New beta-adrenergic sweat test

to assess CFTR function

in patients with acute recurrent/chronic pancreatitis

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PancreasFest 2019

SickKids®
THE HOSPITAL FOR SICK CHILDREN

UNIVERSITY OF TORONTO
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Current criteria for the diagnosis of CF

- One or more characteristic phenotypic features

  - or a history of a CF sibling

  - or positive newborn screening test result

AND

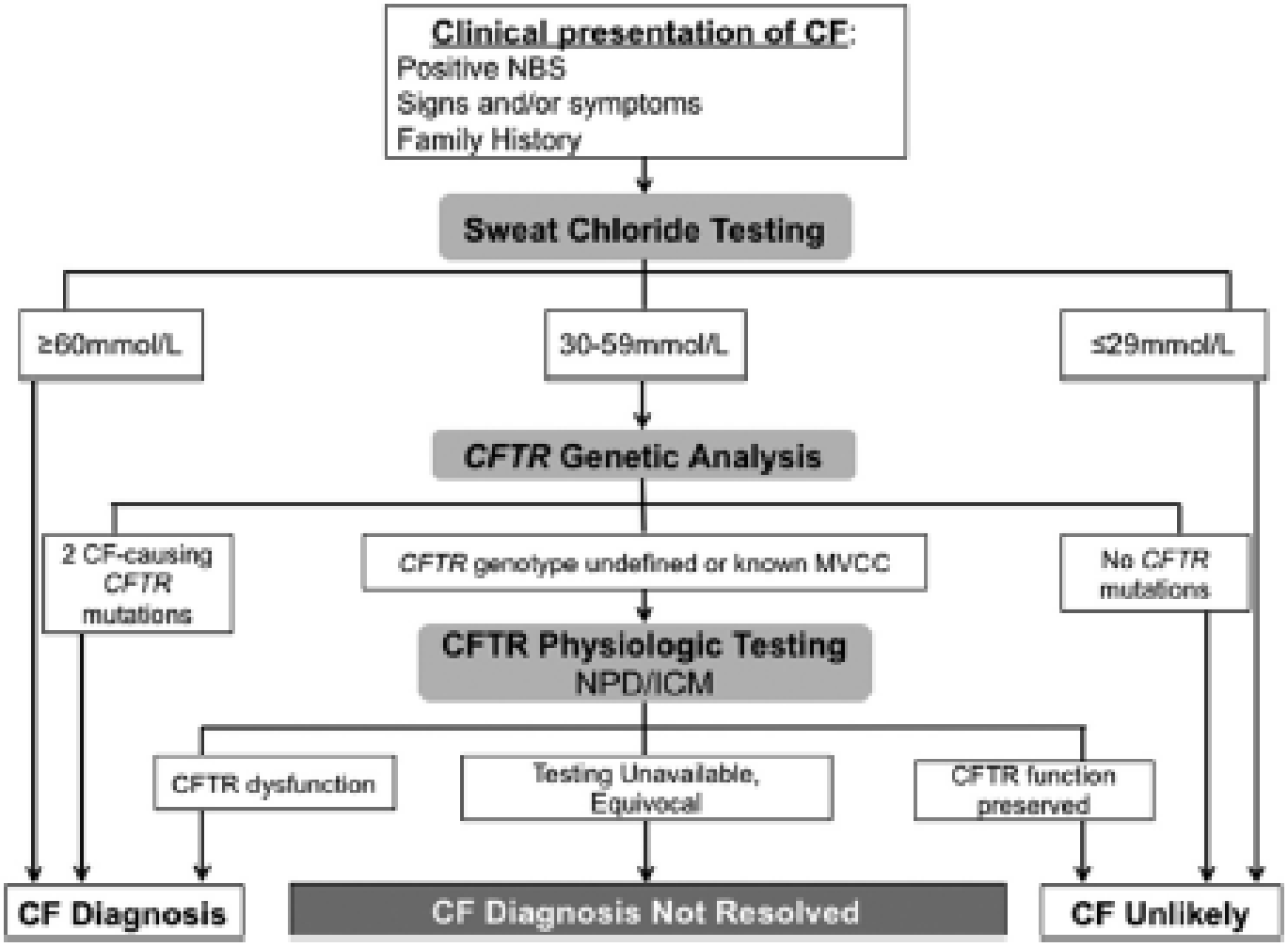
- Increased sweat [Cl^-] on two or more occasions

  - or two CF-causing mutations

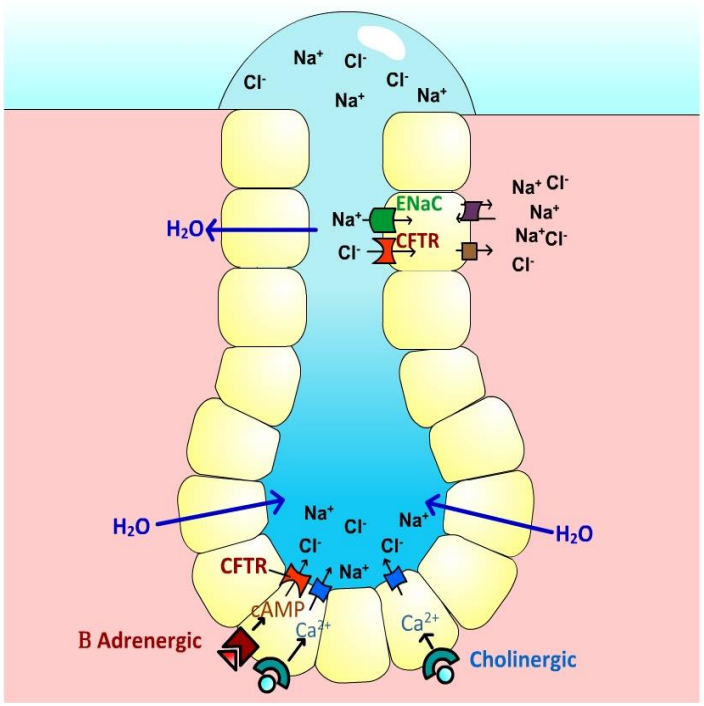
  - or abnormal nasal epithelial ion transport

Farrell , J Pediatr 2017

Current criteria for the diagnosis of CF



Classic sweat test: Determining [sweat Cl^-]



Model Stan Pasyk

1

Wescor©

2

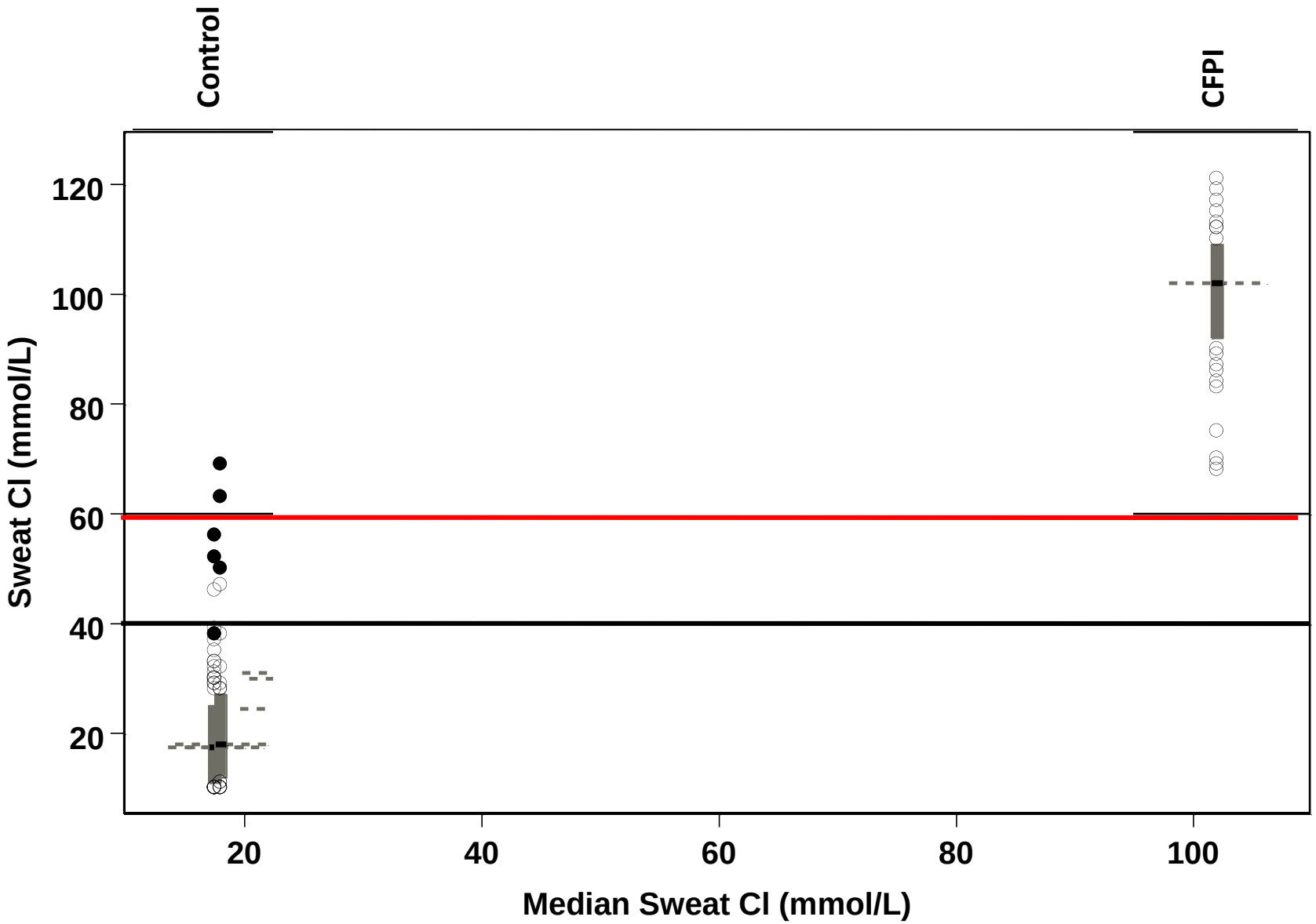
Wescor©

3

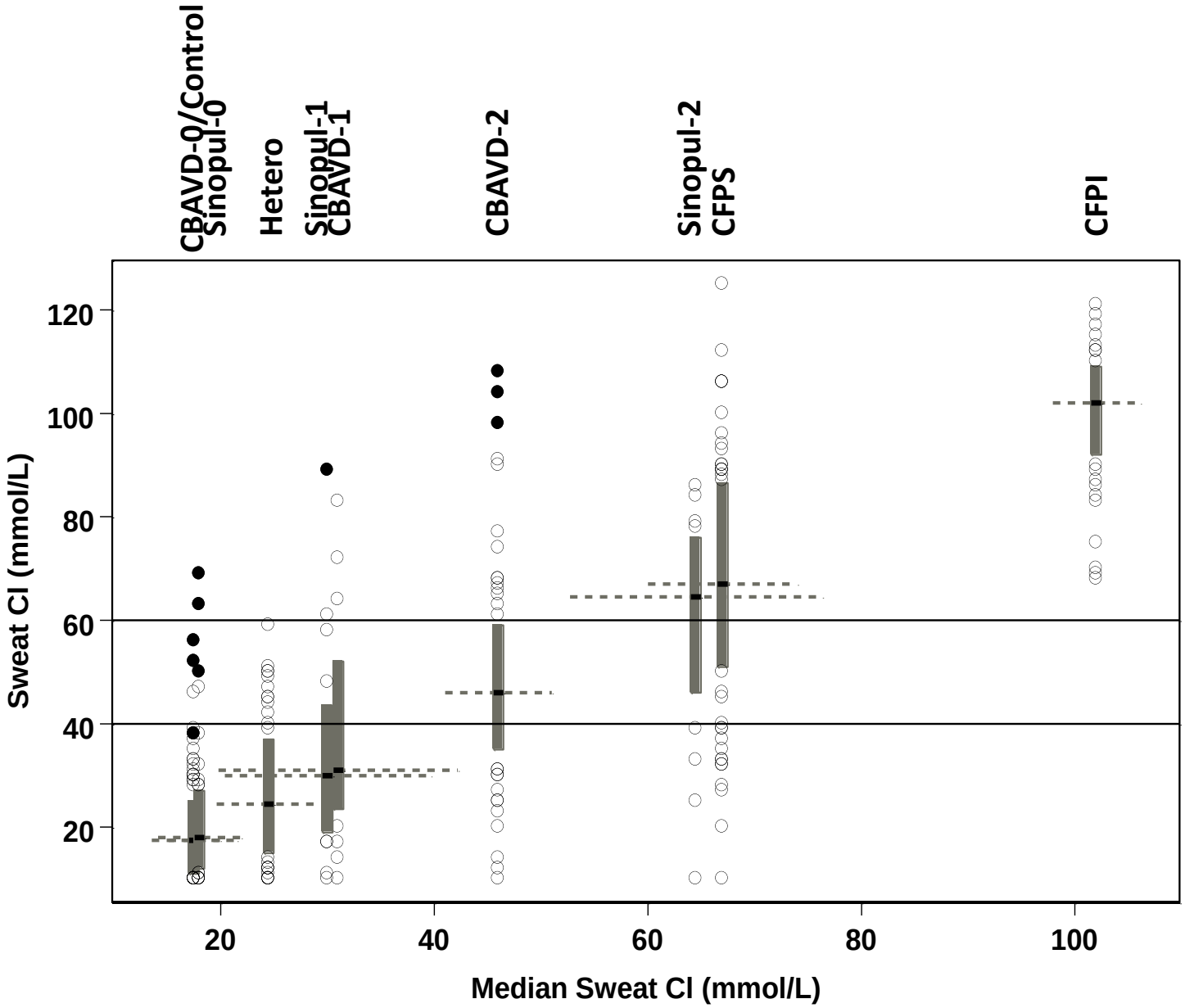
http://www.thomassci.com/_resources/_global/media

Gibson, L., di Sant-Agnese, P. and Shwachman, H. Procedure for the quantitative iontophoretic sweat test for cystic fibrosis. Cystic Fibrosis Foundation, 1972.
National Committee for Clinical Laboratory Standards. Sweat testing: sample collection and quantitative
The Committee, 1994.

CFTR function assessed with Sweat chloride test

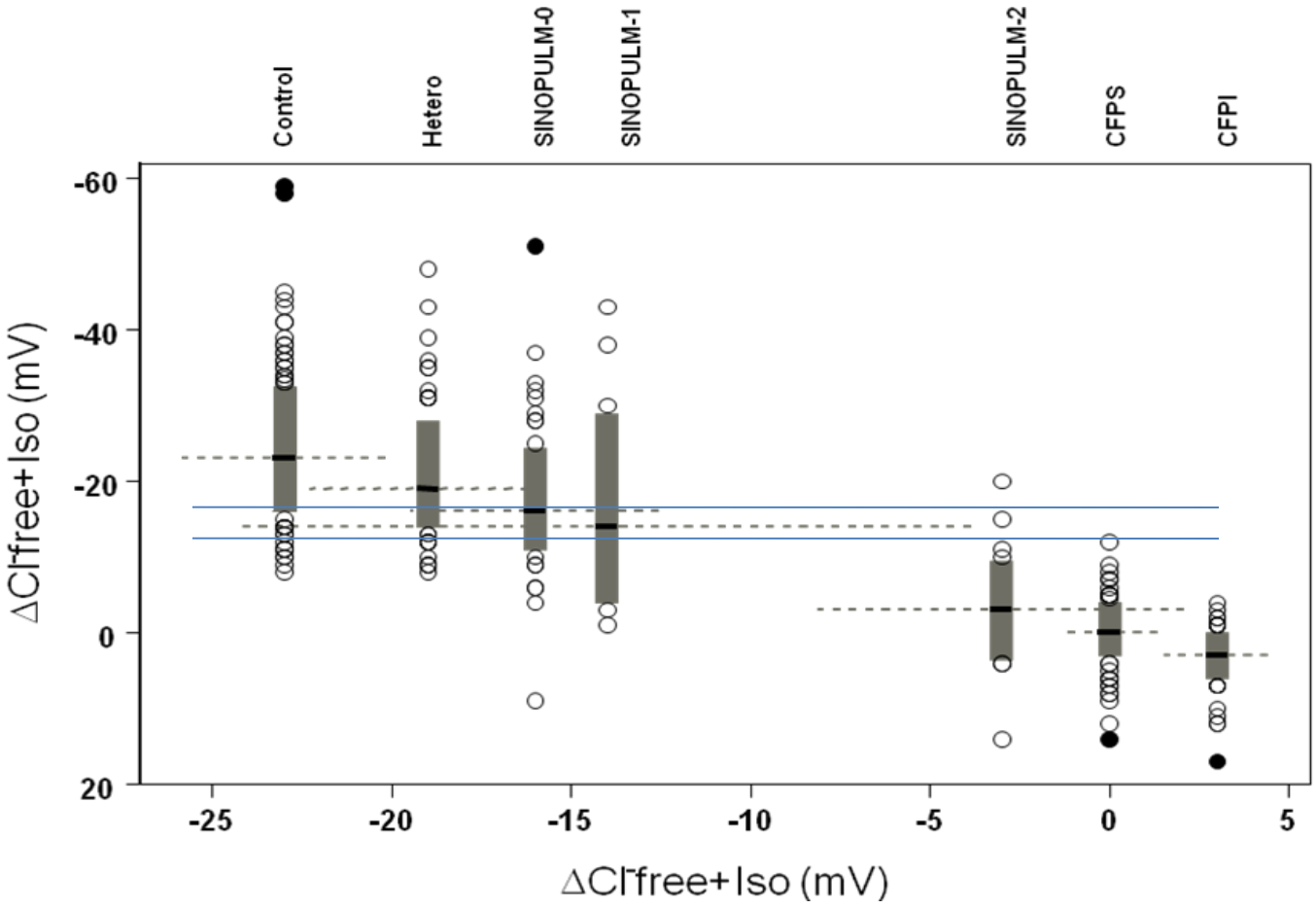


CFTR function assessed with Sweat chloride test



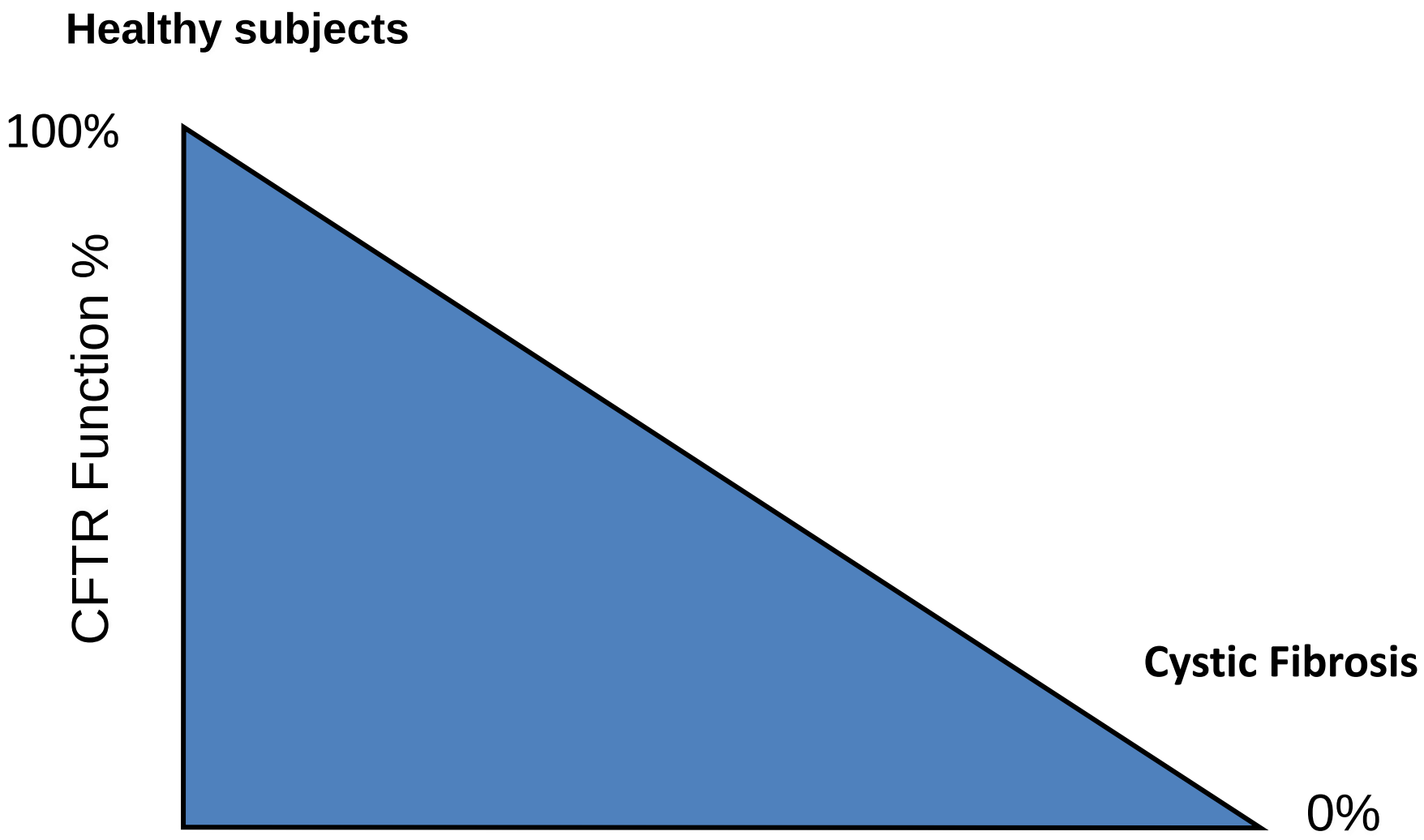
Wilschanski et al. AJRCCM 2010, Gonska et al. Chest 2012

Functional CFTR assessment – NPD ΔISO+Cl free

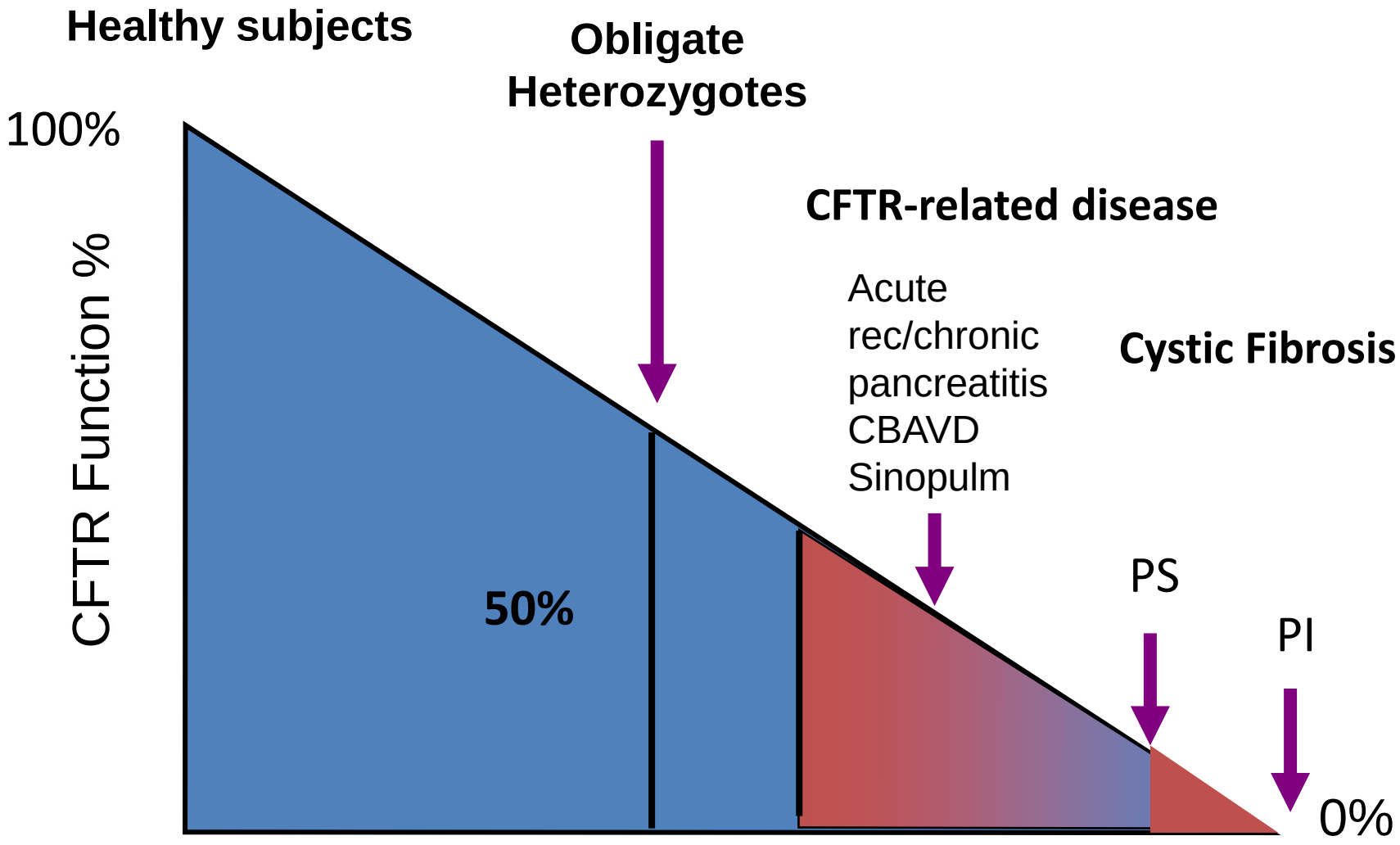


Gonska et al, Chest 2012

Spectrum of CF Phenotypes



Spectrum of CF Phenotypes



Current criteria for the diagnosis of CFTR-related disease

- One or more characteristic phenotypic features

  - bronchiectasis/chronic sinopulmonary disease
  - acute recurrent or chronic pancreatitis
  - male azoospermia

AND

- Borderline sweat [Cl^-] on two or more occasions

  - and 1 or 2 CFTR gene variants, not 2 CF-causing mutations
  - or borderline nasal epithelial ion transport

Bombieri, JCF 2011

Problem of diagnosing CF disease

1) ~2000 CFTR mutations detected

2) phenotype variable

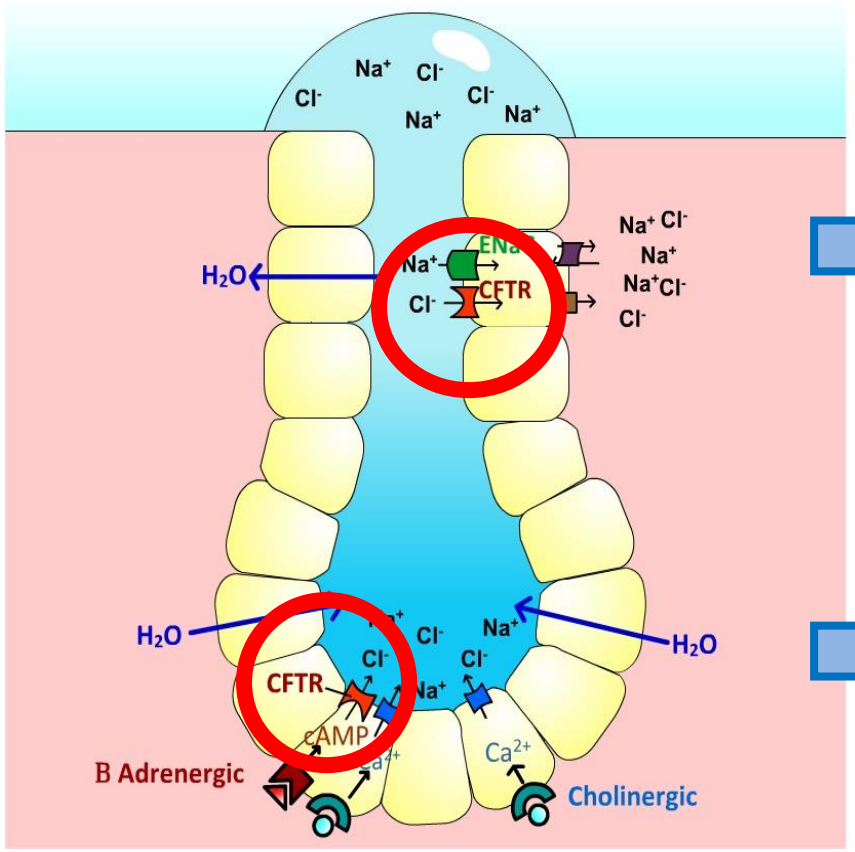
3) gold standard sweat test shows limitation

4) adjunctive NPD test overlaps between groups

Accessing CFTR function in sweat glands

Sweat [Cl^-]

Sweat duct

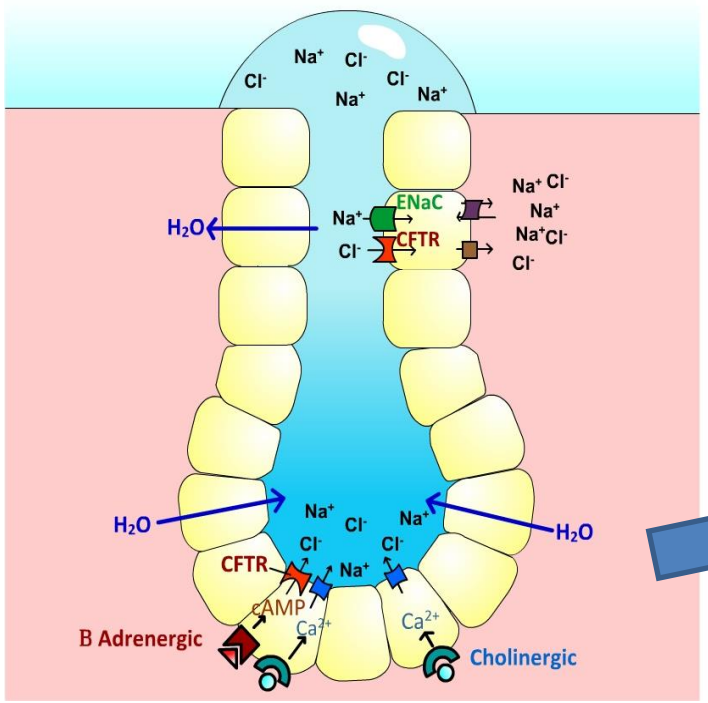


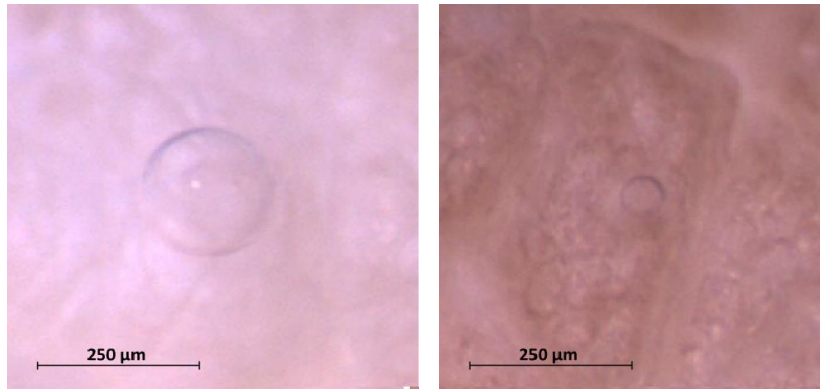
Absorption

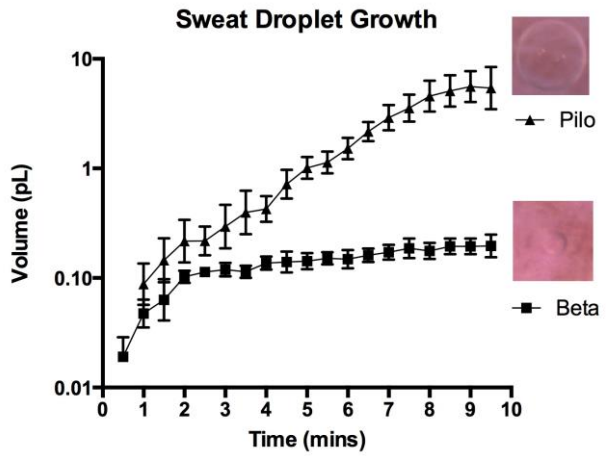
Secretory coil

Secretion

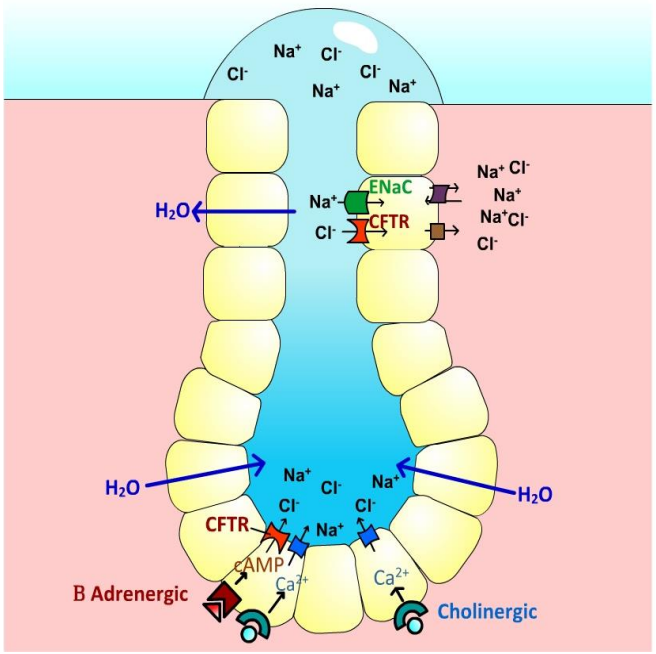
CFTR-mediated β-adrenergic sweat secretion

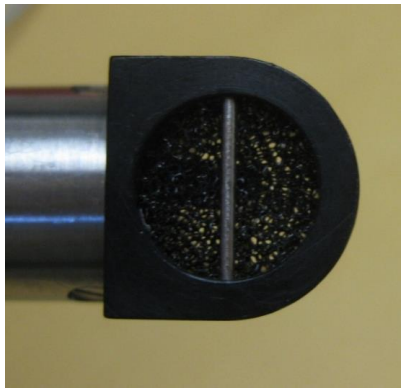


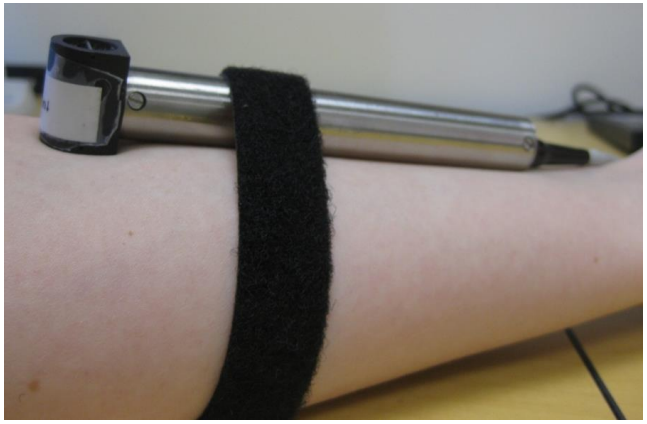




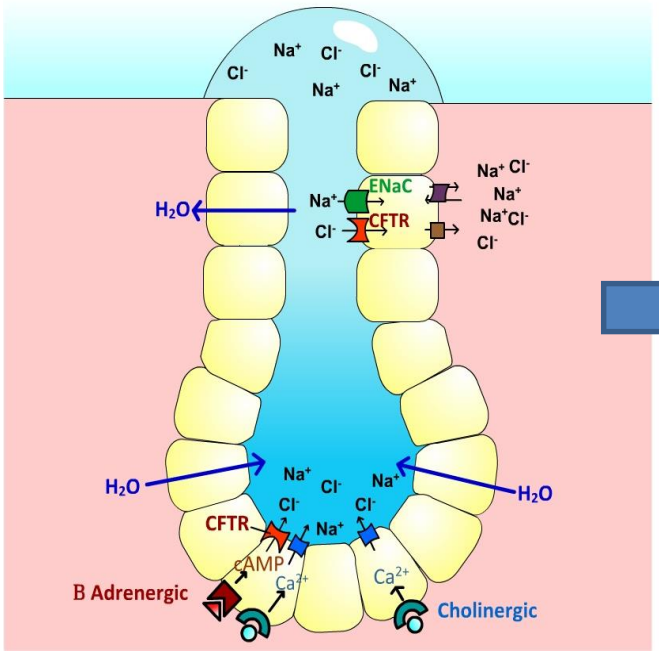
Measuring β-adrenergic sweat secretion using evaporimetry



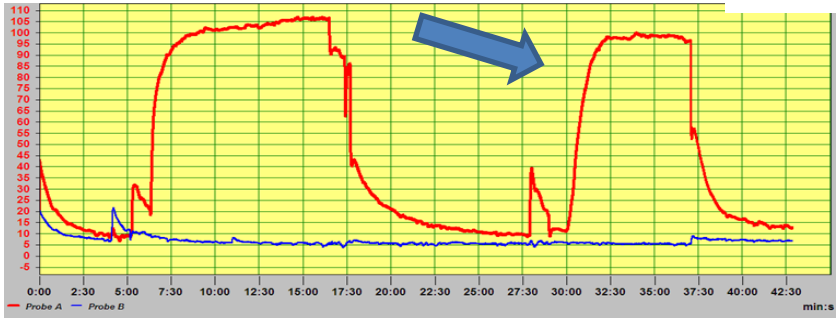




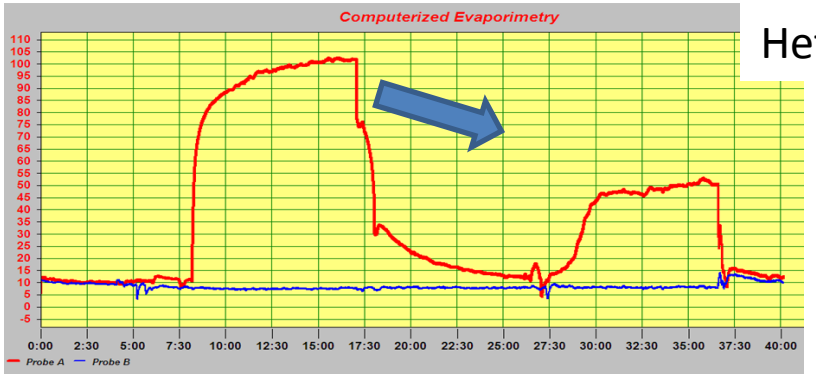
β-adrenergic secretory test using evaporimetry



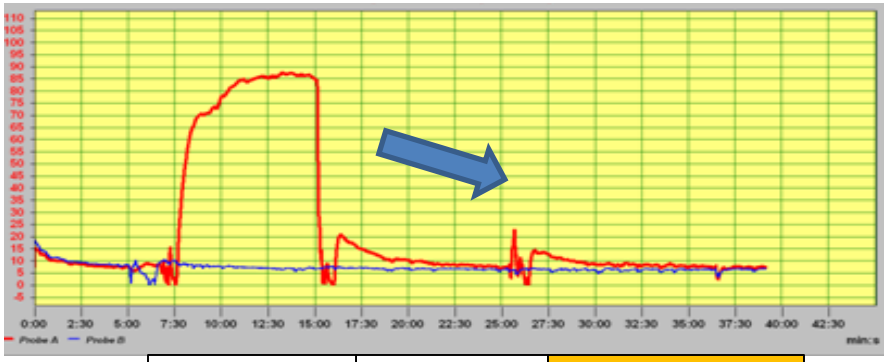
Healthy control



Heterozygoyte



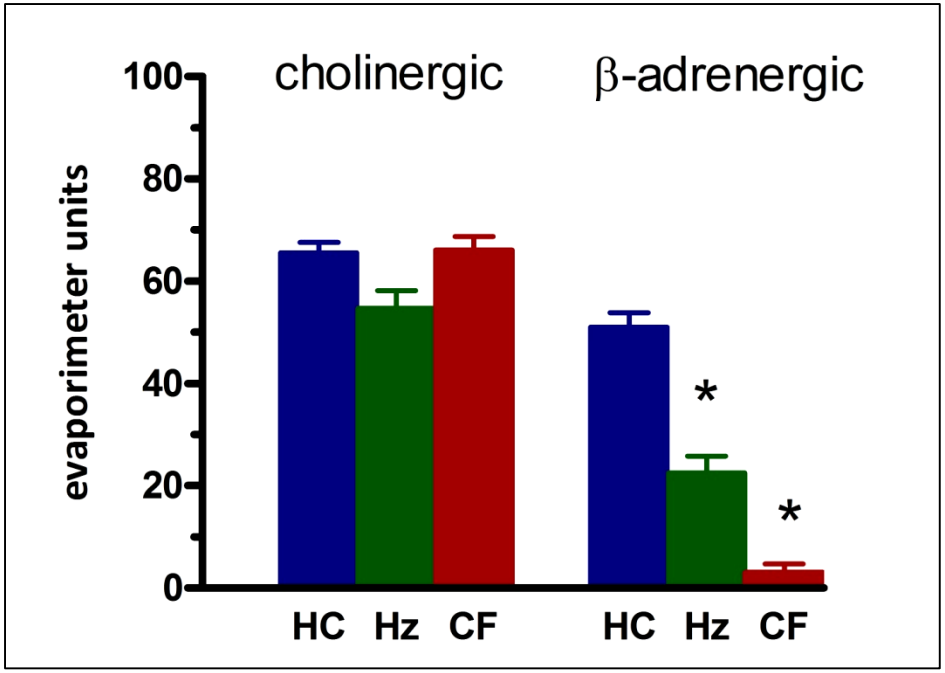
CF



cholinergic	atropine	B-adrenergic

β-adrenergic sweat secretory test identifies CF as well as Heterozygotes

Primary cohort



Primary cohort: 51 healthy controls,
40 heterozygotes,
40 CF patients

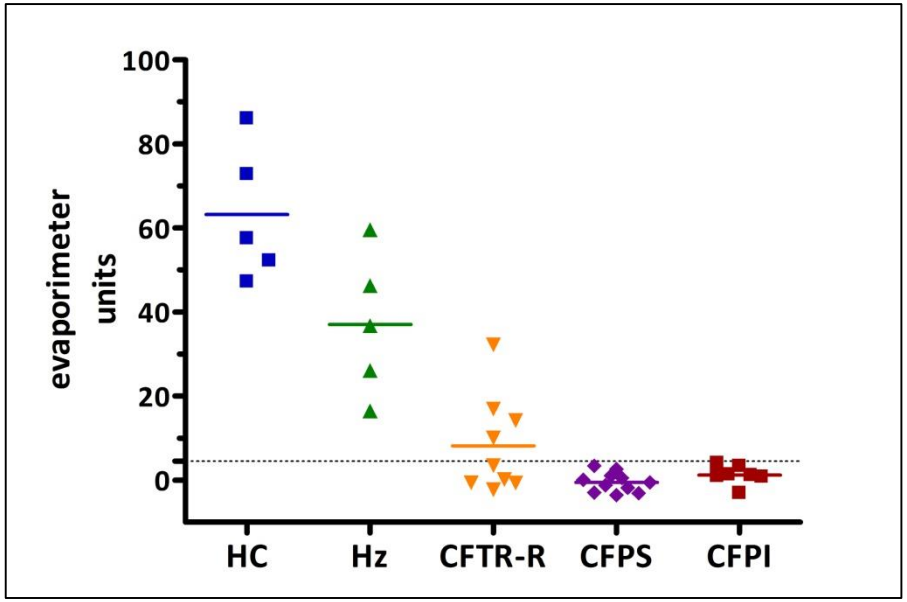
p<0.0001

Quinton and Gonska, AJRCCM 2012

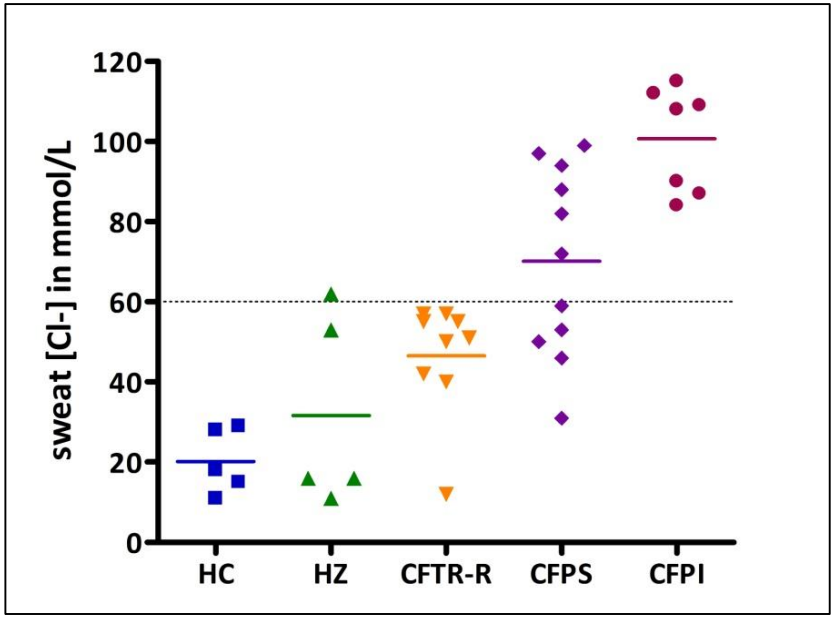
β-adrenergic sweat secretory test-Validation

Validation cohort

β-adrenergic sweat secretory



Sweat Chloride test



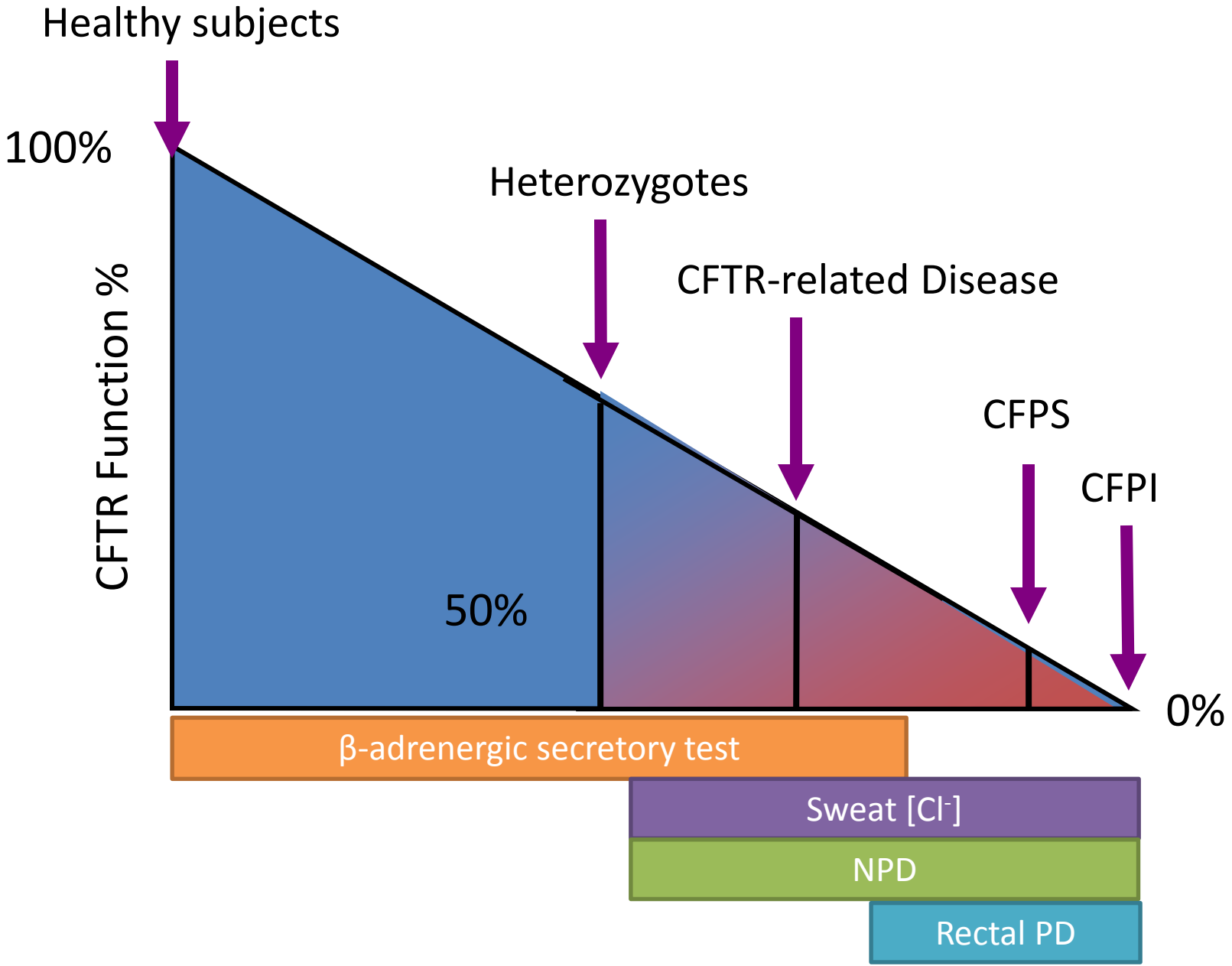
p<0.0001

Validation cohort:

5 healthy controls,
5 obligate heterozygotes,
9 patients with CFTR-related disease,
11 CFPS,
7 CFPI

Quinton and Gonska, AJRCCM 2012

Assessing CFTR function within CF disease spectrum



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