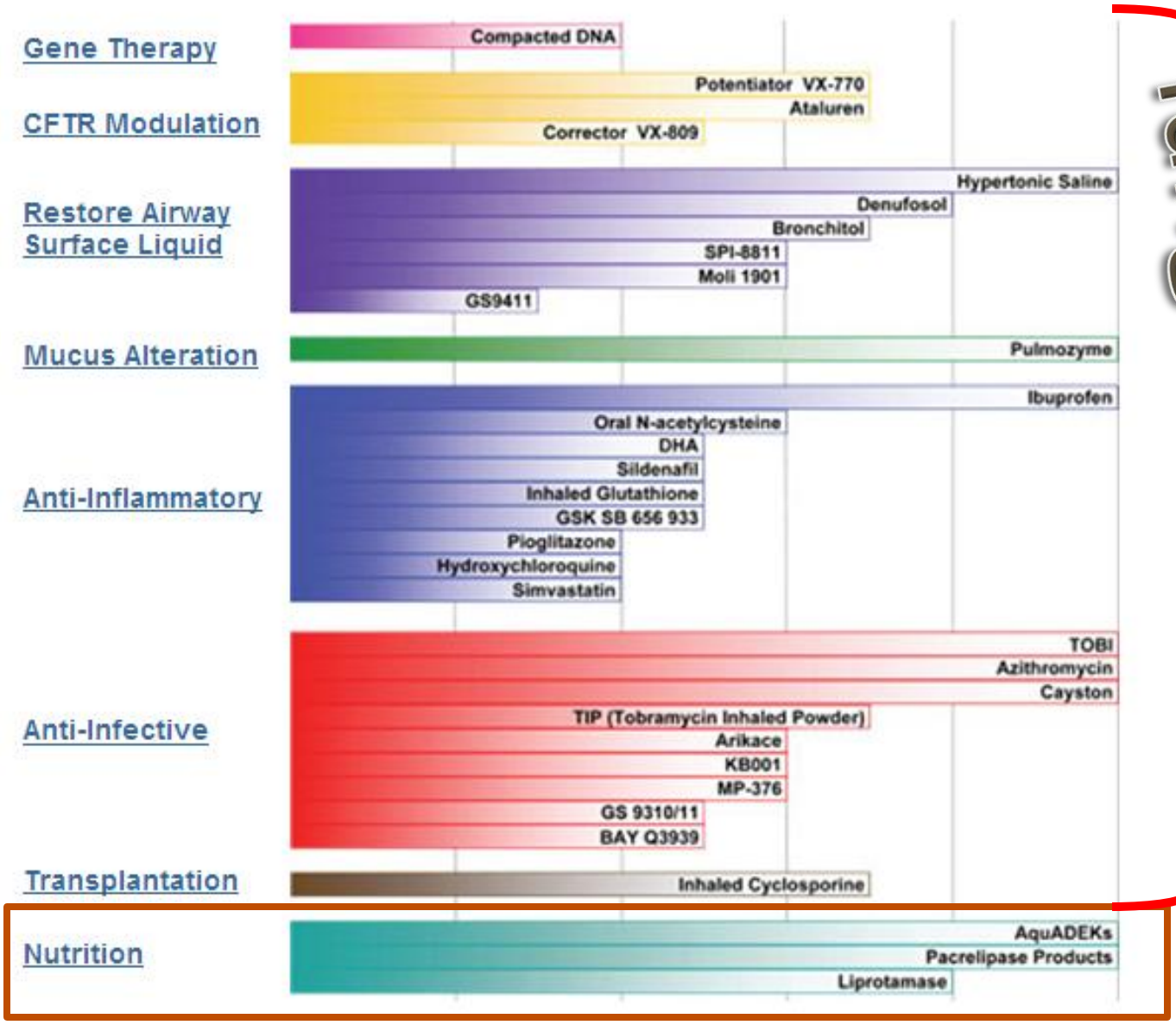
- One written page, once a year
- Real time entry of every visit, every culture, every pft, every lab result
- US…Canada…UK…Australia… Ireland…

Patient data registry

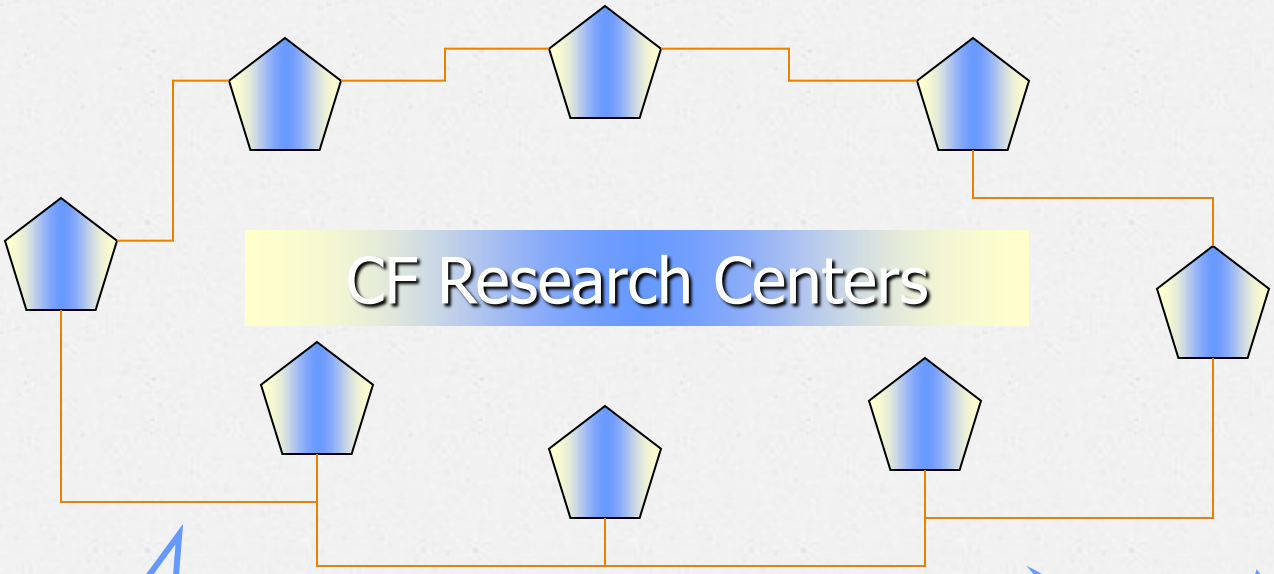
- Lots and lots of information
- Comparison between center outcomes
- Comparison between center treatment approaches
- Published information: www.cff.org
- **Consensus conferences to guide care**
  - **Guidelines**
  - **MORE data requirements**
  - **More guidelines…etc!**

Information!!!

As of Feb 2010



Therapeutics Development Centers



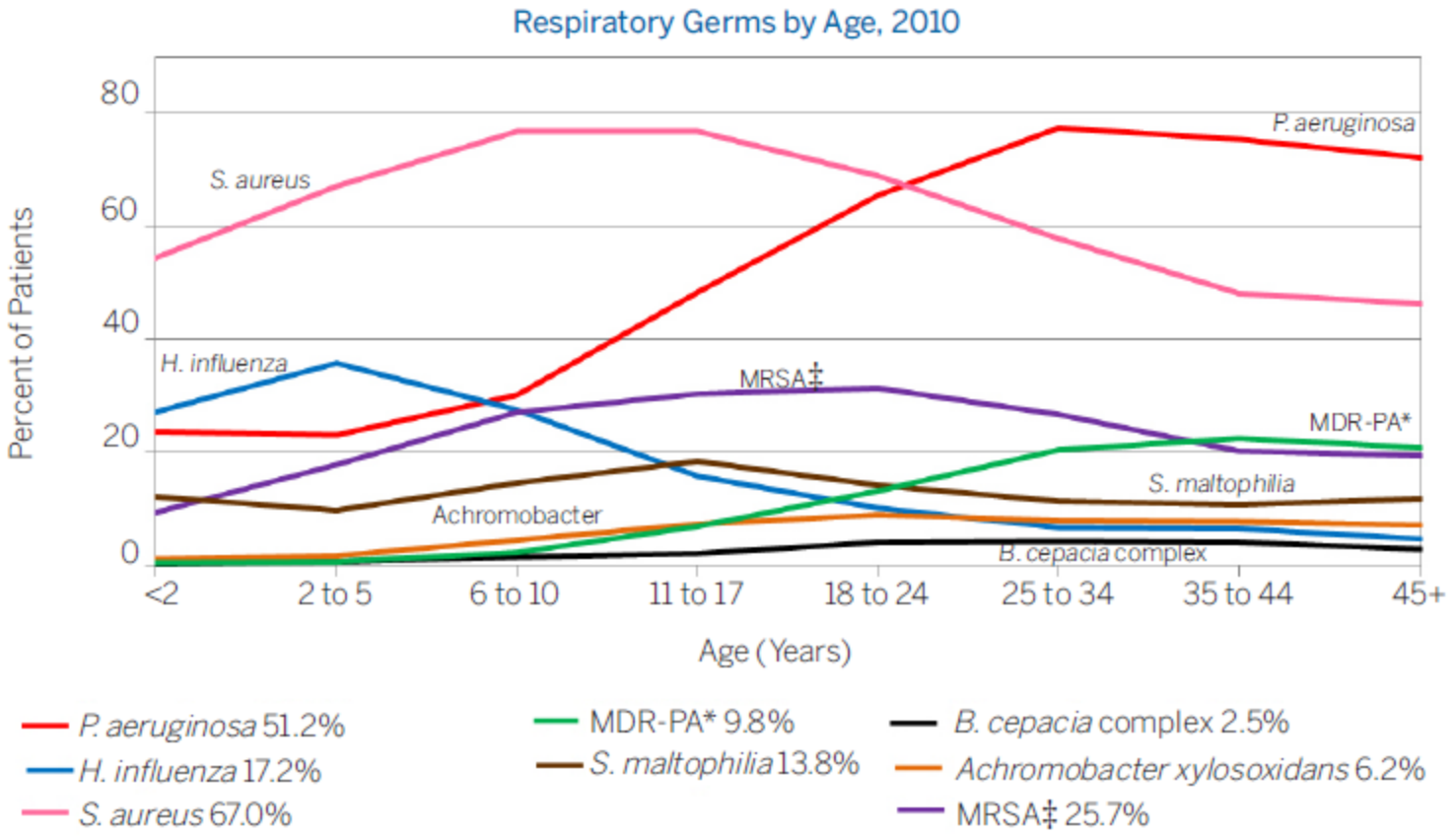
Development of new therapies

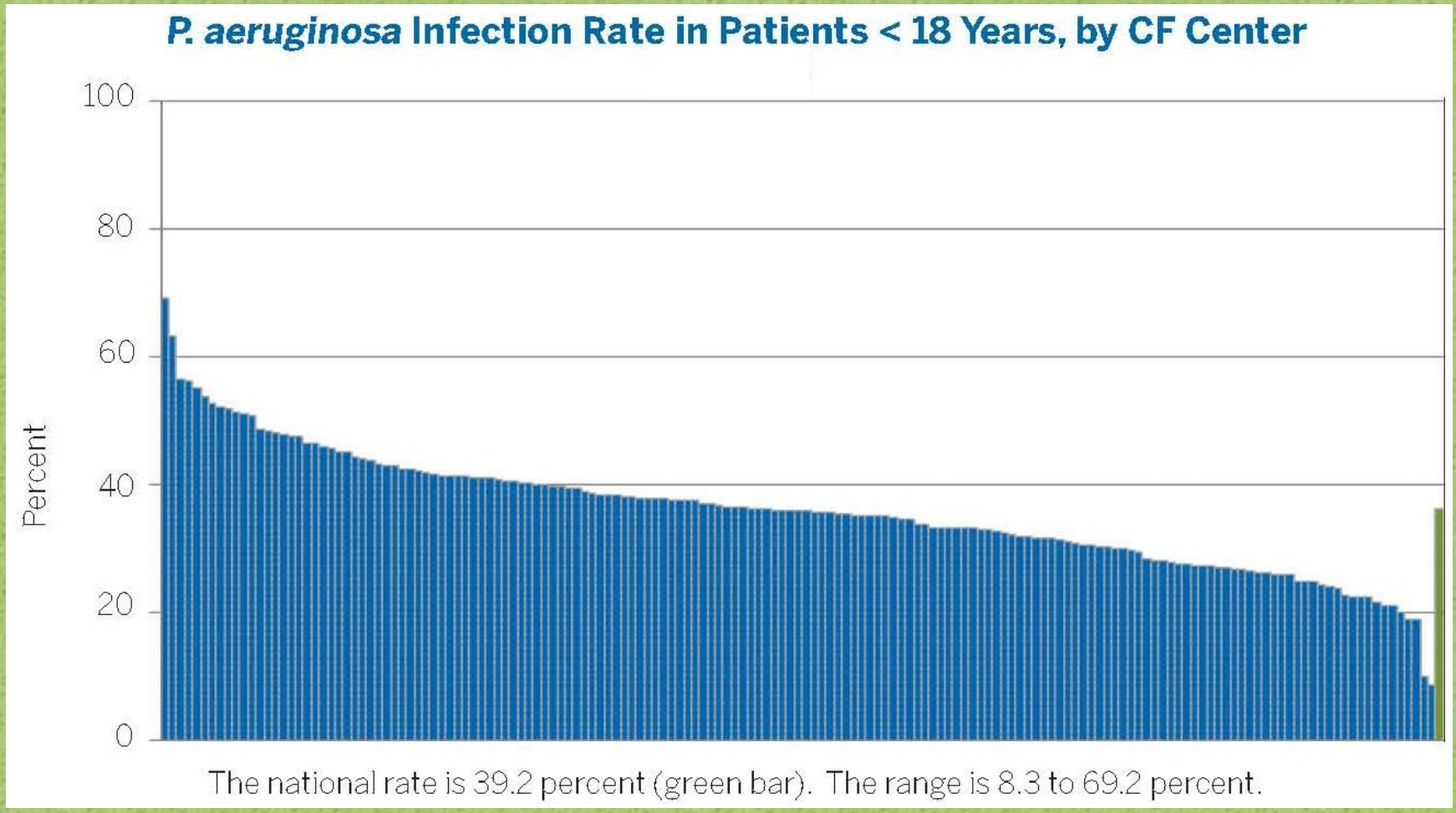
Develop core services to support research

Speed up early phase clinical trials

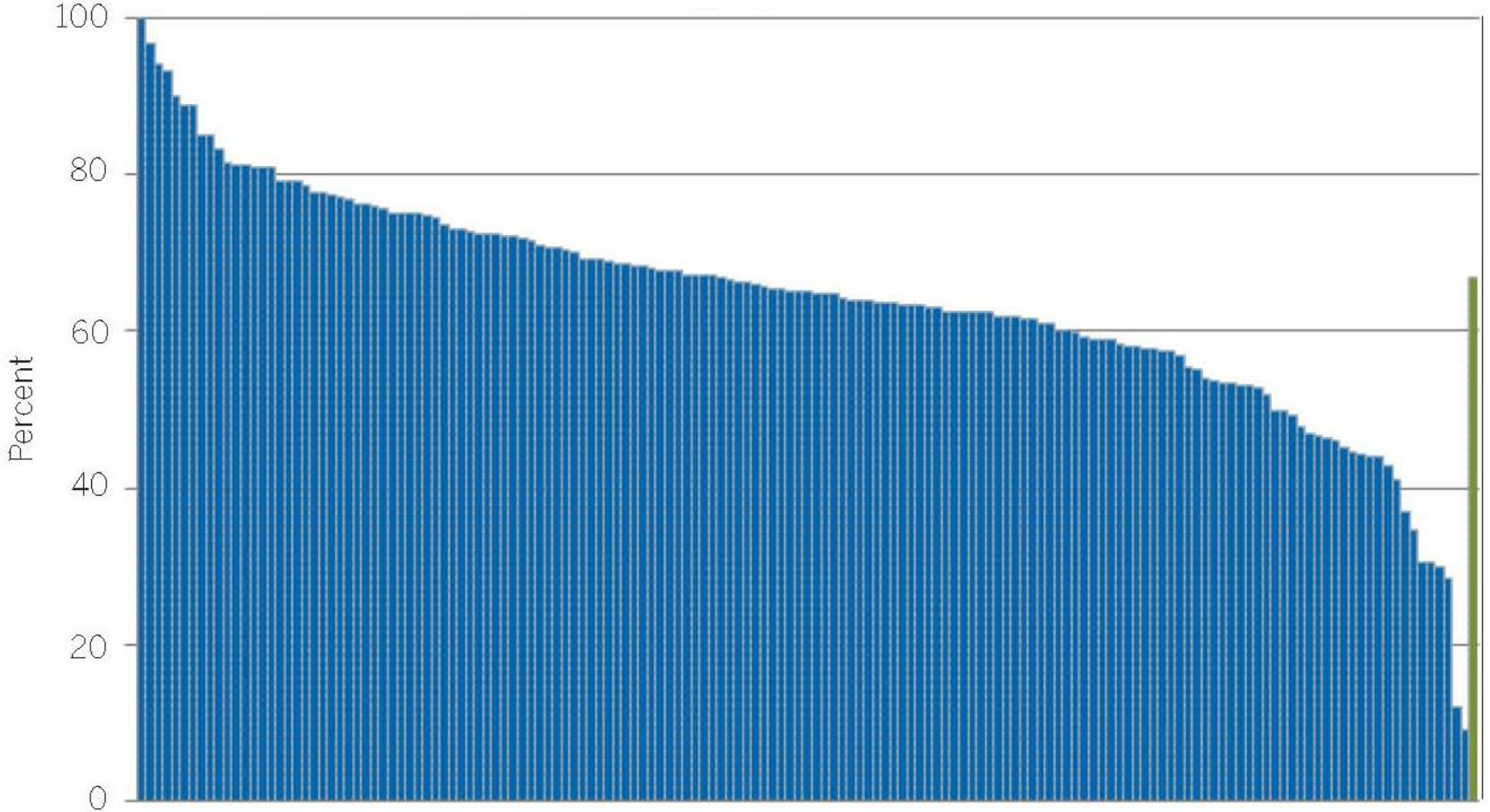
Lung disease is the predominant cause of illness and death (68.3%)

CYSTIC FIBROSIS FOUNDATION PATIENT REGISTRY: ANNUAL DATA REPORT 2010




P. aeruginosa Infection Rate in Patients < 18 Years, by CF Center
100
80
60
40
20
0
Percent
The national rate is 39.2 percent (green bar). The range is 8.3 to 69.2 percent.

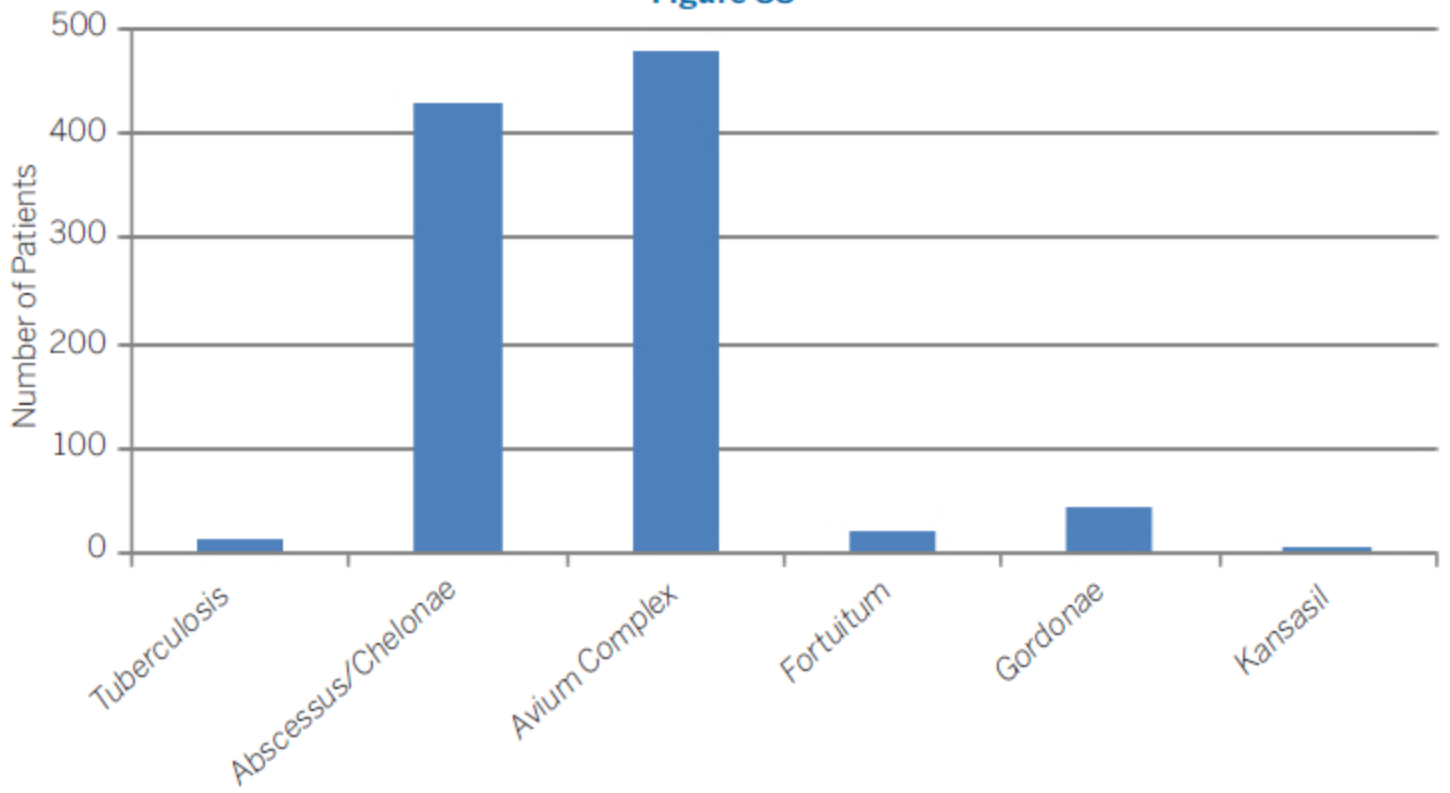
Patients With *P. aeruginosa* Who Were Reported as Mucoid Phenotype, by CF Center



The national rate is 66.8 percent (green bar). The range is 9.1 to 100 percent.

Mycobacterial Species Isolated*

Figure 88



9,462 patients had a mycobacterial culture in 2010 and 939 had a mycobacterial species isolated. The relative proportion of *M. abscessus* isolated in 2010 is higher than that reported over a decade ago in the CF Foundation supported multicenter prevalence study.[20]

Staphylococcus aureus

- MRSA (methicillin resistant Staph aureus)
- MSSA (methicillin sensitive Staph aureus)

Haemophilus influenzae (a

Pseudomonas aeruginosa

- mucoid
- non-mucoid

Burkholderia species

- B. gladioli
- B. cenocepacia
- B. multivorans
- Burkholderia - other

Specify (if other Burkholderia):

B. cepacia	B. stabilis	B. vietnamiensis	B. dolosa
B. anthina	B. ambifaria	B. pyrrocinia	B. ubonensis
B. arboris	B. latens	B. lata	B. metallica
B. seminalis	B. contaminans	B. diffusa	B. pseudomallei

Was the identification of Burkholderia species confirmed at the CFF reference Lab?

Yes No Unknown

Other Microorganisms:

- Alcaligenes (Achromobacter) xylosoxidans
- Stenotrophomonas (Xanthomonas)/Maltophilia
- Other types

Other types of Microorganisms

Acinetobacter baumannii	Acinetobacter species - other*	Agrobacterium species
Bordetella species	Brevundimonas species	Chryseobacterium species
Cupriadidus metallidurans	Cupriavidus pauculus	Cupriavidus respiraculi
Delftia acidivordans	Delftia species - other*	Enterobacter species

Fungal/Yeast:

- [ ] Aspergillus (any species)
- [ ] Candida (any species)
- [ ] Scedosporium species

Specify if additional species were found

- [ ] Other bacterial or fungal species

Specify: _____

Mycobacterial Culture

Was Mycobacterial culture done? [ ]

Date of culture __/__/____ (MM DD YYYY)

Type of specimen:

- ( ) sputum
- ( ) induced sputum
- ( ) bronchoscopy

AFB Smear

- ( ) Positive
- ( ) Negative
- ( ) Not done

Mycobacterial Species:

- [ ] Mycobacterial tuberculosis
- [ ] Mycobacterium abscessus/chelonae
- [ ] Mycobacterium avium complex (MAC)
- [ ] Mycobacterium fortuitum group
- [ ] Mycobacterium gordonae
- [ ] Mycobacterium kansasii
- [ ] Mycobacterium marinum
- [ ] Mycobacterium terrae

Respiratory cultures

- Quarterly
- With sensitivities
- Expanded “bug” list
- Qualified lab

Pulmonary Function Tests

- Quarterly
- During hospitalizations
- Evaluate when sick

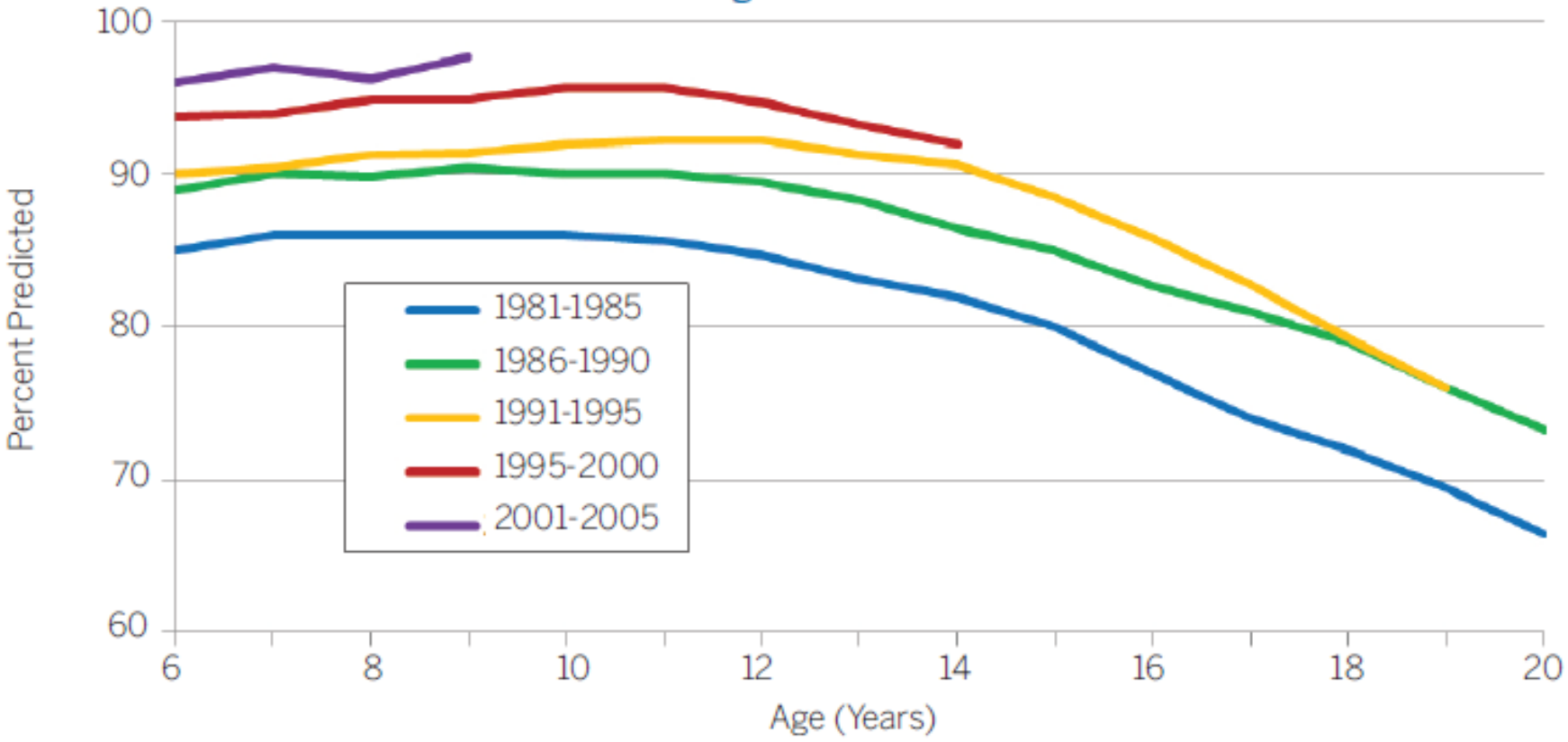
    - Evaluate: PFT data entered for exacerbations along with treatment data = outcomes to compare

CXR/CT Scans

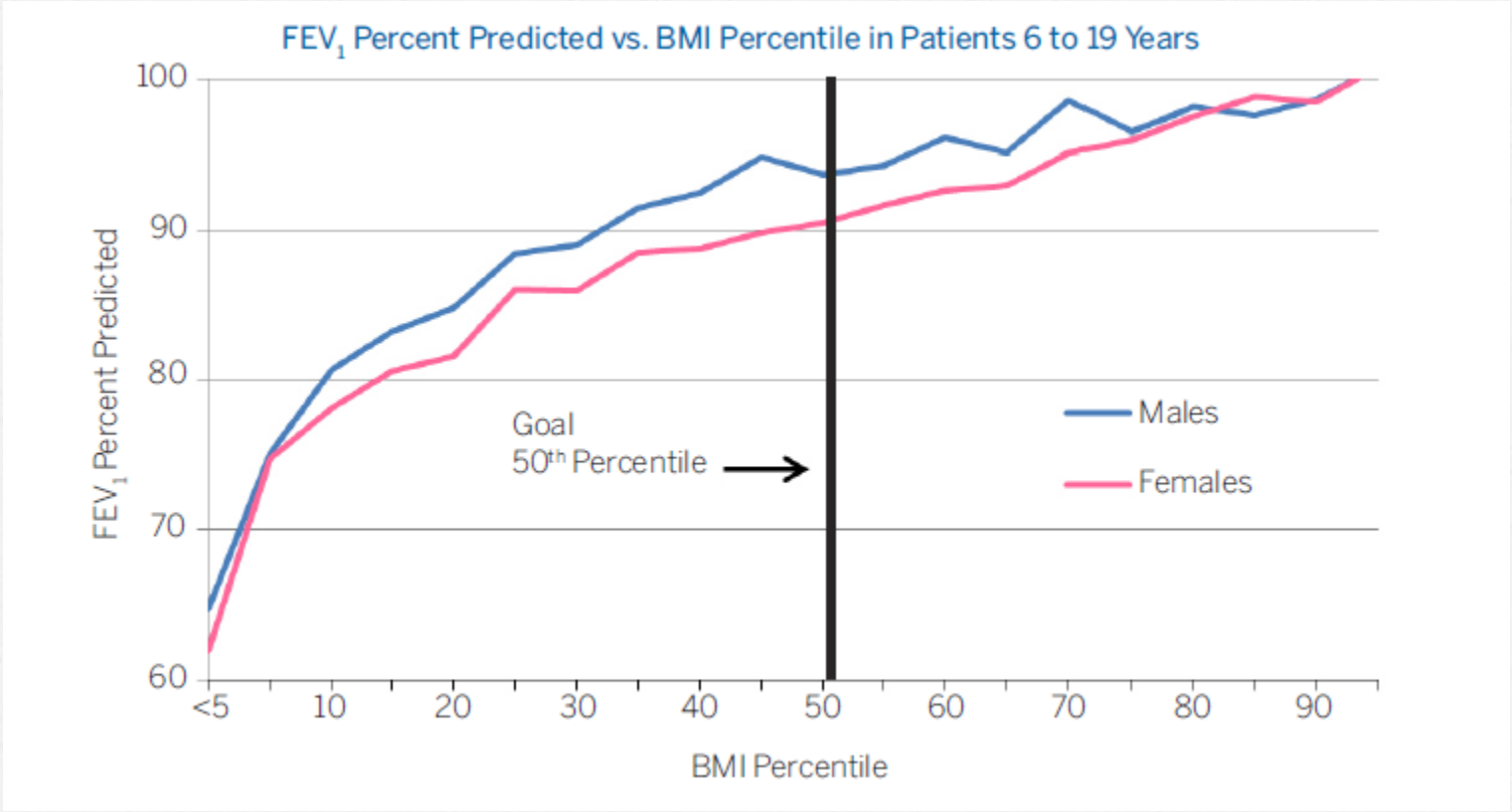
Bronchoscopy

Median FEV_1 Percent Predicted vs. Age by Birth Cohort

Figure 61

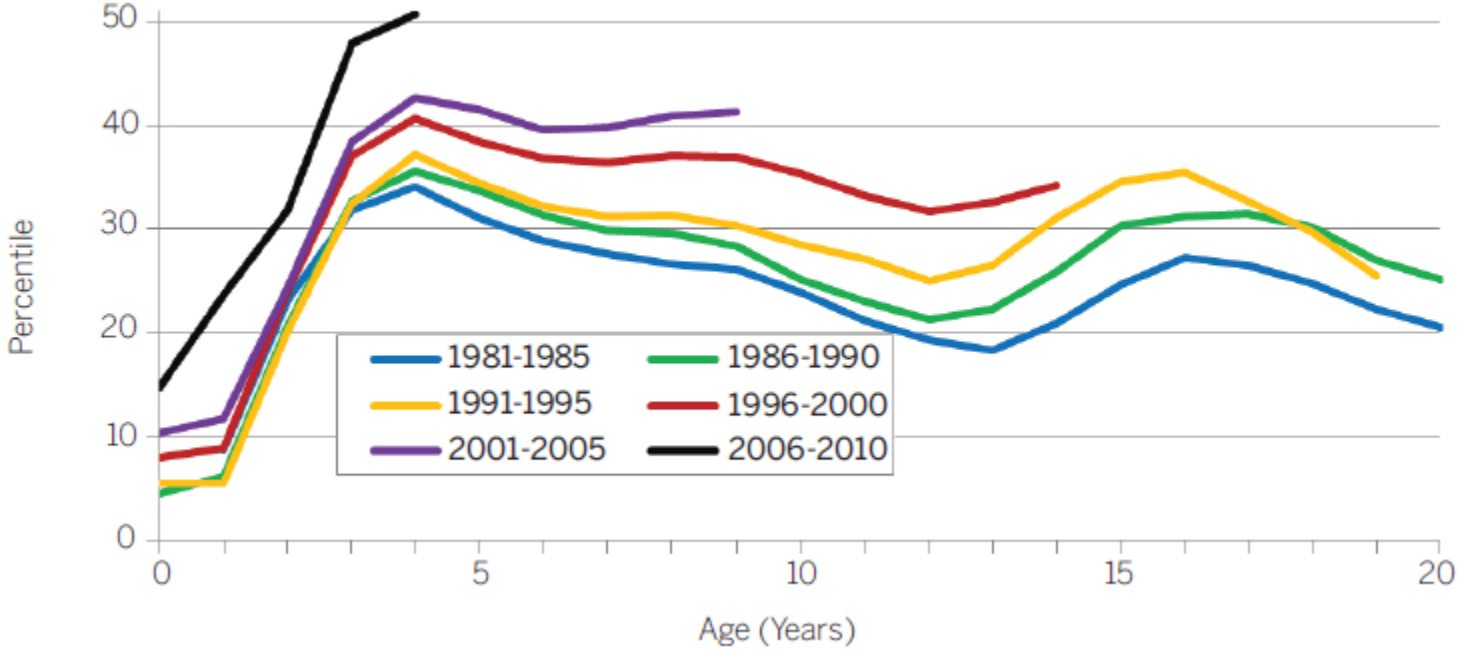


FEV_1 is steadily improving and stays above 90 percent predicted into early adolescence.


FEV1 Percent Predicted vs. BMI Percentile in Patients 6 to 19 Years
100
90
80
70
60
FEV1 Percent Predicted
Goal
50th Percentile
Males
Females
<5
10
20
30
40
50
60
70
80
90
BMI Percentile

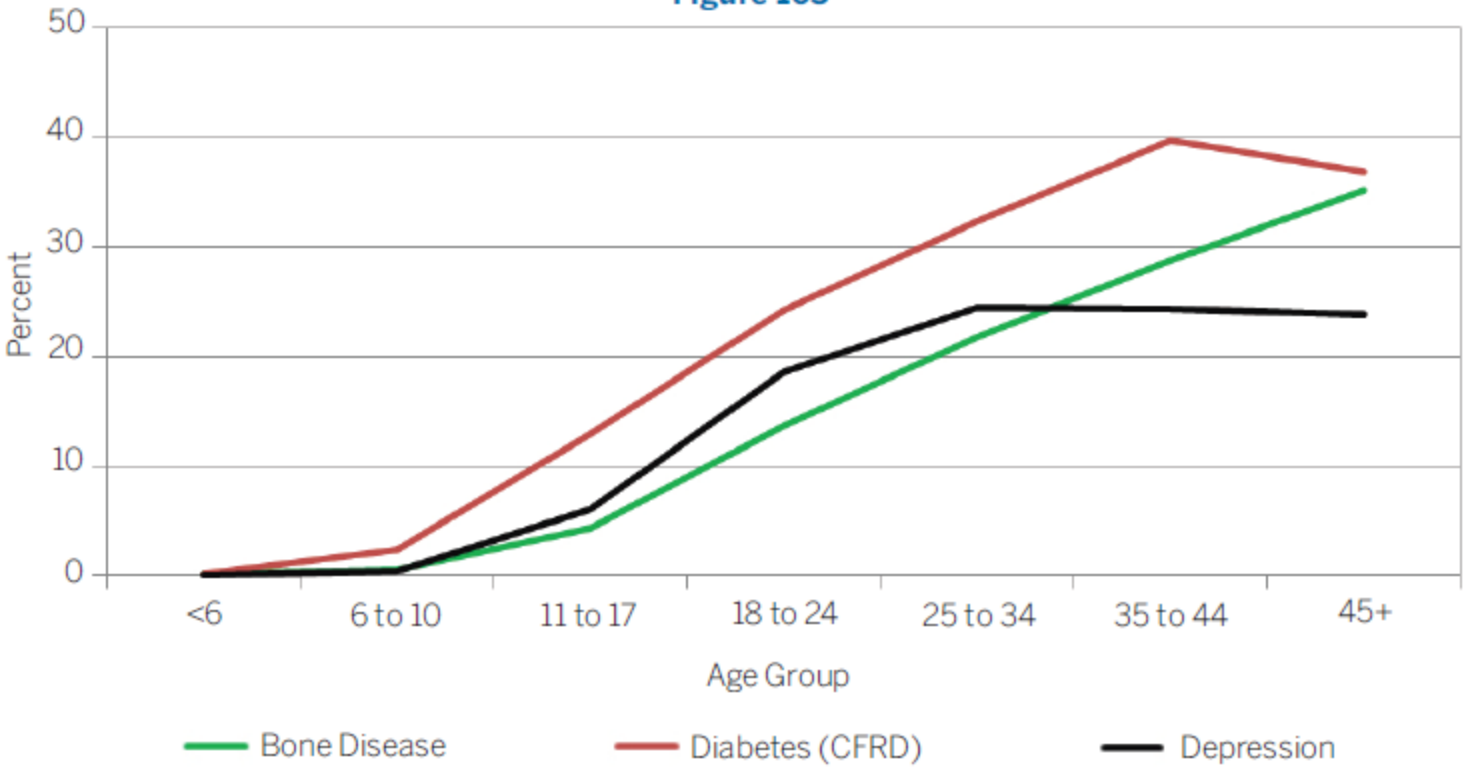
Median CDC Weight Percentile vs. Age by Birth Cohort

Figure 32



Common Complications vs. Age

Figure 103



Vitamin K

What is my blood vitamin K level and how does it compare to the recommended level?

Vitamin A

Vitamin D

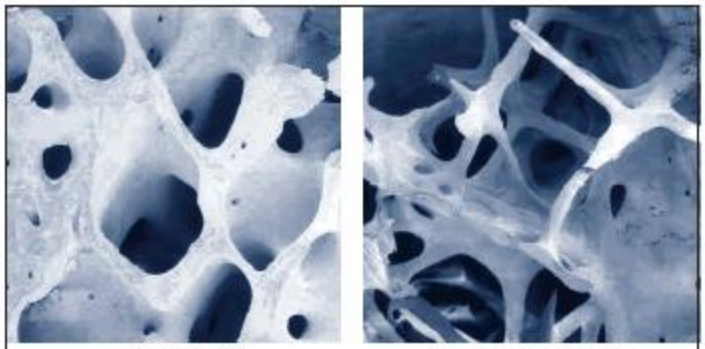
Vitamin E

Nutrition

Bone Health and Cystic Fibrosis

Bone Disease: Causes & Risk Factors

- Low body weight
- Low vitamin D
- Low calcium intake
- Malabsorption
- Not enough pancreatic enzymes
- Tobacco, alcohol, and caffeine use
- Moderate to severe lung illness
- Chronic infections
- Chronic bone and joint swelling
- CF-Related Diabetes
- Organ transplant
- Long-term steroid use
- Low *sexual hormones*
- Lack of exercise, especially weight-bearing



Normal *Osteoporosis*

Image Copyright 2001, David W. Dempster, PhD

…and so

Along with “bloodwork”
To watch liver and kidney function

- vitamin levels annually
- Glucose testing begins in preteens
- Bone scans in older adolescents

Genotype Data — All Patients, 2010

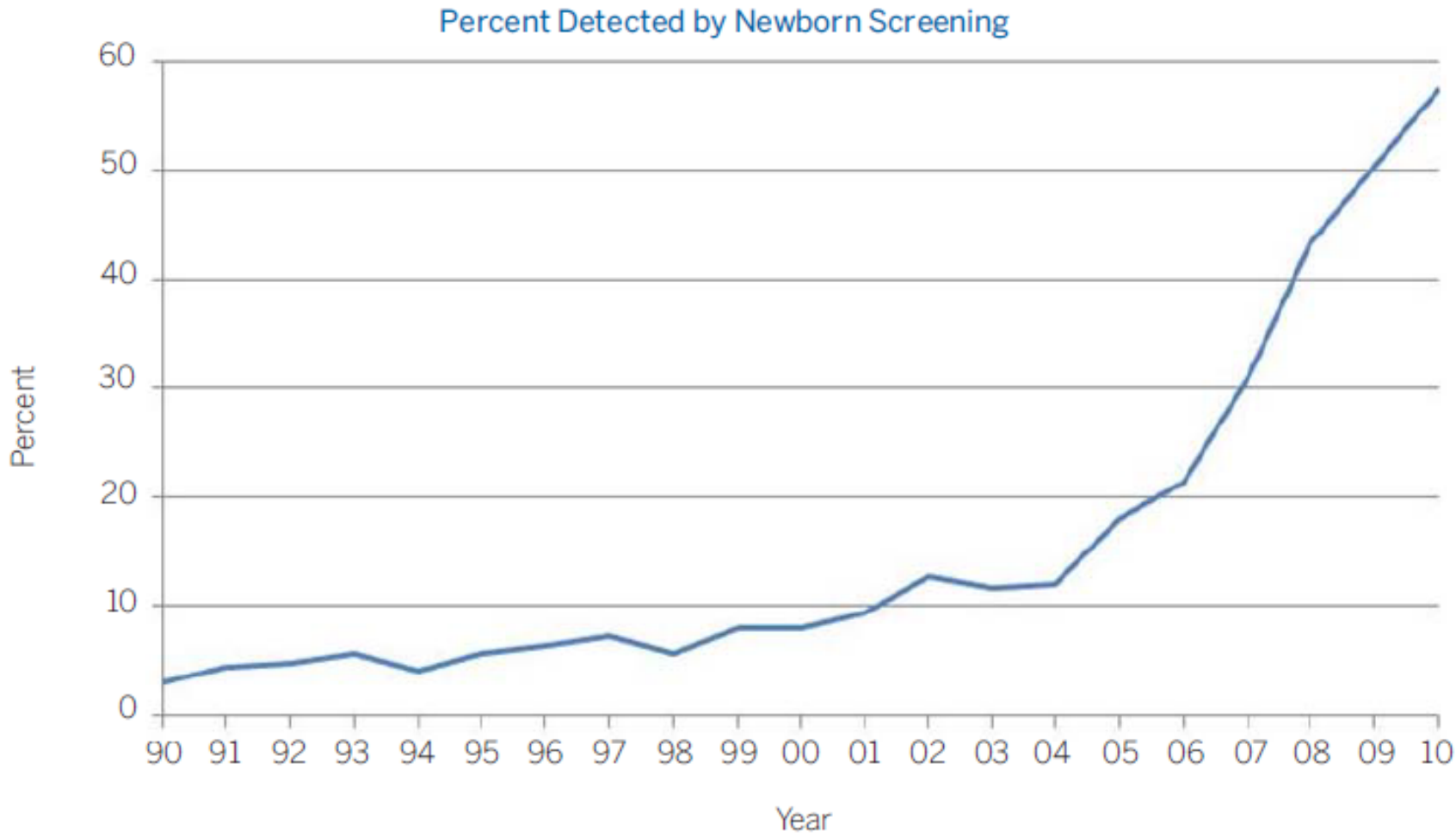
Total Number of Patients Genotyped = 24,125

Percent of Patients Genotyped = 91.7%

delF508 Mutation (% of patients):	
Homozygotes F508	48.4
Heterozygotes F508	40.1
Neither F508	11.5

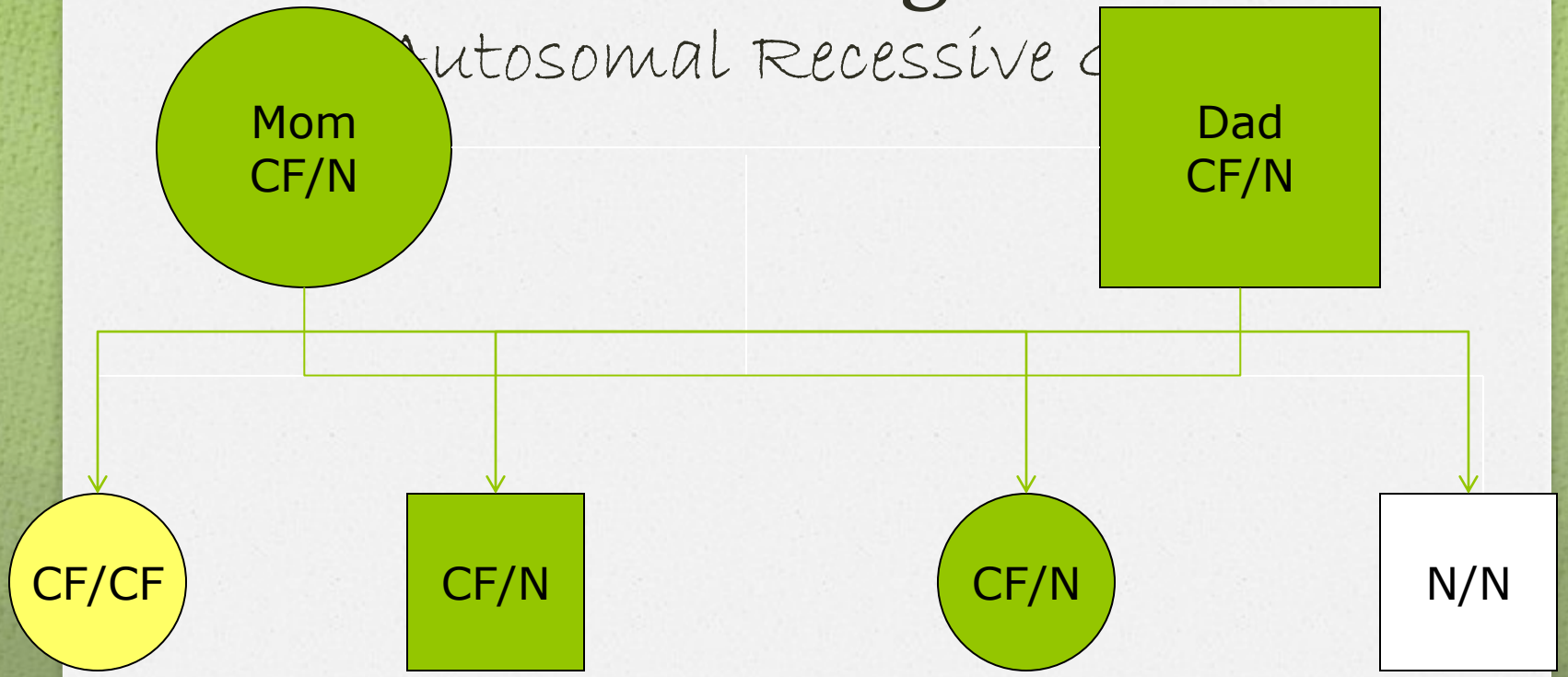
Mutation	Number of Alleles	Percent of Alleles
F508del	32,499	67.4
G542X	1,104	2.3
G551D	1,055	2.2
R117H	643	1.3
W1282X	621	1.3
N1303K	599	1.2
R553X	436	0.9
621+1G->T	425	0.9
3849+10kbC->T	402	0.8
1717-1G->A	394	0.8
Other	6,808	14.1
Unidentified	2,518	5.3

Mutation	Number of Patients*	Percent of Patients*
F508del	21,015	88.5
G542X	1,086	4.6
G551D	1,035	4.4
R117H	636	2.7
N1303K	593	2.5
W1282X	565	2.4
R553X	432	1.8
621+1G->T	419	1.8
1717-1G->A	392	1.7
3849+10kbC->T	373	1.6
2789+5G->A	308	1.3
3120+1G->A	237	1.0
I507del	193	0.8
R1162X	184	0.8
1898+1G->A	174	0.7
3659delC	159	0.7
G85E	148	0.6
R560T	142	0.6
R347P	141	0.6
D1152H	131	0.6


Percent Detected by Newborn Screening
60
50
40
30
20
10
0
Percent
90 91 92 93 94 95 96 97 98 99 00 01 02 03 04 05 06 07 08 09 10
Year

Inheriting CF

Autosomal Recessive d



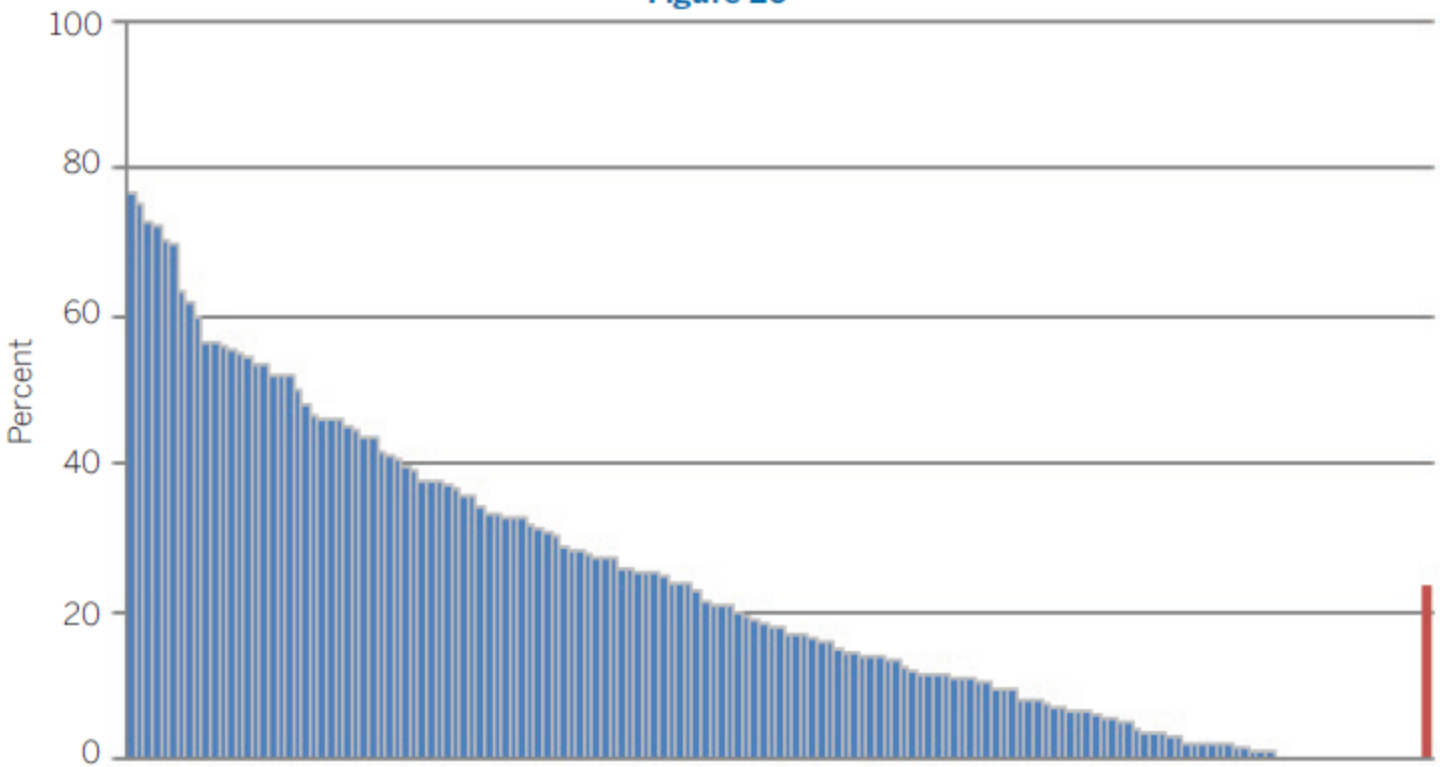
Same risk with EVERY pregnancy!

It used to be “simple”…

- Chest PT
- Oral/IV antibiotics for infections
- Enzymes
- A little lab work every year
- A Chest xray every 2 years
- PFT’s
- Sputum cultures in the “home” lab
- Oxygen when it got necessary

OGTT Screening in Non-Diabetic Patients 10 Years and Older, by CF Center

Figure 20

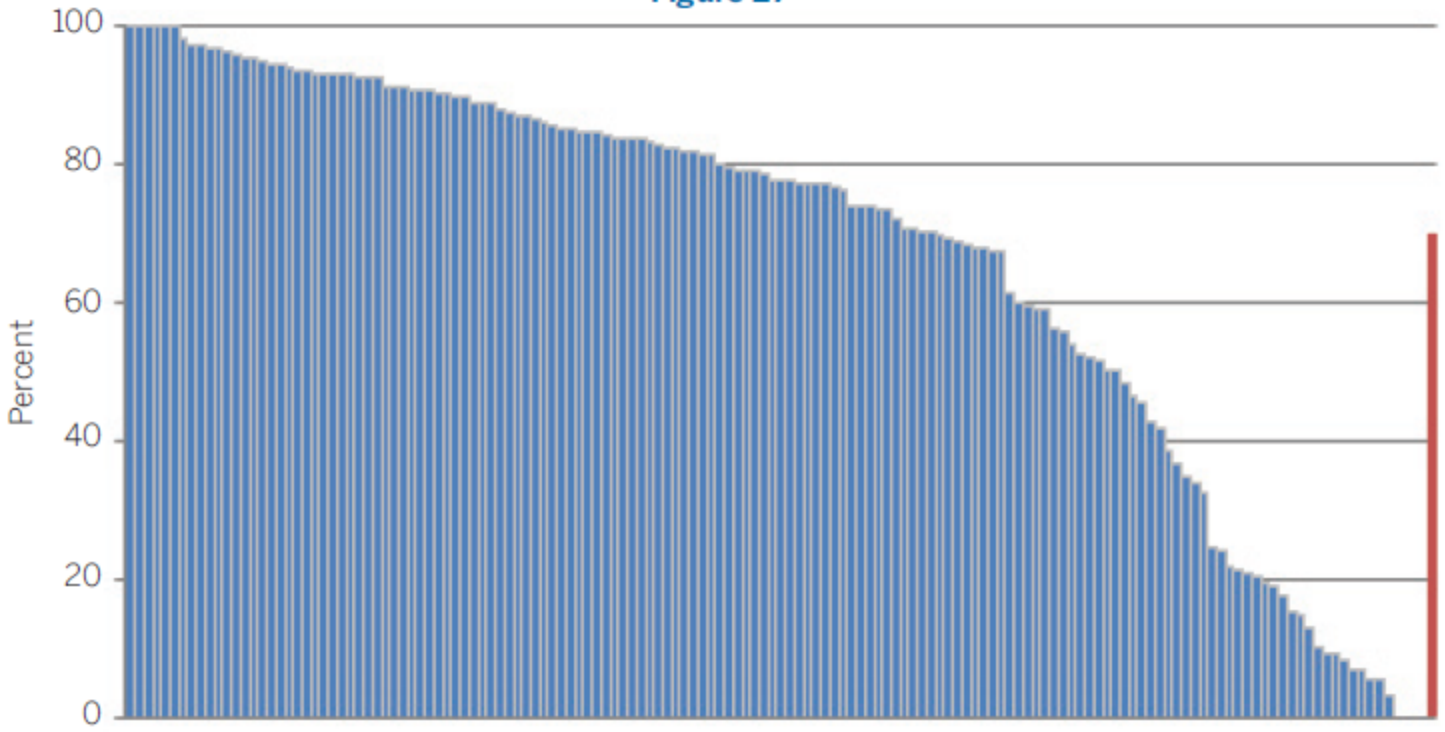


The national rate is 23.5 percent (red bar). The range is 0 to 76.5 percent. The CF Foundation CFRD Guidelines recommend annual screening for CFRD in patients 10 years and older with an OGTT.[8]

Recommend, see who is doing the testing, see their results…fold those into guidelines

Percent of Patients 6 to 17 Years with an IgE Measurement, by CF Center

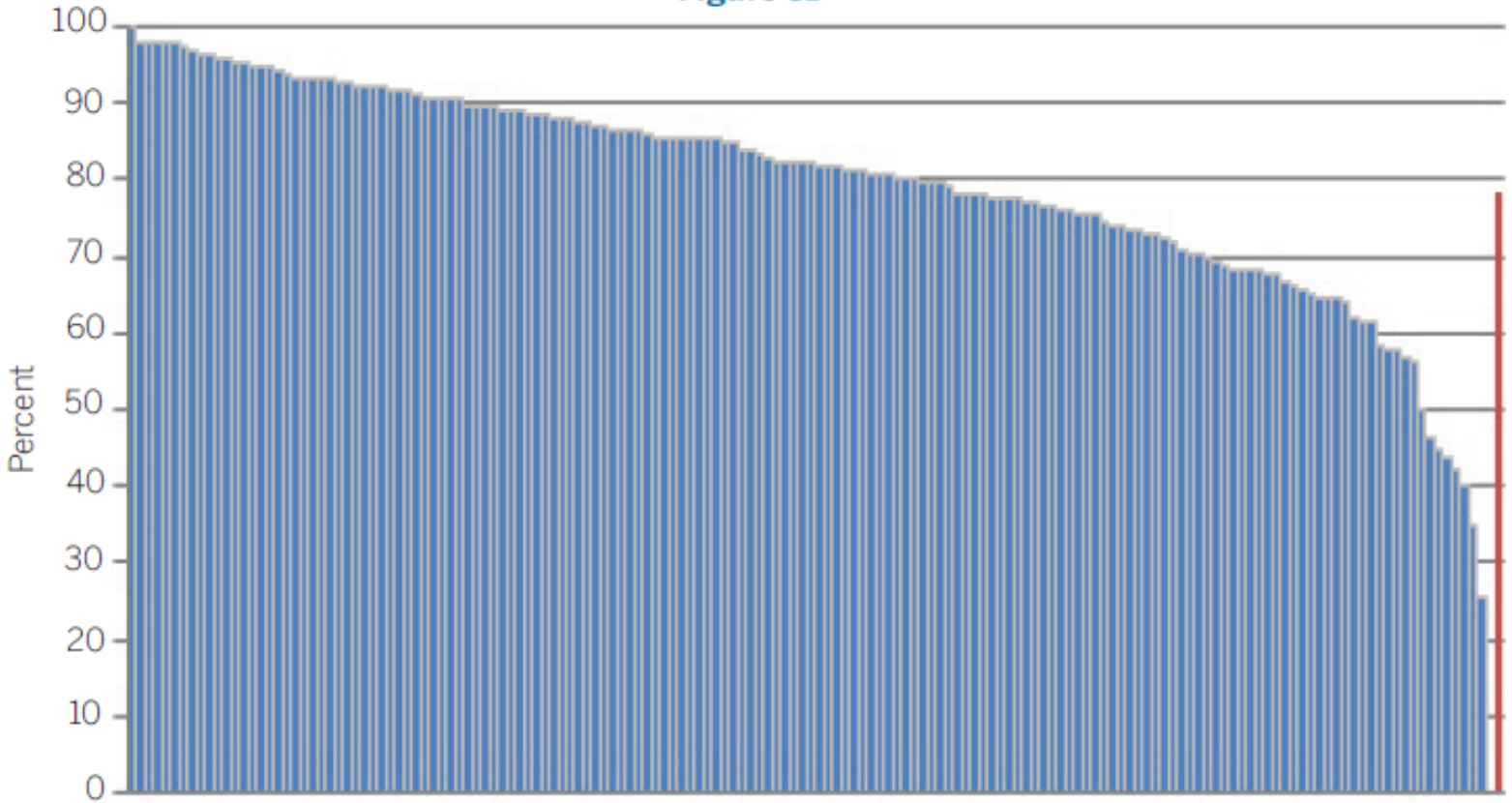
Figure 27



The national rate is 69.8 percent (red bar). The range is 0 to 100 percent. The CF Foundation Consensus Statement on ABPA recommends screening patients 6 years and older for ABPA by annual measurement of total serum IgE concentration.[11]

Percent of Patients with Fat Soluble Vitamins Measured, by CF Center

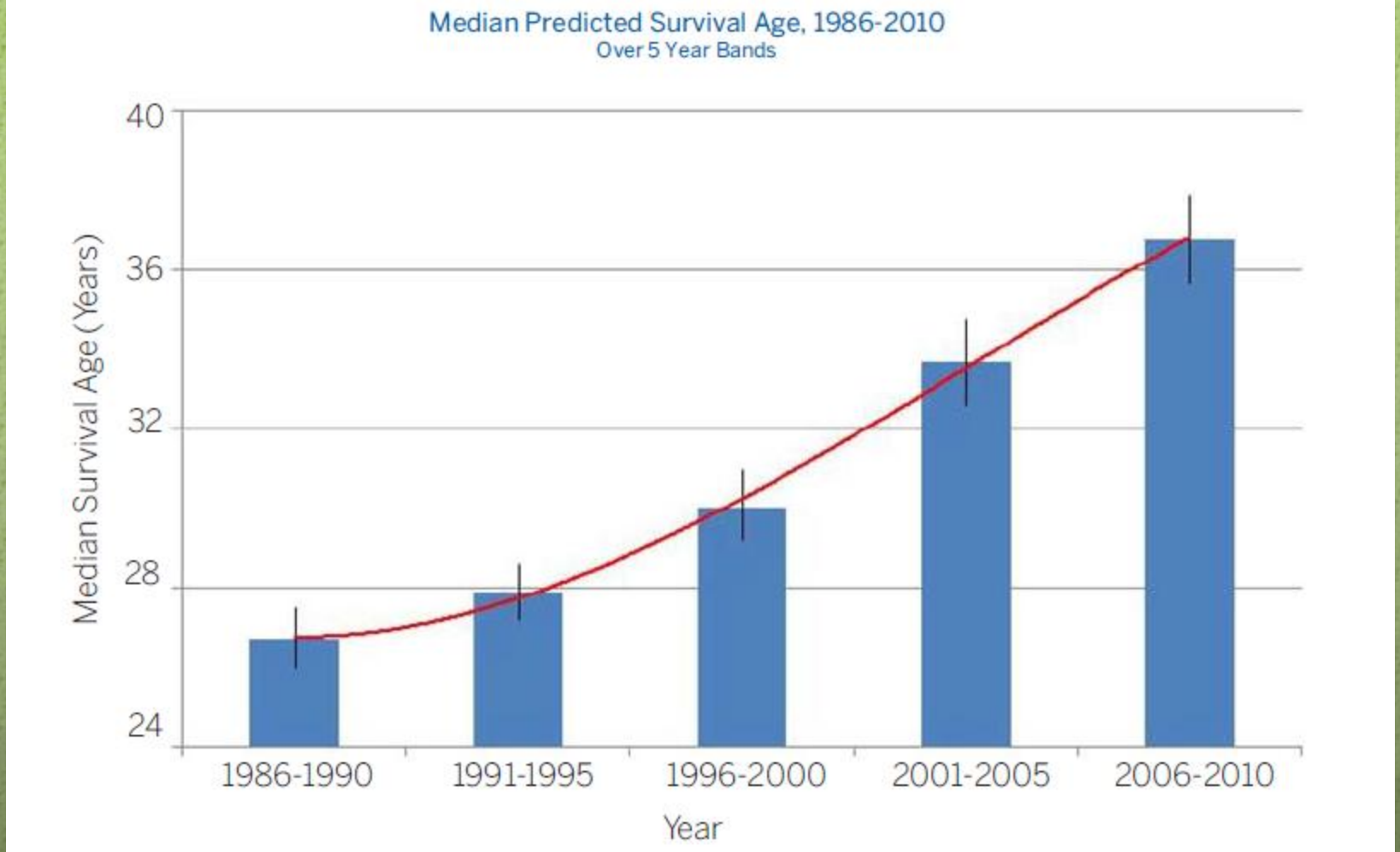
Figure 31

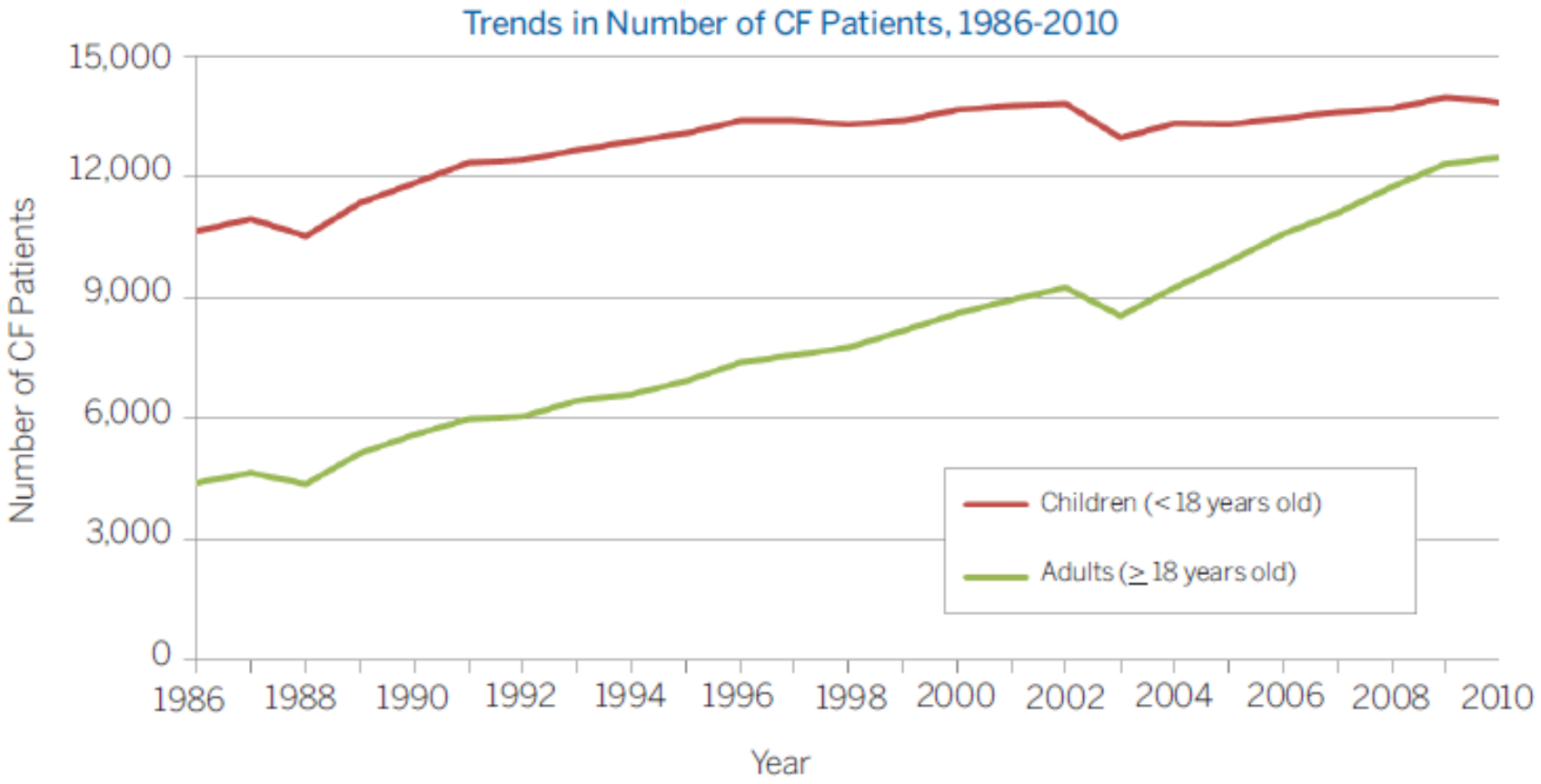


The national rate is 80.6 percent (red bar). The range is 12.5 to 100 percent.
CF Foundation Guidelines recommend annual measurement of fat soluble vitamins.[6, 13]

Consensus Statements/Evidence Based Guidelines:

Guide to Bone Health and Disease
Guide to Biliary tract and Liver Disease
Guidelines: Care, Screening and Prevention
Guidelines: Care of the Adult
Guidelines: Care of the Infant
Guidelines: Use of Preventive Therapies


Median Predicted Survival Age, 1986-2010
Over 5 Year Bands
Median Survival Age (Years)
40
36
32
28
24
1986-1990
1991-1995
1996-2000
2001-2005
2006-2010
Year


Trends in Number of CF Patients, 1986-2010
15,000
12,000
9,000
6,000
3,000
0
Number of CF Patients
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
Year
Children (< 18 years old)
Adults (≥ 18 years old)

www.cff.org

For data

For studies

For accredited centers

For educational info

In short?

That’s why we do the things we do

☺