

# Mycket förbättrade behandlingsmöjligheter vid cystisk fibros

Terapigrupp Barn och Ungdom

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Anders Lindblad, överläkare, docent

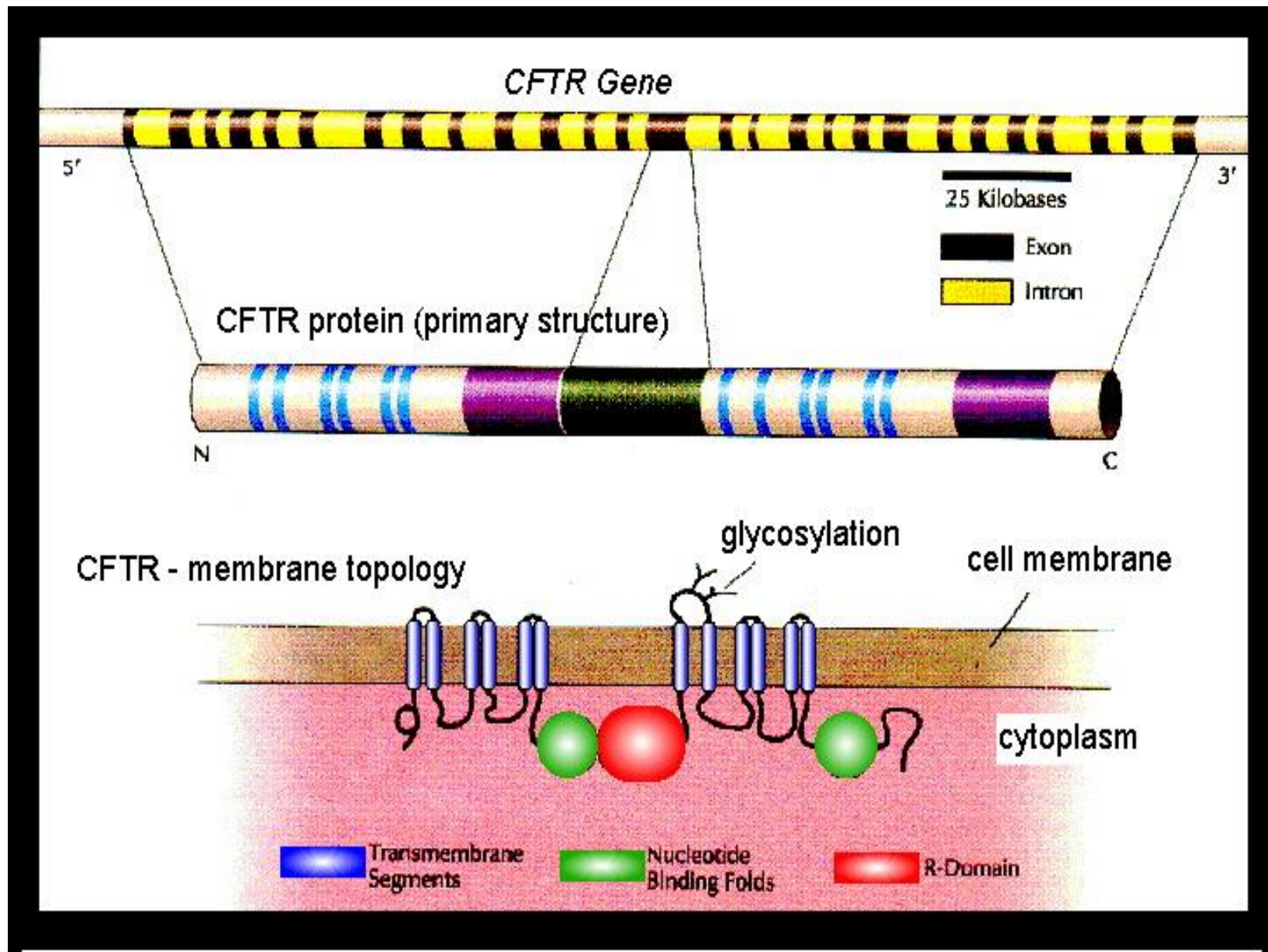
Drottning Silvias Barnsjukhus

Sahlgrenska Universitetssjukhus

Göteborg, Sverige

# Disposition

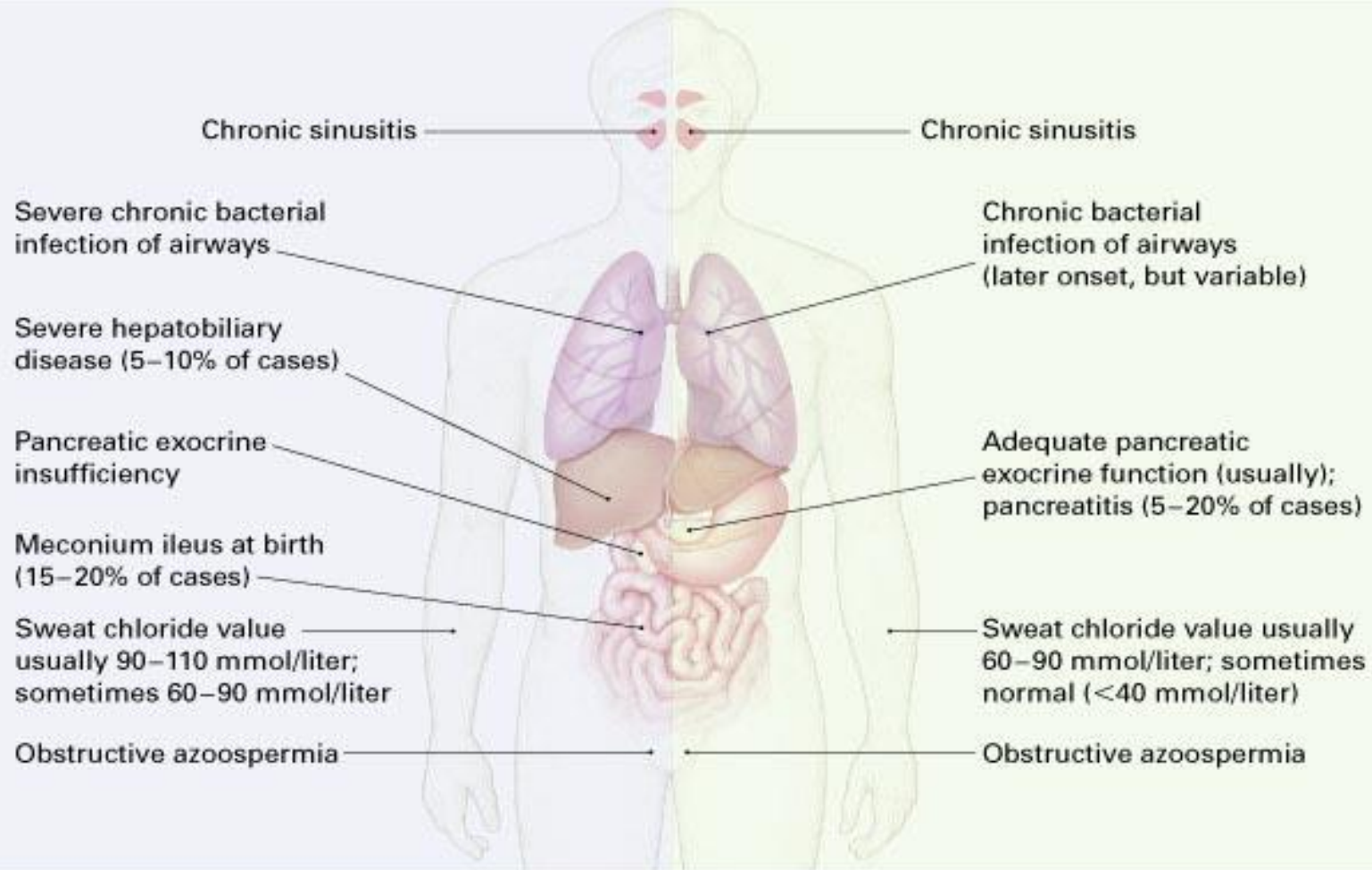
- Vad är grundorsaken till CF
- Vilka behandlingar och vilka resultat hade vi innan nya läkemedel (CFTR modulatorer)
- Hur fungerar de nya läkemedlena
- Hur har det påverkat patienten och behandlingen
- Framtiden



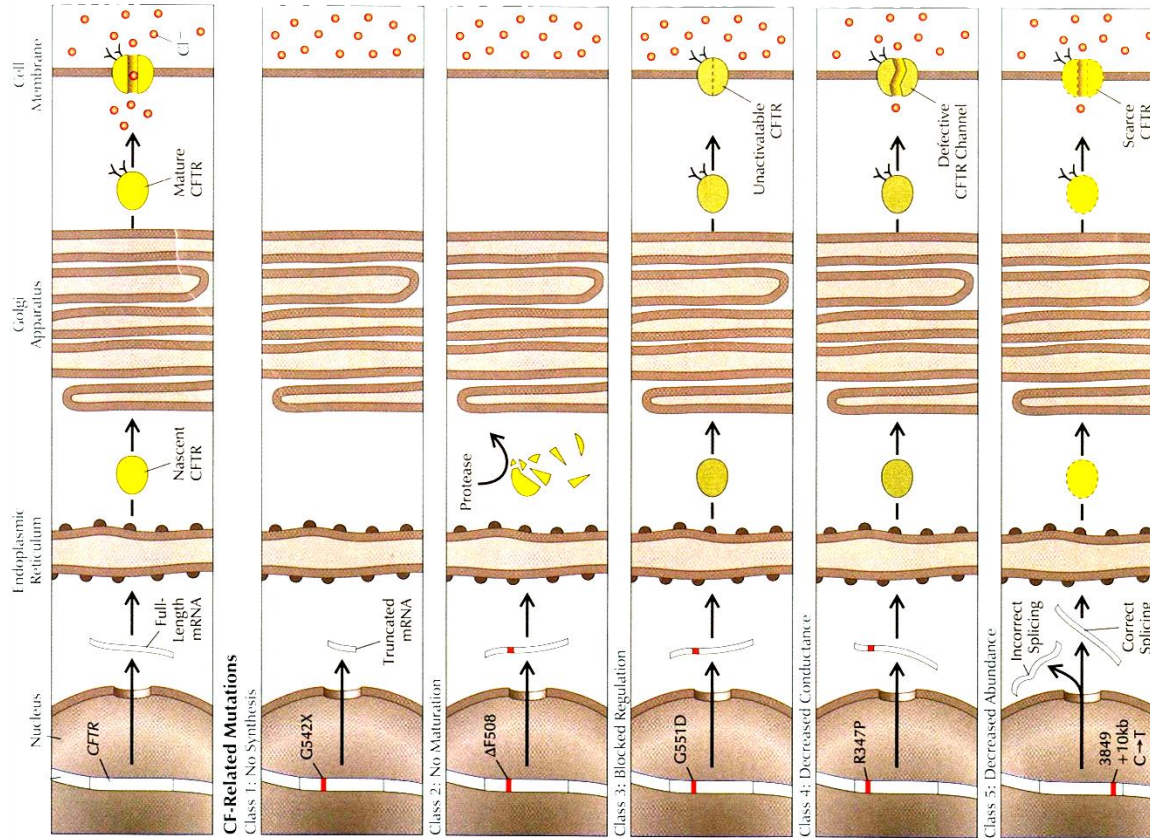
## Classic and Nonclassic Cystic Fibrosis

Classic cystic fibrosis  
(no functional CFTR protein)

Nonclassic cystic fibrosis  
(some functional CFTR protein,  
providing survival advantage)



# Olika typer av mutationsklasser



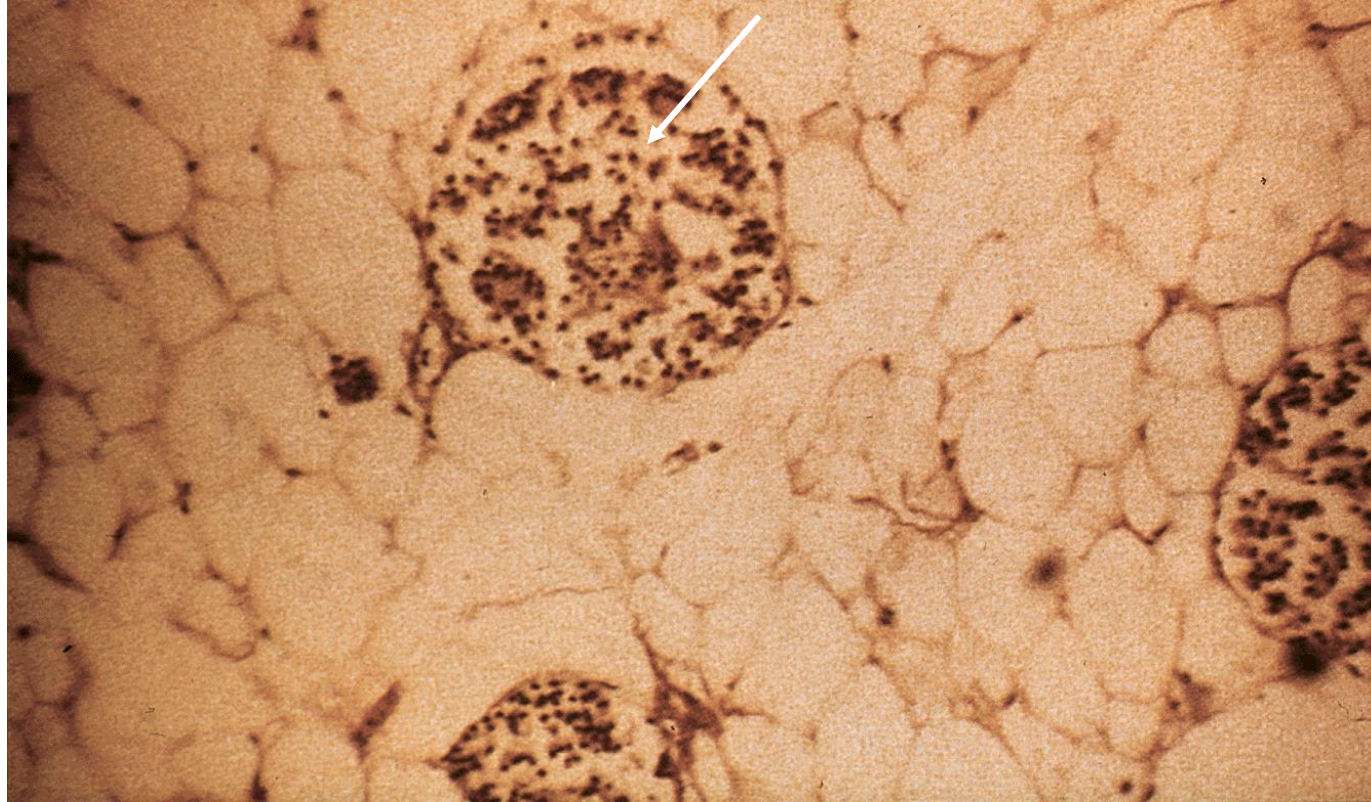
## I, II, III (severe)

- Pancreatic Insufficiency
- Risk of:
  - Meconium ileus, DIOS
  - CFRD
  - Severe hepatobiliary disease

## IV, V (mild)

- Pancreatic Sufficiency
- Risk of:
  - Acute, recurrent pancreatitis
  - Chronic pancreatitis

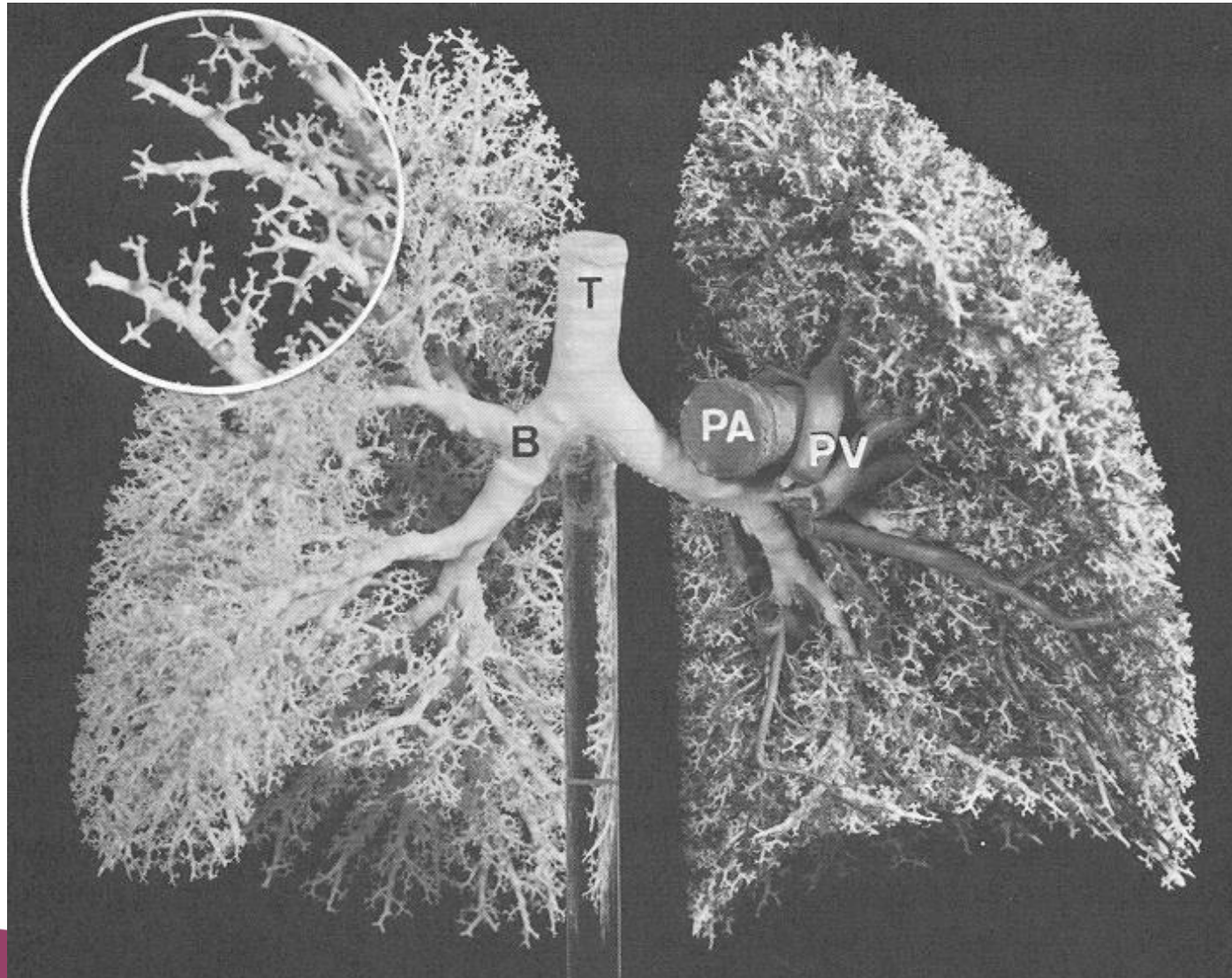


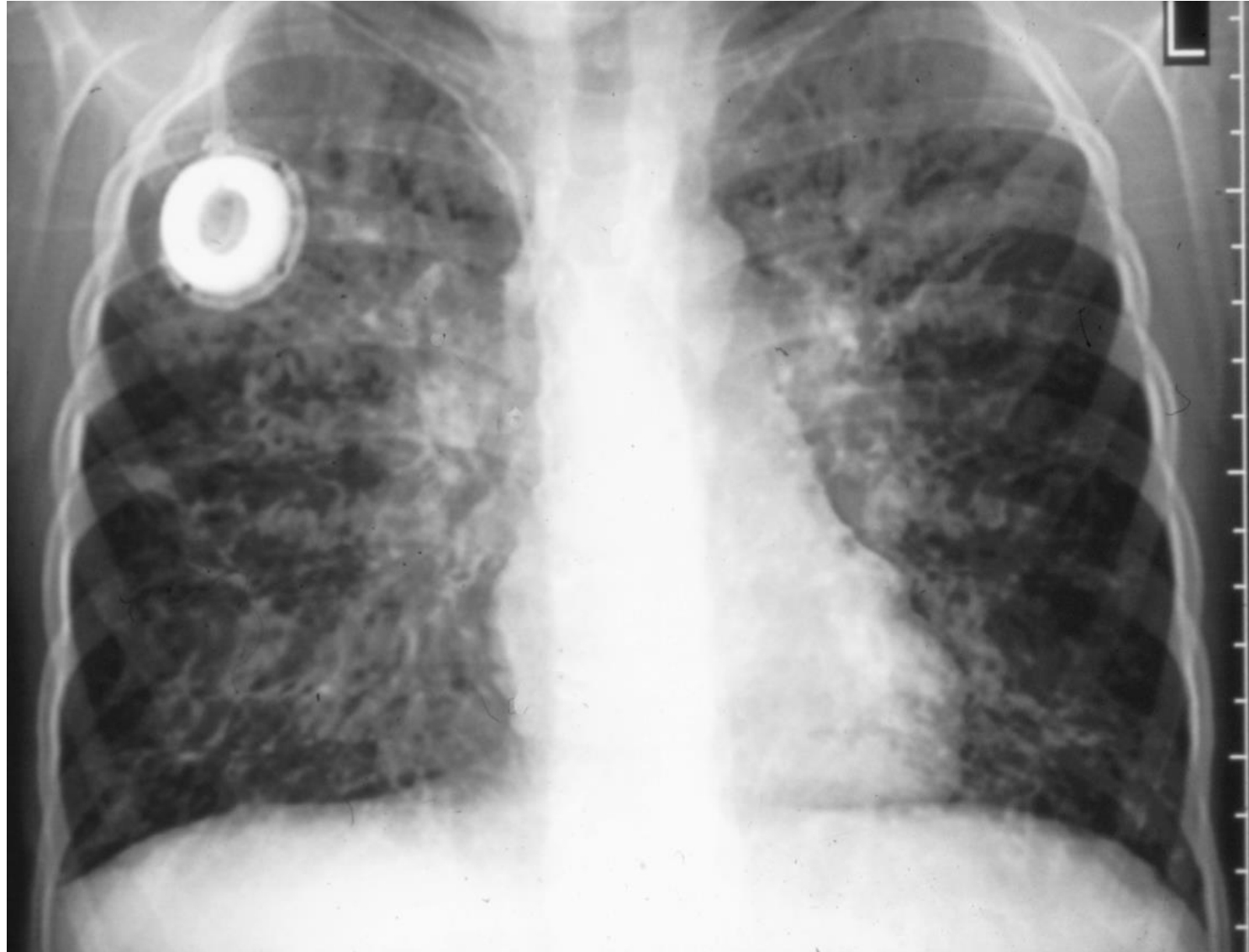


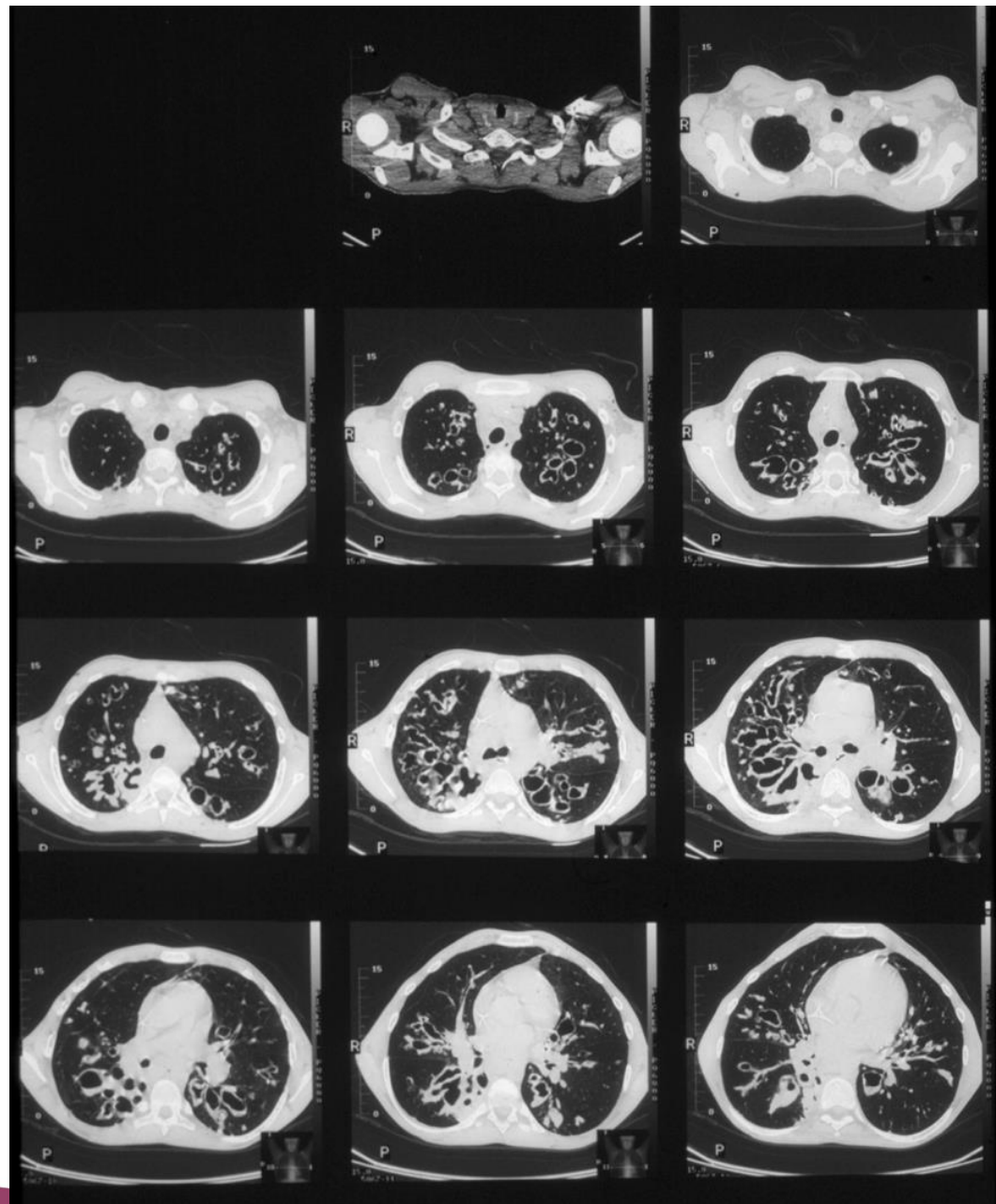
# Behandling av pankreasinsufficiens

- Pankreasenzymer
- Fettlösliga vitaminer (ffa ADE)
- Fettrik kost (40%)
- 120% RDA energi
- Vid dålig viktuppgång- PEG

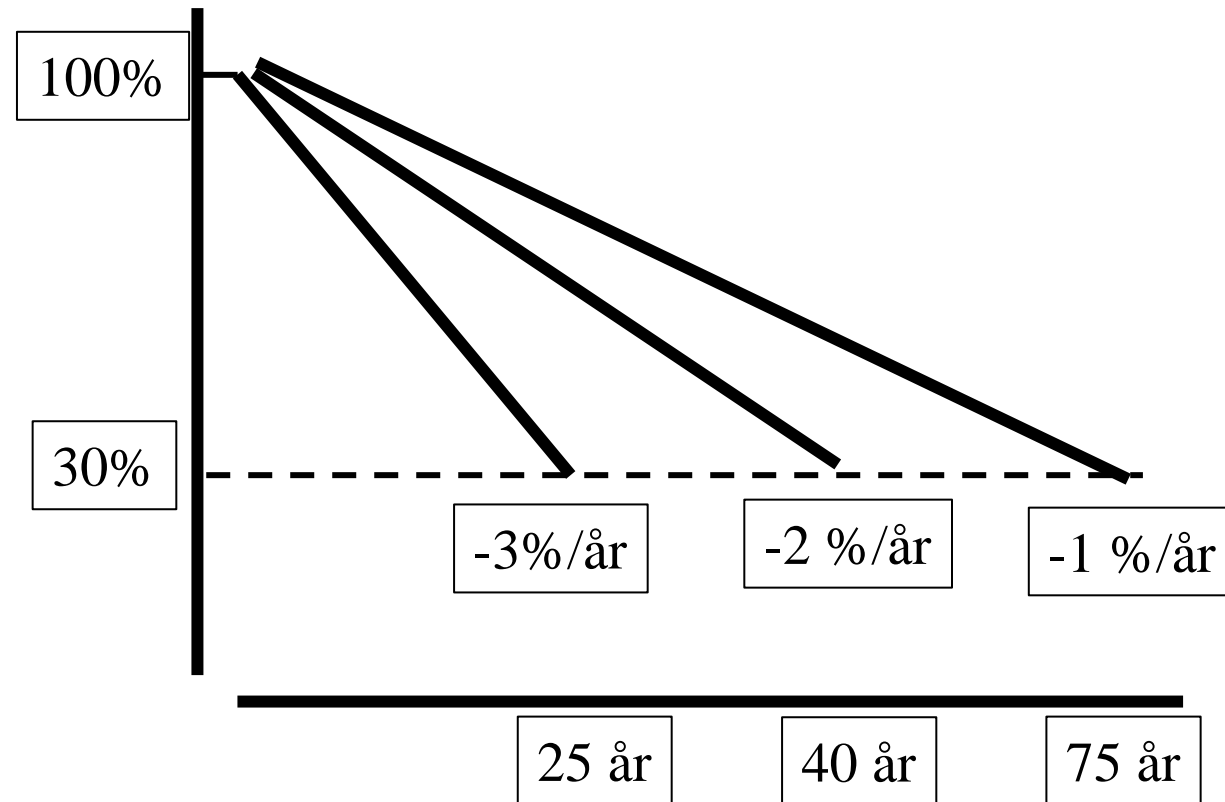






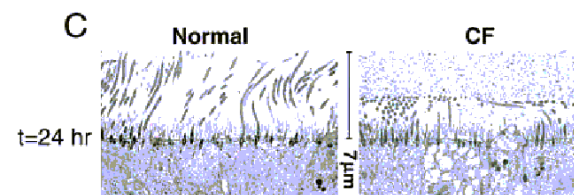
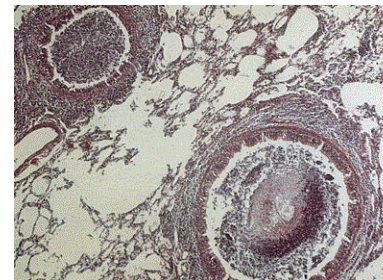
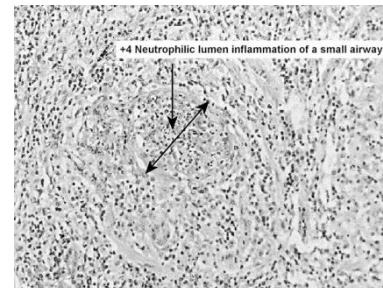


# Förlust av lungfunktion uttryckt som FEV1.0 (%)



# Lungbehandling

- Antiinflammatoriska
  - Perorala steroider
- Slemlösande
  - Pulmozyme (rhDNAse)
- Återskapa Airway surface liquid, lösa slem
  - Hyperton koksalt 3-7%
  - Mannitol



# Lungbehandling, forts

- Antibiotika ffa mot St.aureus, HI, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Burkholderia cepacia, Mycobacterium abscessus (oralt, intravenöst, inhalation)
- Ex inhalation: tobramycin, colistin, azactam
- Ex iv: tobramycin, ceftazidim, piperacilin, meropenem. Alltid två iv antibiotika. oftast i hemmet



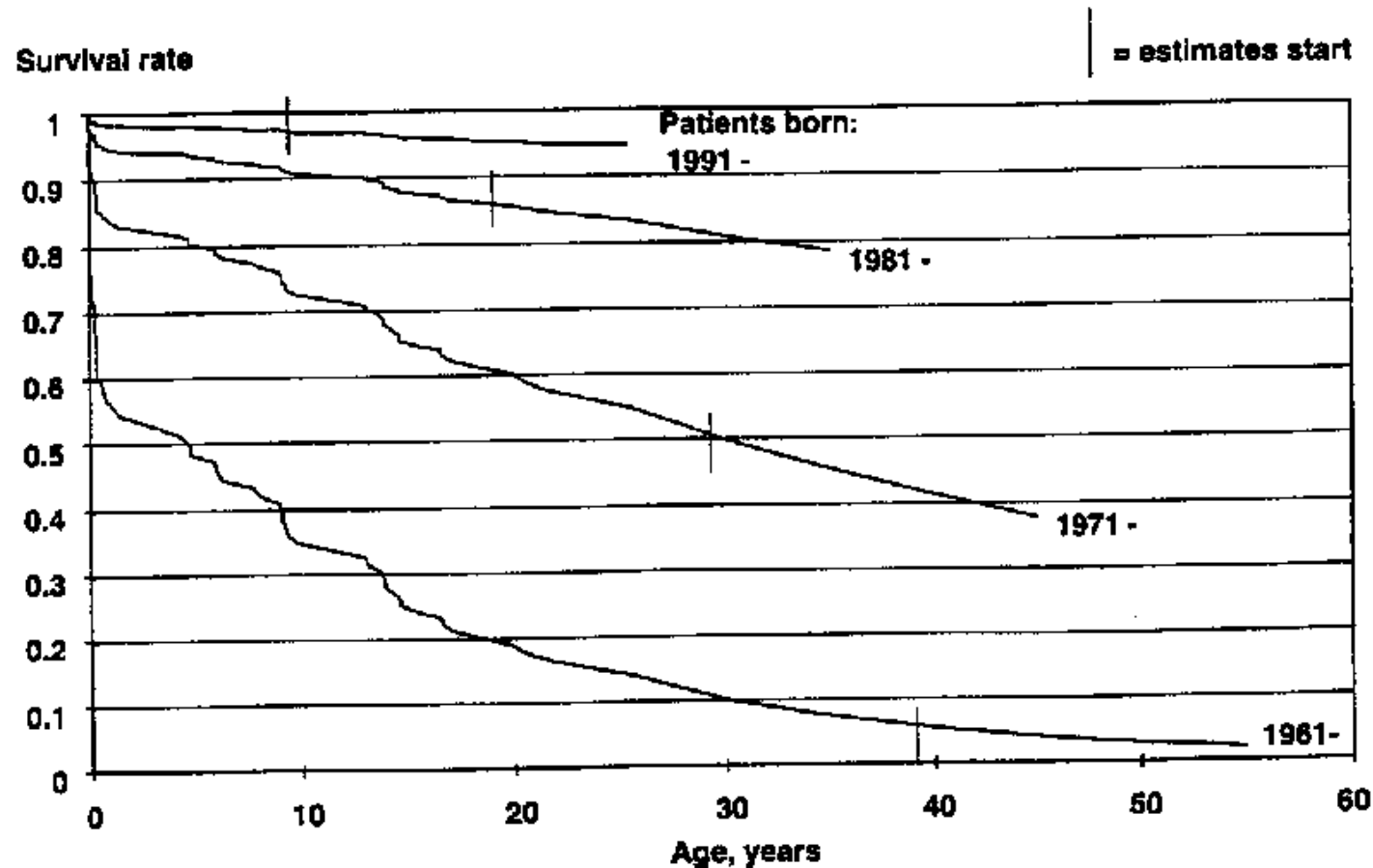
# Normal behandlingsdag för vuxen

- Inhalation hyperton koksalt, Pulmozyme morgon och kväll samt andningsgymnastik (slemmobilisering) 2 timmar
- Tabletter morgon och kväll (5-10 st)
- Pankreasenzymmer till varje måltid (2-8/gång)
- Inhalation antibiotika morgon och kväll
- Iv antibiotika 10-60 dagar per år

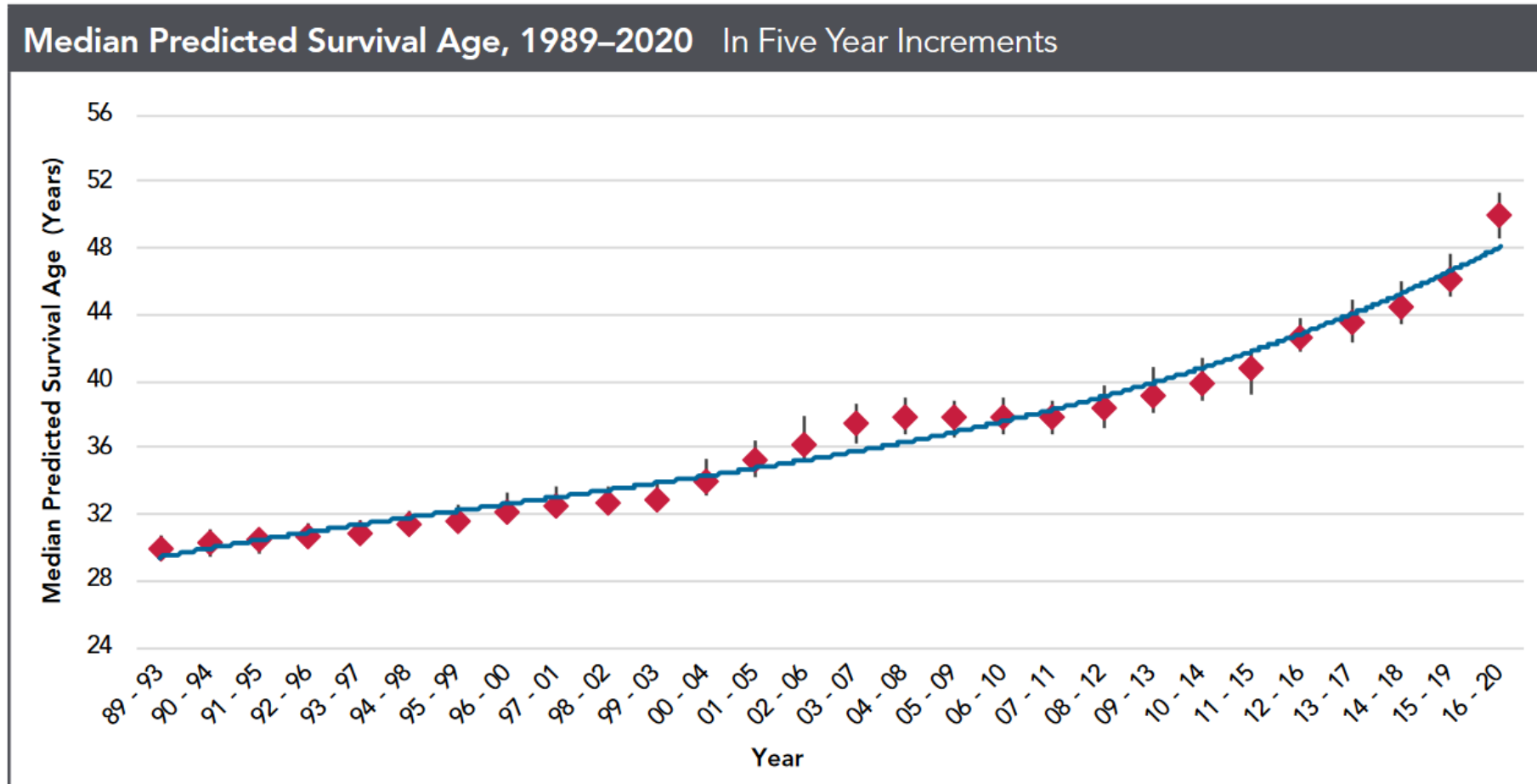
# Övriga vanliga komplikationer

- Diabetes mellitus (25- 30% vid 30 års ålder)
- Kronisk sinuit – FESS operation
- DIOS- distalt intestinalt obstruktivt syndrome
- Pancreatit
- Levercirrhos med portal hypertension
  - ca 2-3% svår leversjukdom
  - Levertransplantation

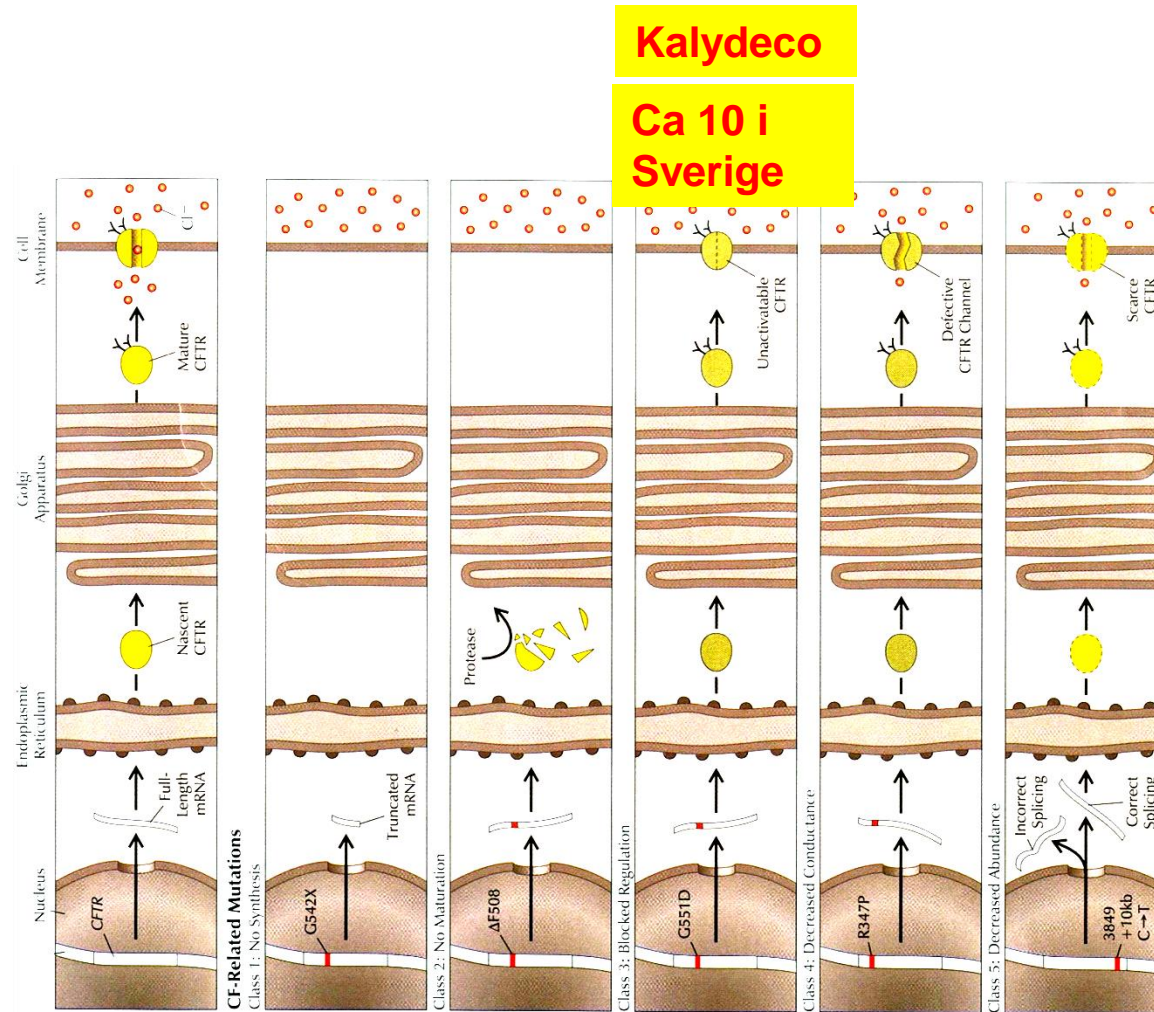
# Aktuell och uppskattad överlevnad av 4 olika födelsekohorter i den svenska CF-populationen



# Förväntad överlevnad över tid



# Olika typer av mutationsklasser



## I, II, III (severe)

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  - Meconium ileus, DIOS
  - CFRD
  - Severe hepatobiliary disease

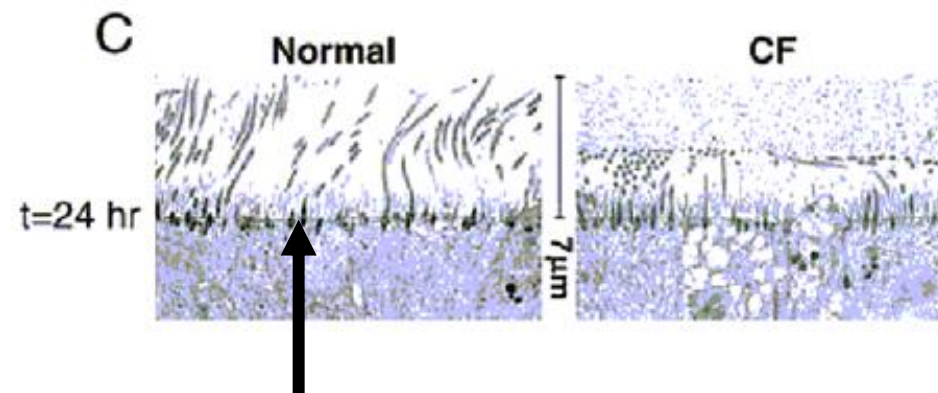
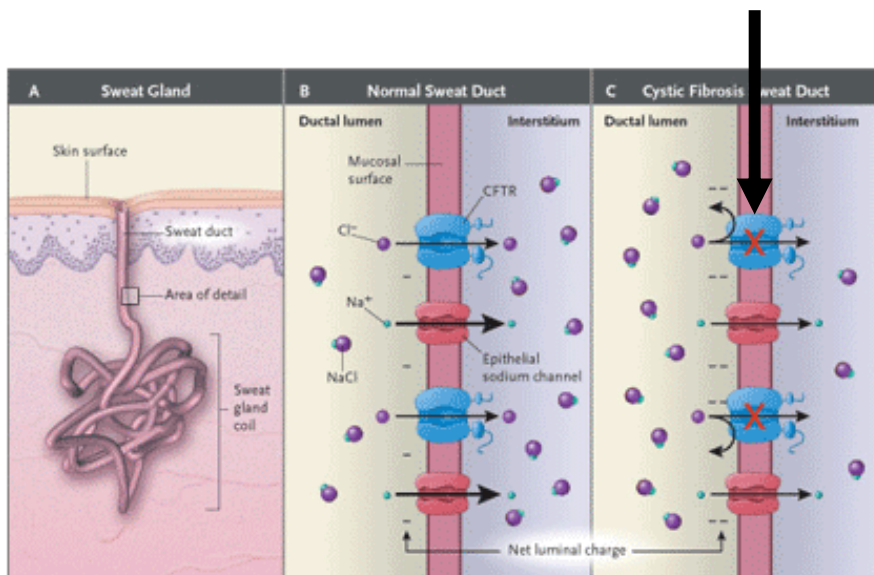
## IV, V (mild)

- Pancreatic Sufficiency
- Risk of:
  - Acute, recurrent pancreatitis
  - Chronic pancreatitis

# Vad gör de nya läkemedlena?

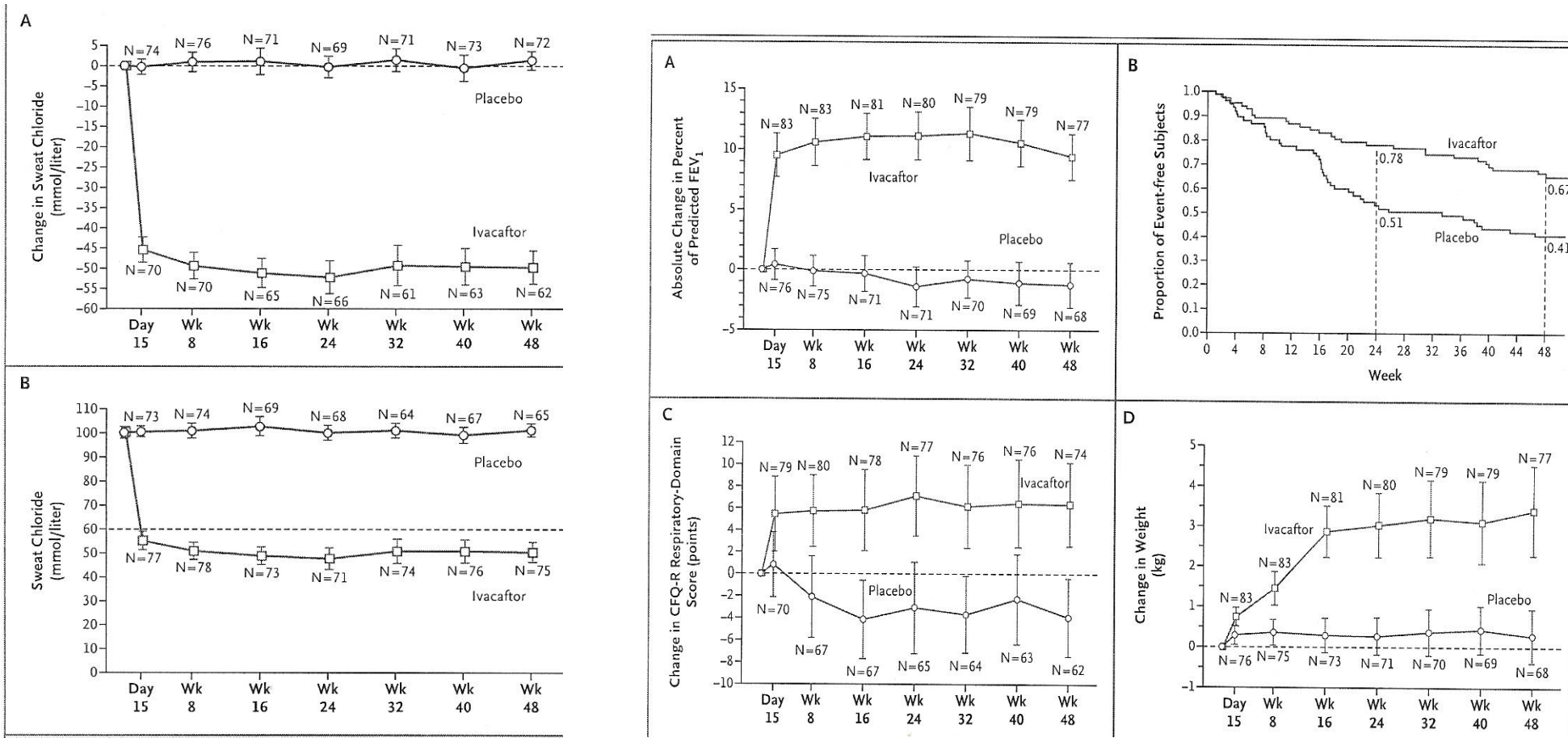
- Svettkörtel

- Lunga/luftvägar



# Behandlingseffekt av ivacaftor (Kalydeco)

Patienter med mutation G551D och andra gatingmutationer, ("potentiator")

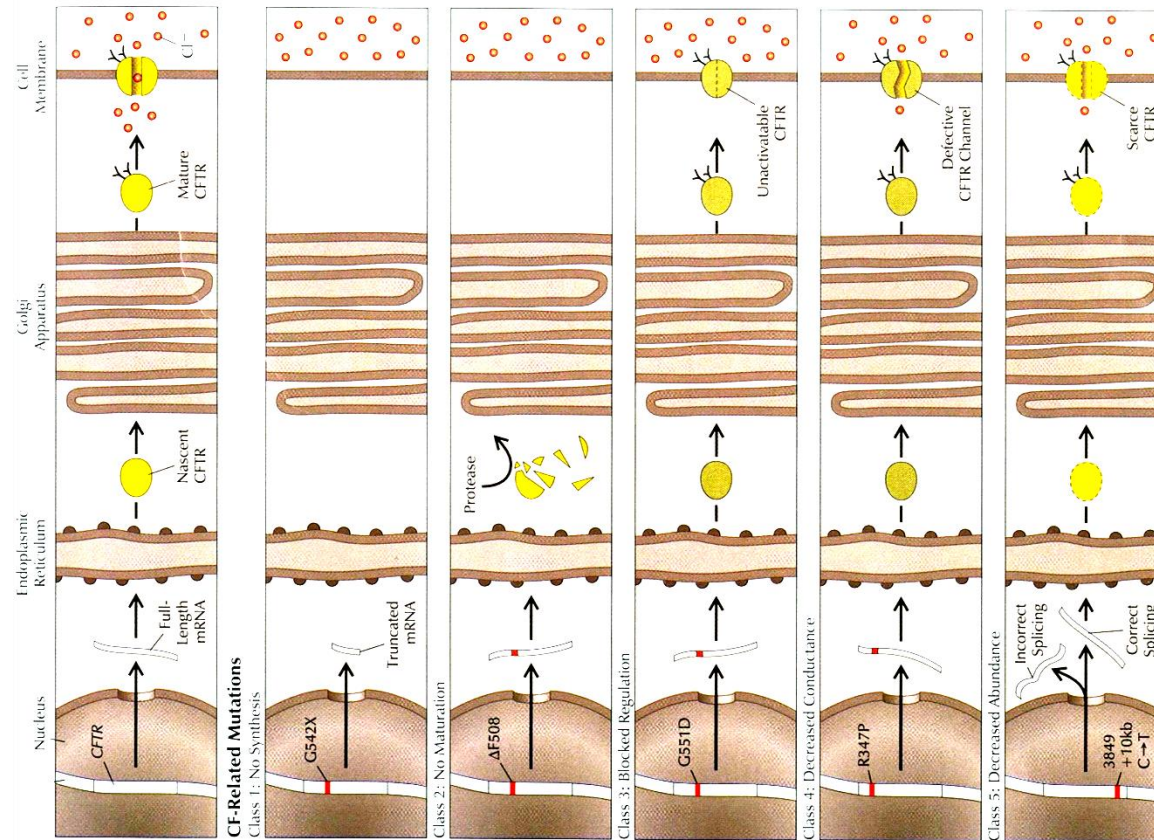


# Olika typer av mutationsklasser

Kaftrio

Orkambi

Kalydeco



## I, II, III (severe)

- Pancreatic Insufficiency
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  - Severe hepatobiliary disease

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## Articles

### Efficacy and safety of the elexacaftor plus tezacaftor plus ivacaftor combination regimen in people with cystic fibrosis homozygous for the *F508del* mutation: a double-blind, randomised, phase 3 trial

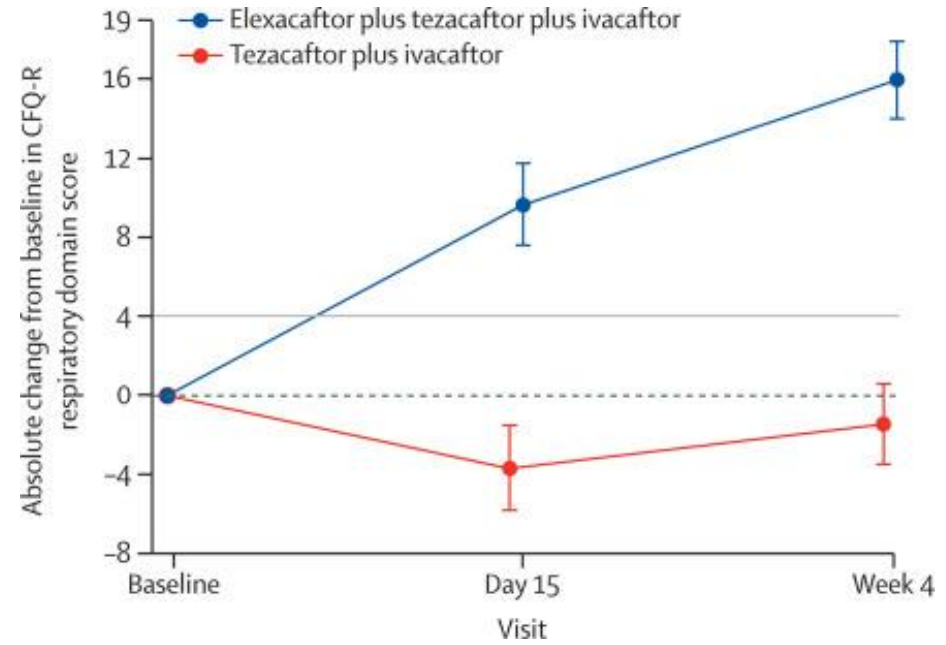
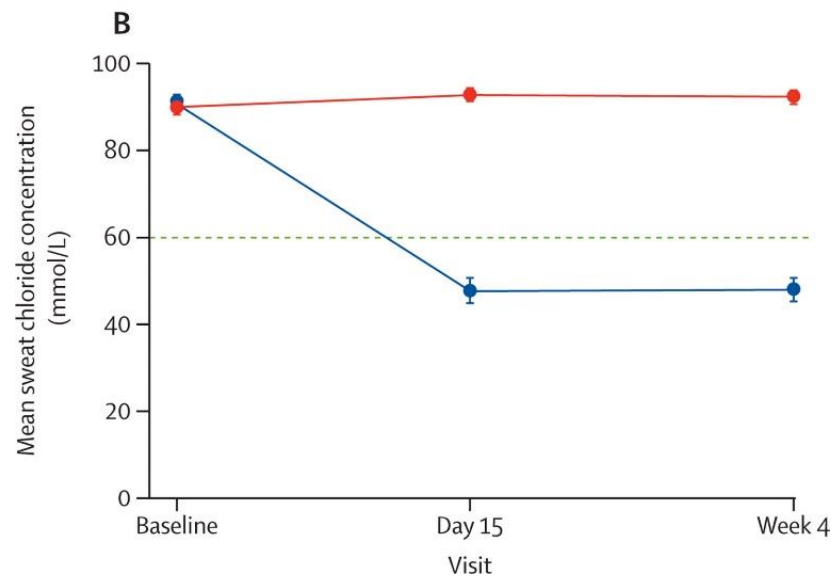
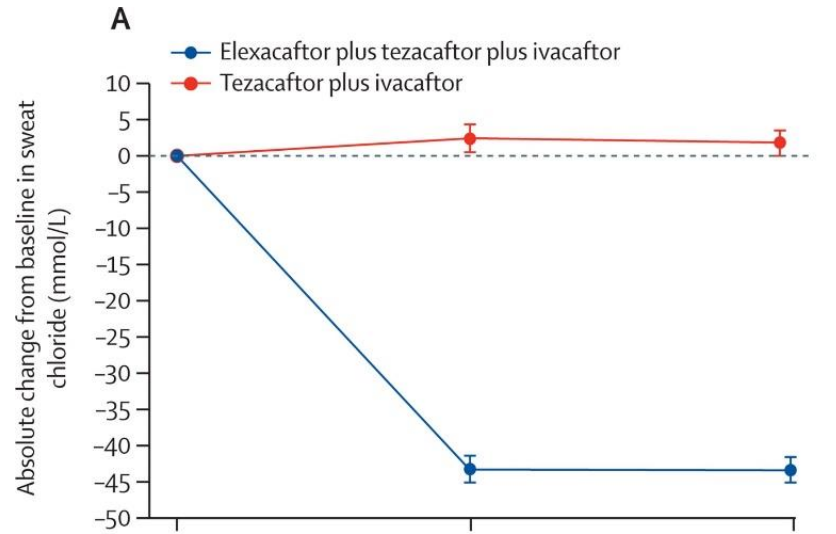
Prof Harry G M Heijerman MD <sup>a\*</sup>  , Edward F McKone MD <sup>b\*</sup>, Damian G Downey MD <sup>c</sup>, Eva Van Braeckel MD <sup>d</sup>, Steven M Rowe MD <sup>e</sup>, Elizabeth Tullis MD <sup>f</sup>, Marcus A Mall MD <sup>g, h, i</sup>, John J Welter MD <sup>j</sup>, Bonnie W Ramsey MD <sup>k</sup>, Charlotte M McKee MD <sup>l</sup>, Gautham Marigowda MD <sup>l</sup>, Samuel M Moskowitz MD <sup>l</sup>, David Waltz MD <sup>l</sup>, Patrick R Sosnay MD <sup>l</sup>, Christopher Simard MD <sup>l</sup>, Neil Ahluwalia MD <sup>l</sup>, Fengjuan Xuan PhD <sup>l</sup>, Yaohua Zhang PhD <sup>l</sup> ... Christof Majoor

ORIGINAL ARTICLE

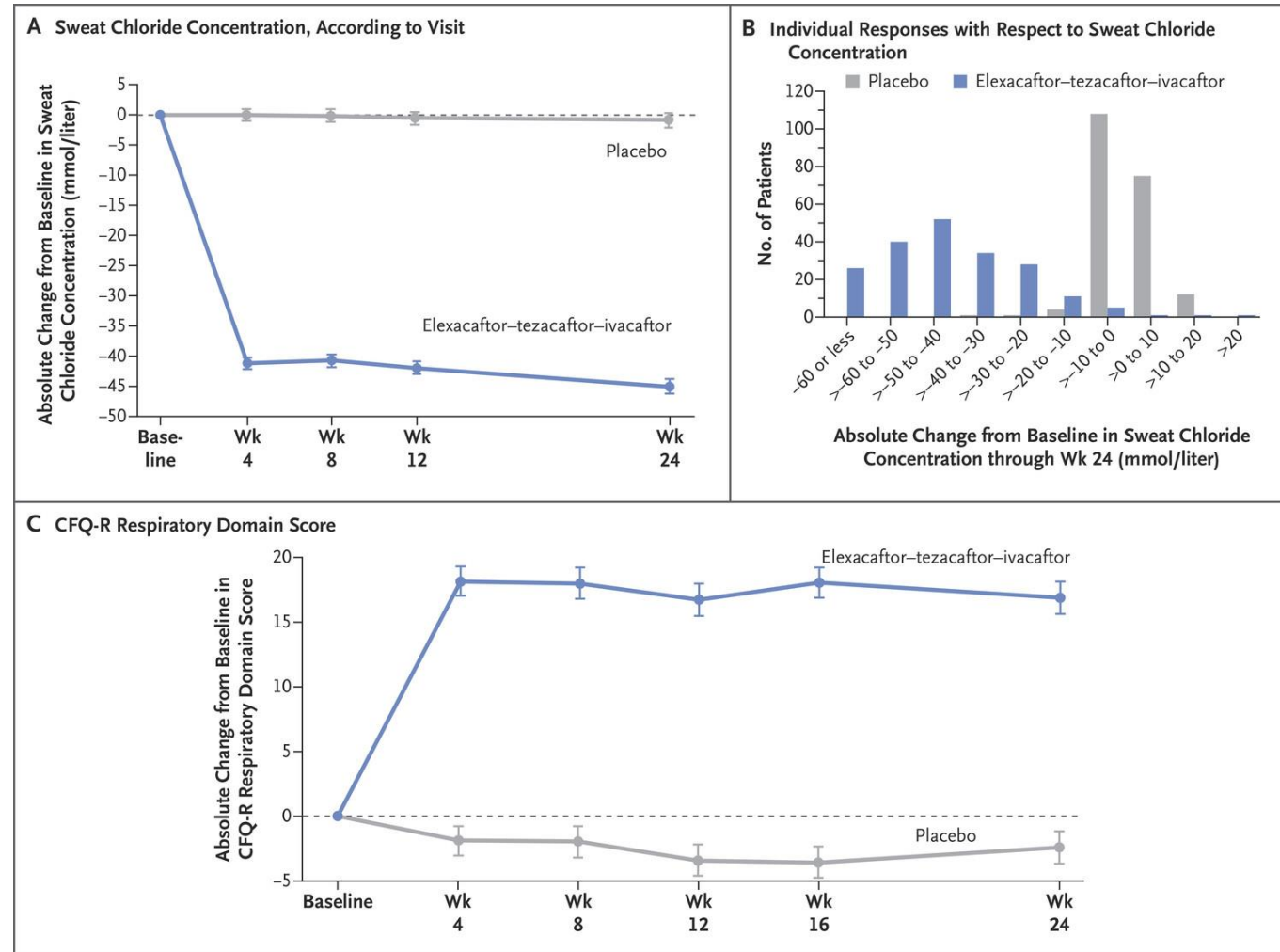
## Elexacaftor–Tezacaftor–Ivacaftor for Cystic Fibrosis with a Single Phe508del Allele

Peter G. Middleton, M.D., Marcus A. Mall, M.D., Pavel Dřevínek, M.D., Larry C. Lands, M.D., Edward F. McKone, M.D., Deepika Polineni, M.D., Bonnie W. Ramsey, M.D., Jennifer L. Taylor-Cousar, M.D., Elizabeth Tullis, M.D., François Vermeulen, M.D., Gautham Marigowda, M.D., Charlotte M. McKee, M.D., et al., for the VX17-445-102 Study Group\*

Ca 50 %  
av alla

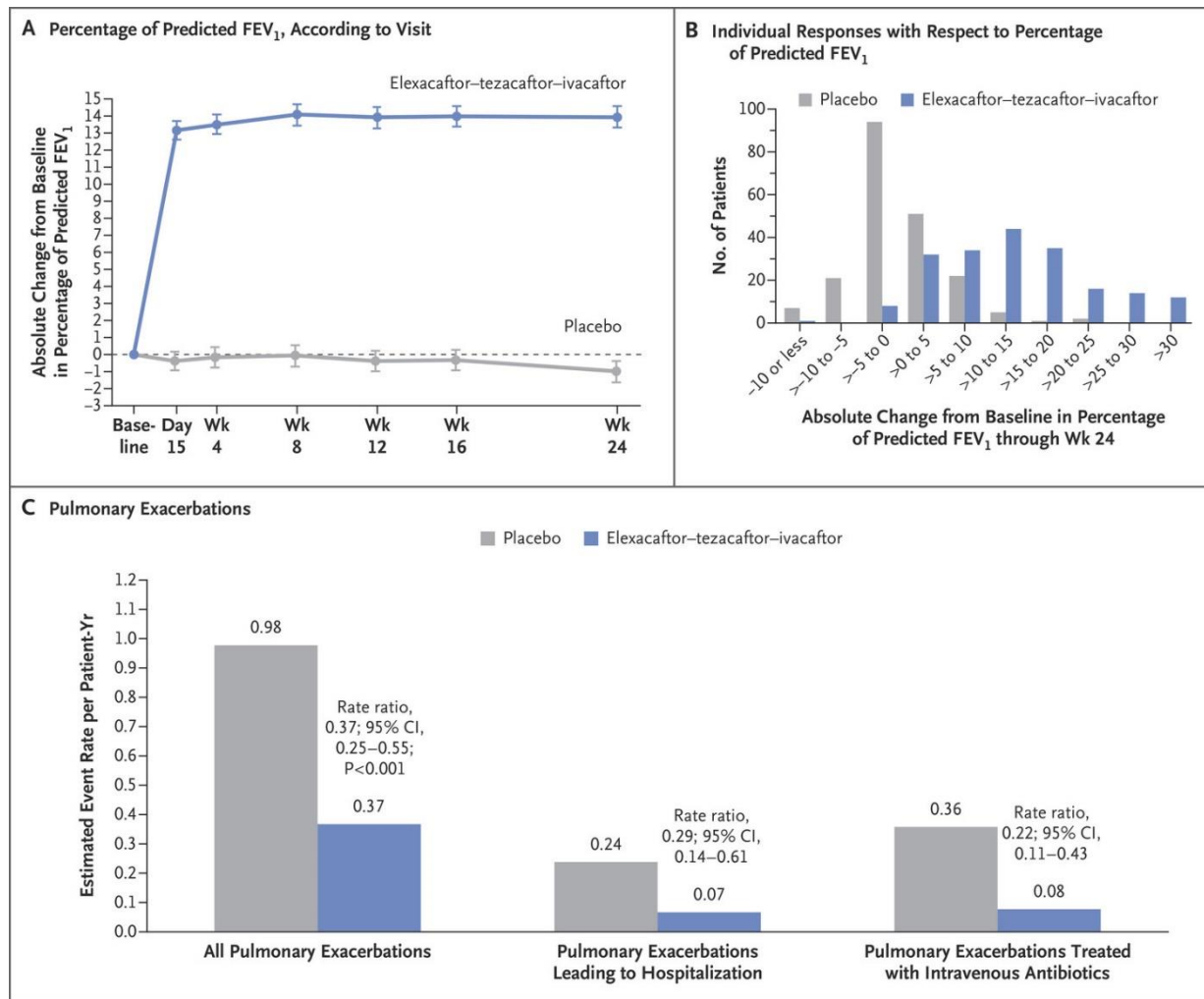


# Absolute Change from Baseline in Sweat Chloride Concentration and CFQ-R Respiratory Domain Score



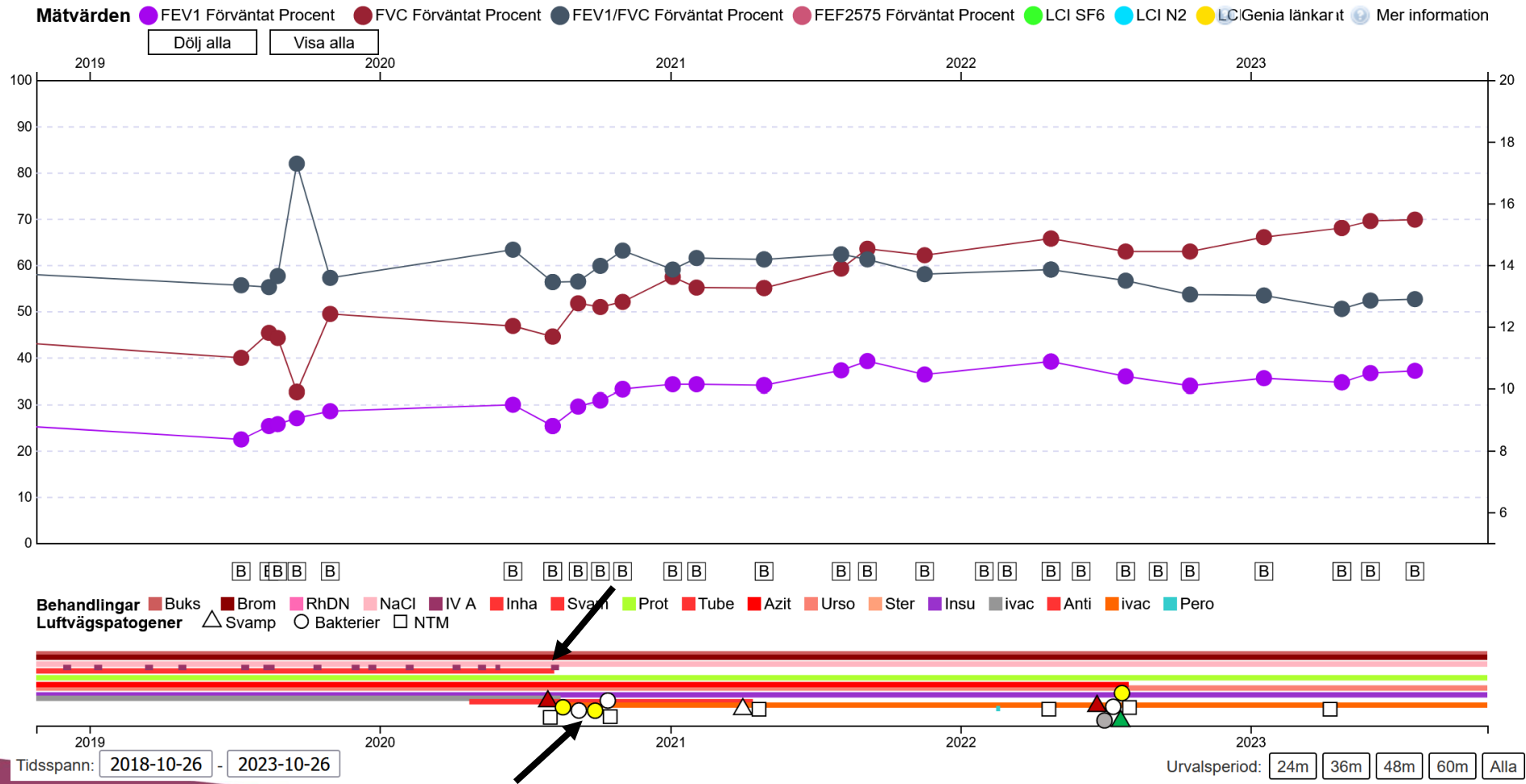
PG Middleton et al. N Engl J Med 2019.

# Absolute Change from Baseline in Percentage of Predicted FEV<sub>1</sub>, and Rate of Pulmonary Exacerbations

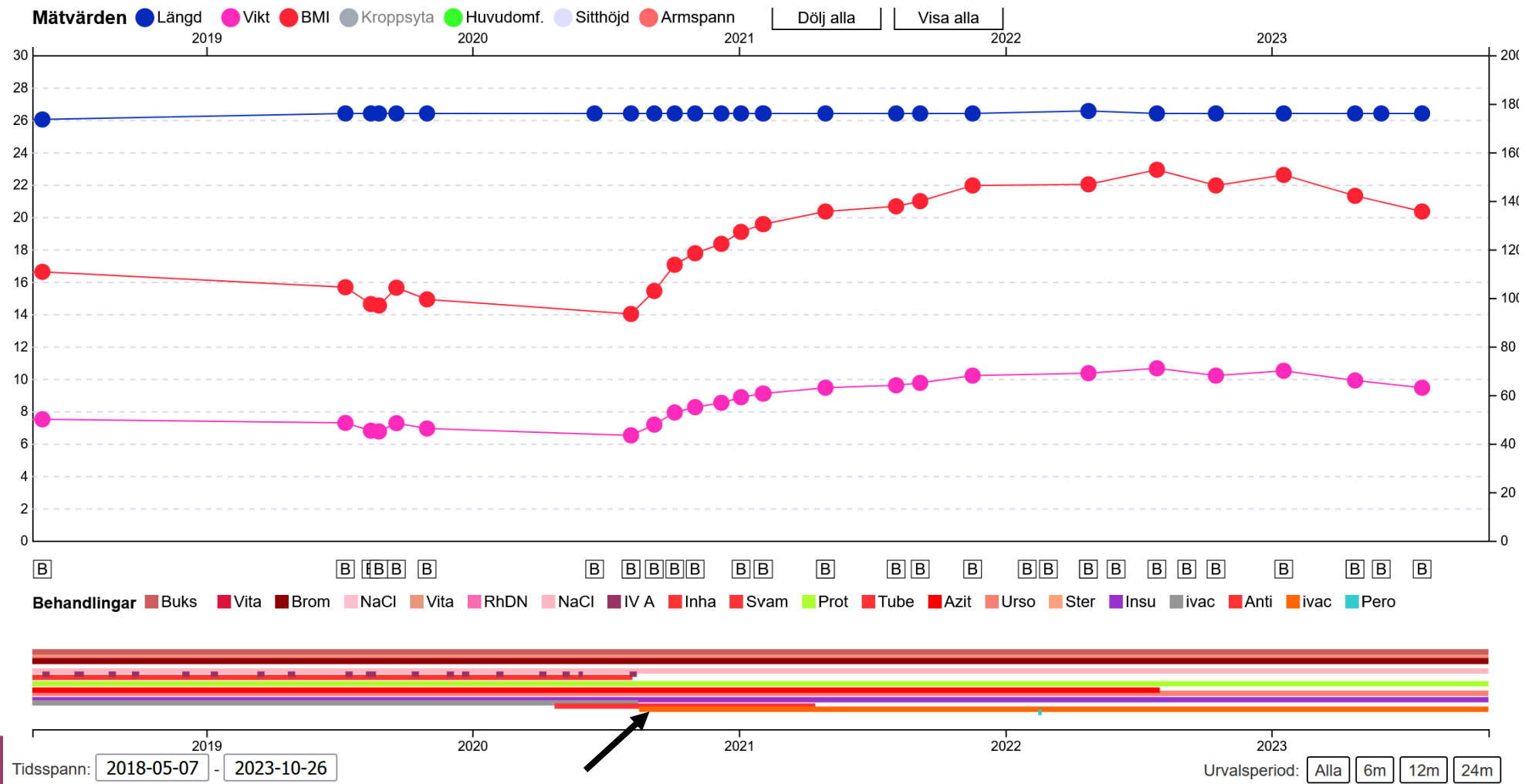


PG Middleton et al. N Engl J Med 2019.

# Pojke 21 år, dF508/dF508, kronisk P aeruginosa



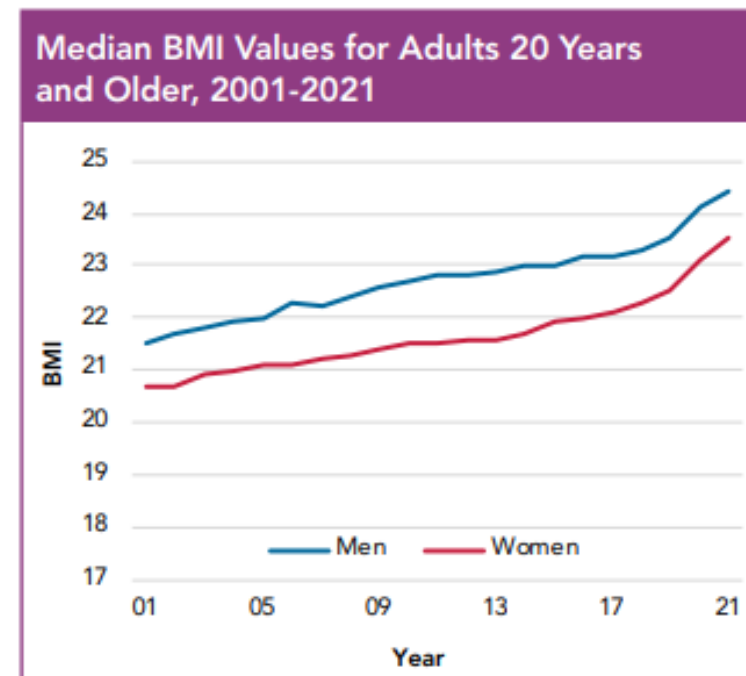
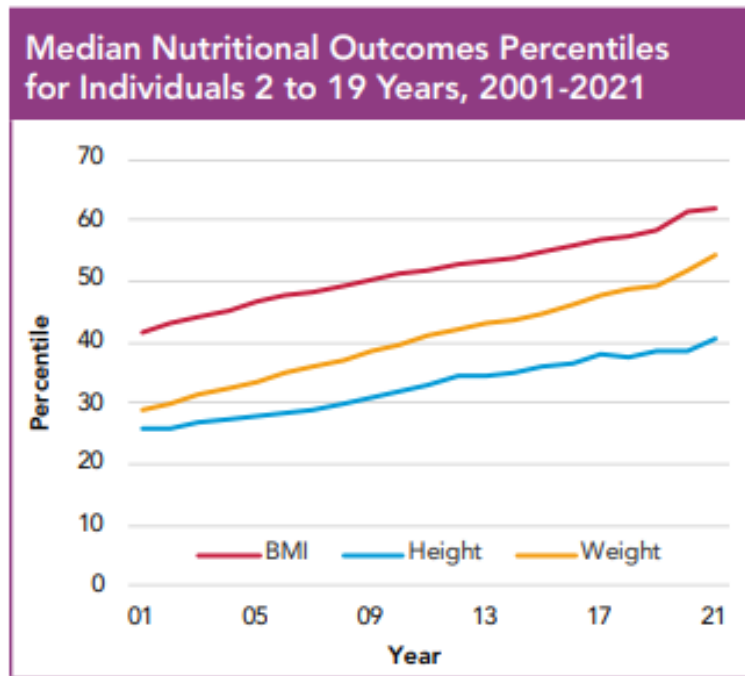
# Pojke 21 år, dF508/dF508, kronisk P aeruginosa



# Hur ser det ut på sikt?

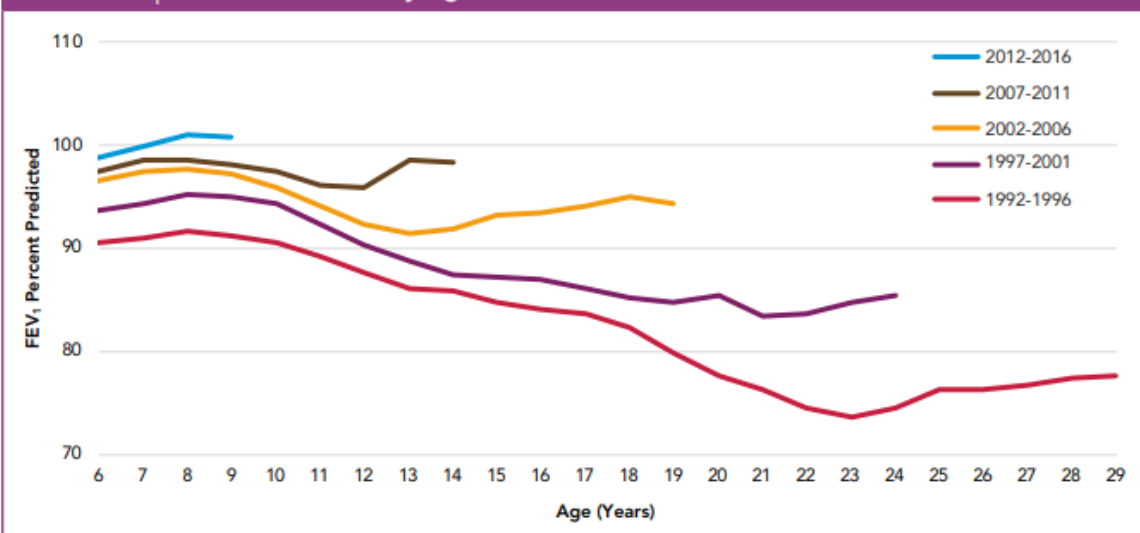
- Låt oss titta på USA siffror som kunnat behandla med CFTRmodulatorer sedan december 2019

# Nutrition

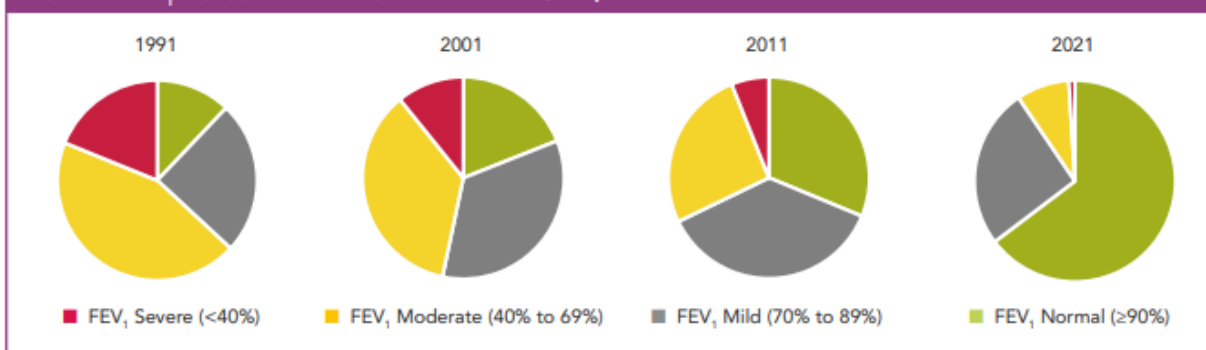


# Lungfunktion

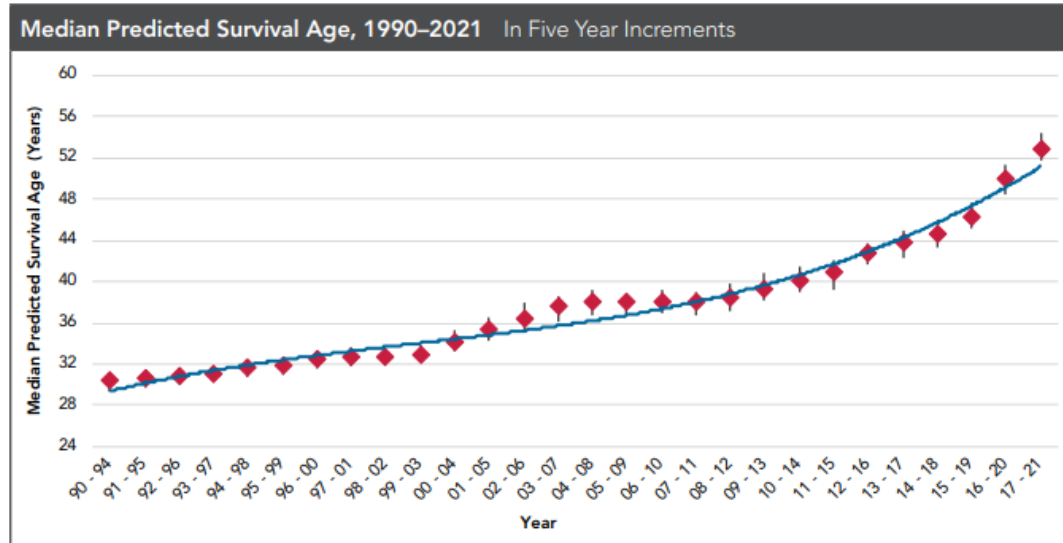
Median FEV<sub>1</sub> Percent Predicted, by Age and Birth Cohort



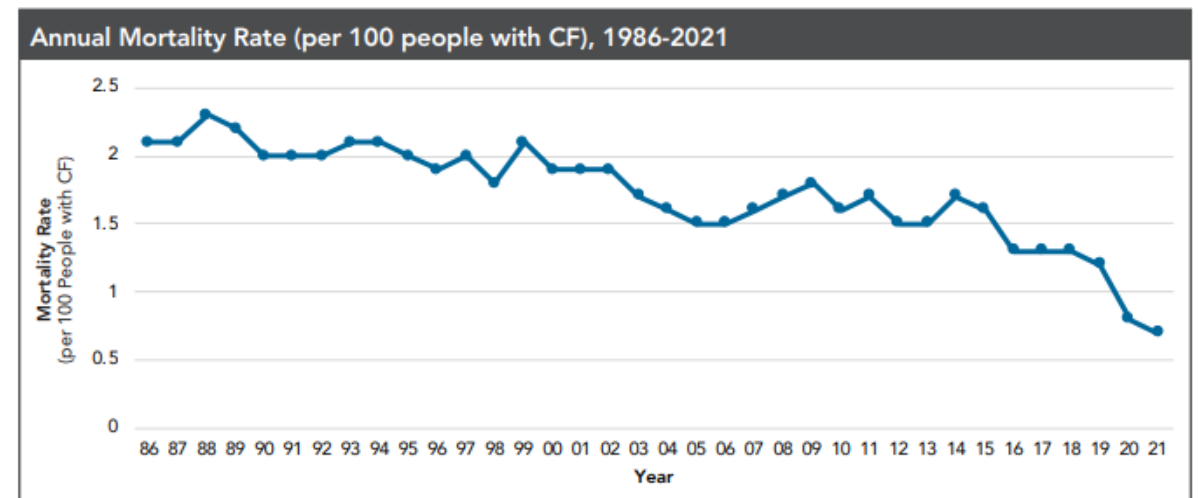
Median FEV<sub>1</sub> Percent Predicted in 18-Year-Olds, 1991–2021



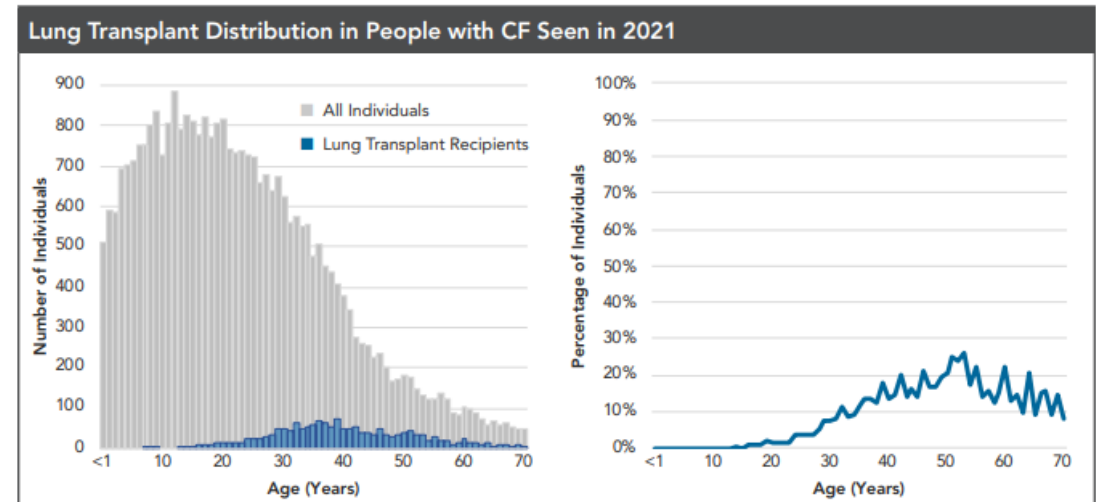
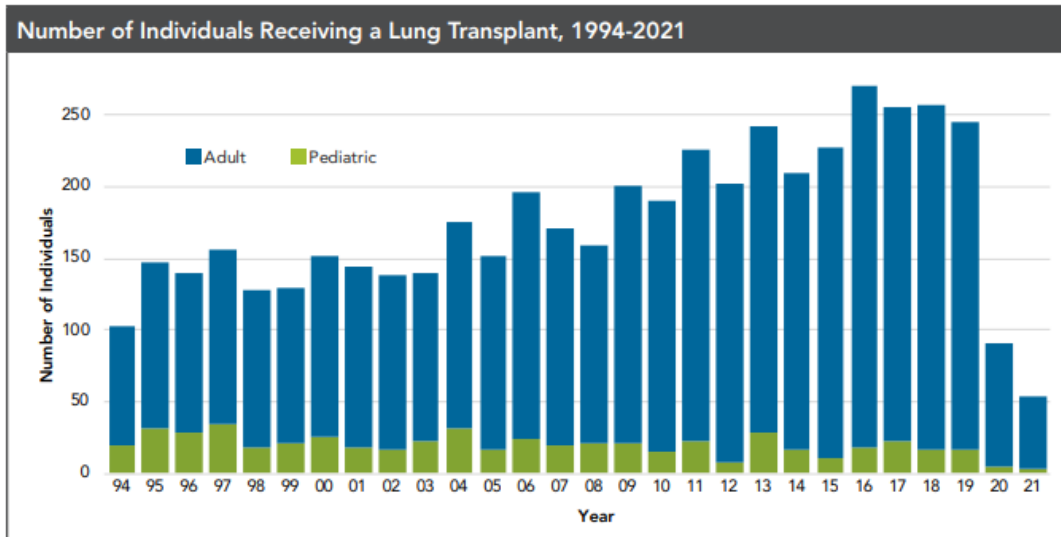
# Mortalitet



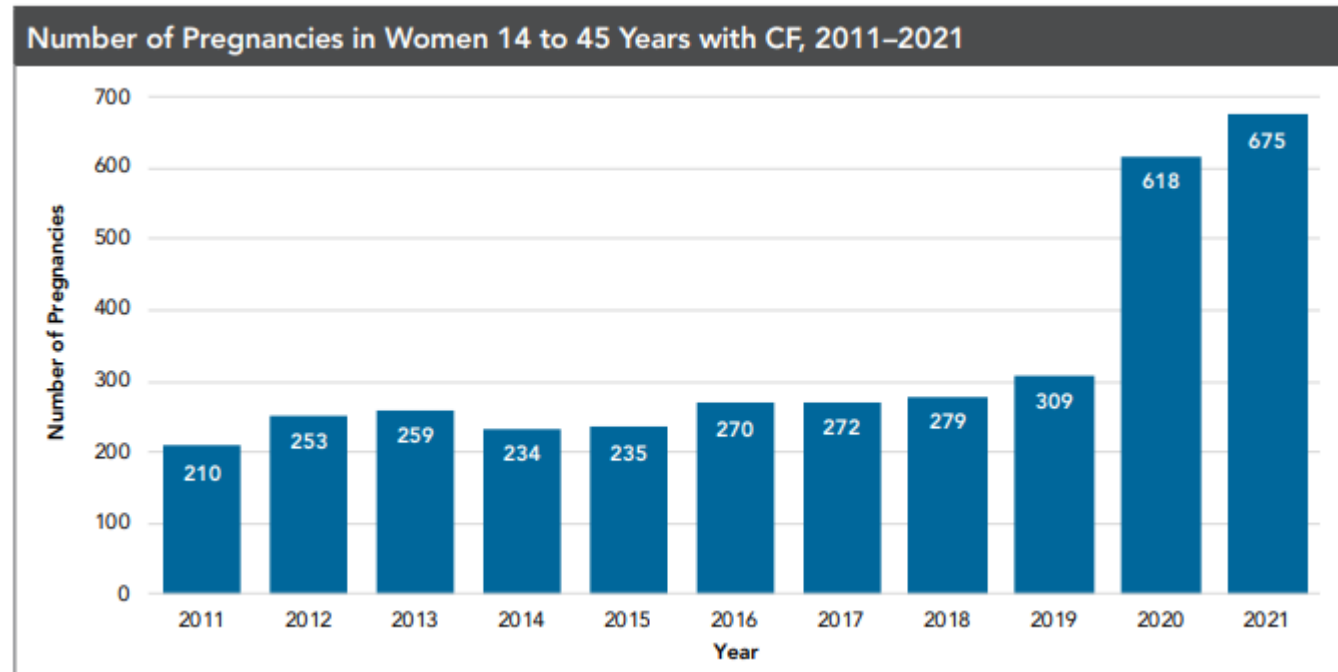
*\*Using the currently recommended method for calculating median predicted survival. For more information about the methodology, please see the Technical Supplement available at [cff.org](http://cff.org).*



# Lungtransplantation



# Graviditeter



# Framtid

## Överlevnad och lungfunktion

Normal lungfunktion?

Närma sig normal överlevnad?

Skillnad på barn med lite lungskada  
och vuxna med mycket lungskada

## Komplikationer

Diabetes mellitus?

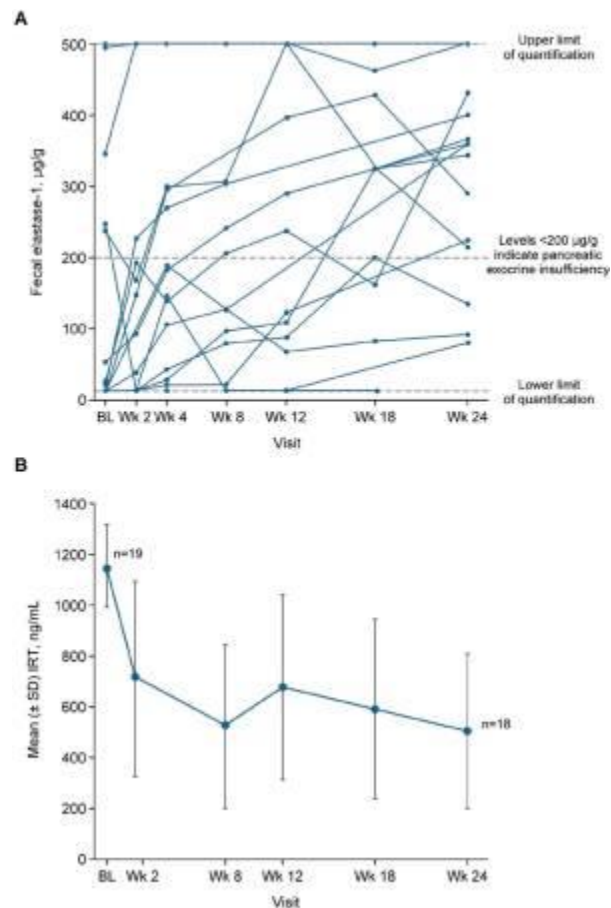
Grav leversjukdom?

Allergisk aspergillos?

Sinuititer?

Förebygga pankreasinsufficiens?

# Barn med gating mutationer 1-2 år vid start av behandling med ivacaftor



# Barn med gating mutationer 2-5 år vid start av behandling med ivacaftor

