# Debunking Myths and Dogma in Pulmonary Function Testing


Jeffrey M. Haynes RRT RPFT FAARC
Elliot Health System
Manchester, New Hampshire

# Learning Objectives

- Appreciate the weakness of many revered myths and examples of dogma
- Understand the negative impact of myths and dogma on PF testing
- Understand the need for evidence based practice in the PFT laboratory

# Disclosures

Paid Consultant

Morgan Scientific Inc.

Myth: an idea or story that is believed by many people but is not true

# What is dogma?

Something held as an established opinion; *especially* **:** a definite authoritative tenet

Merriam-Webster

# So where do myths and dogma in pulmonary diagnostics originate?

- Ideas based on common sense, what sounds right, what makes sense
- The way we've always done it
- Old text books

# So where do myths and dogma in pulmonary diagnostics originate?

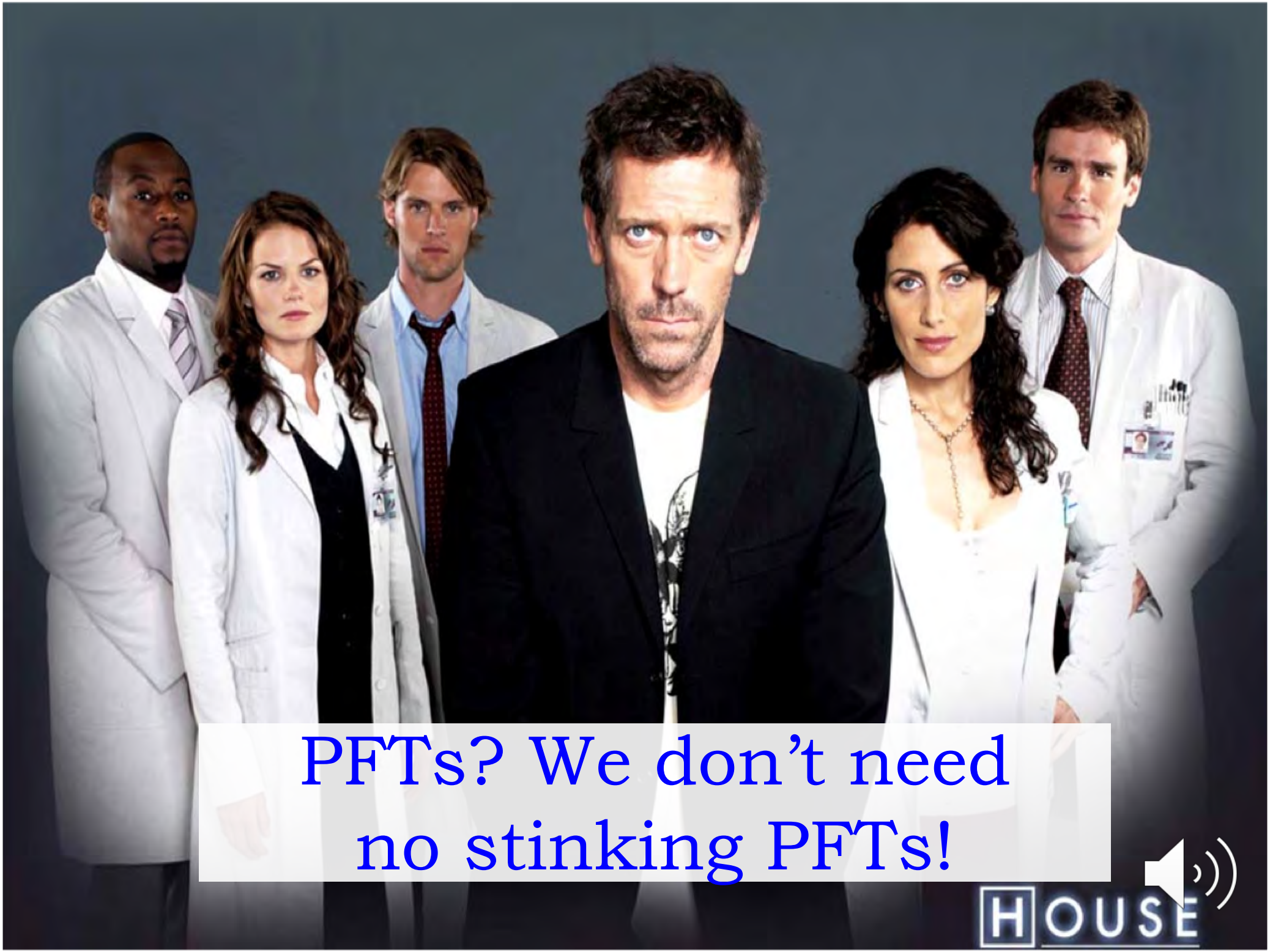
AMERICAN THORACIC SOCIETY DOCUMENTS

**Standardization of Spirometry 2019 Update**

An Official American Thoracic Society and European Respiratory Society Technical Statement

Brian L. Graham, Irene Steenbruggen, Martin R. Miller, Igor Z. Barjaktarevic, Brendan G. Cooper, Graham L. Hall, Teal S. Hallstrand, David A. Kaminsky, Kevin McCarthy, Meredith C. McCormack, Cristine E. Oropez, Margaret Rosenfeld, Sanja Stanojevic, Maureen P. Swanney†, and Bruce R. Thompson; on behalf of the American Thoracic Society and the European Respiratory Society

THIS OFFICIAL TECHNICAL STATEMENT WAS APPROVED BY THE AMERICAN THORACIC SOCIETY AND THE EUROPEAN RESPIRATORY SOCIETY SEPTEMBER 2019


PFTs? We don't need
no stinking PFTs!
HOUSE

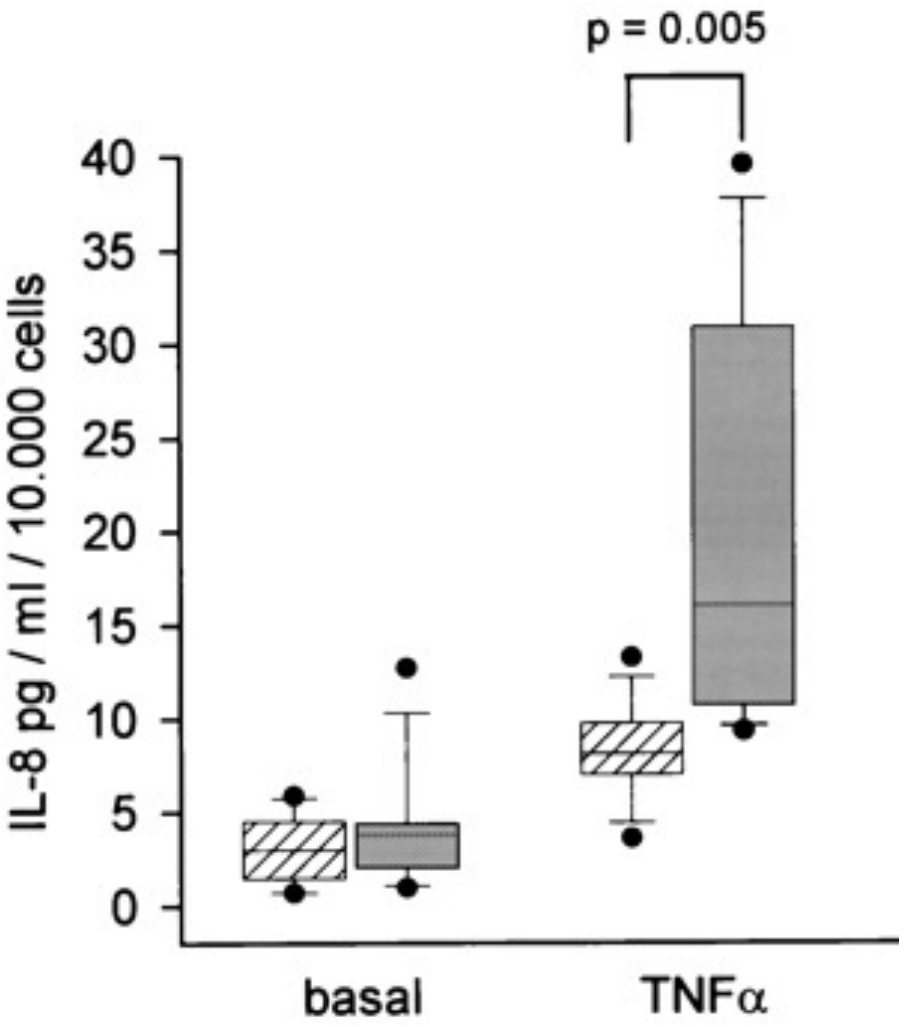
# “Most long-term smokers have COPD”

“Most long-term smokers have COPD”

~20%

# COPD Susceptibility

Schulz. Chest. 2004;125;1706



# Mary: "COPD & Emphysema"

80-year-old female with chronic cough and mild doe
Smokes 1 ppd for 62 years 452,600 cigarettes

Diagnosed several years ago with "COPD/emphysema"
No pulmonary function testing

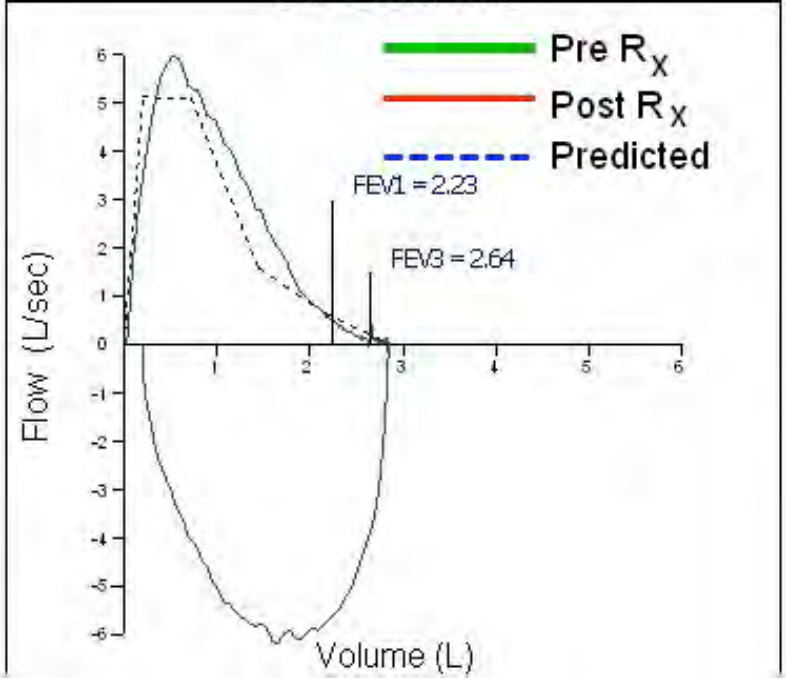
| | | |
|---|---|---|
| Rx: | Combivent | $214.60 |
| | Advair | $254.30 |
| | Albuterol | $51.85 |

Scheduled for PFT preoperatively for needle biopsy

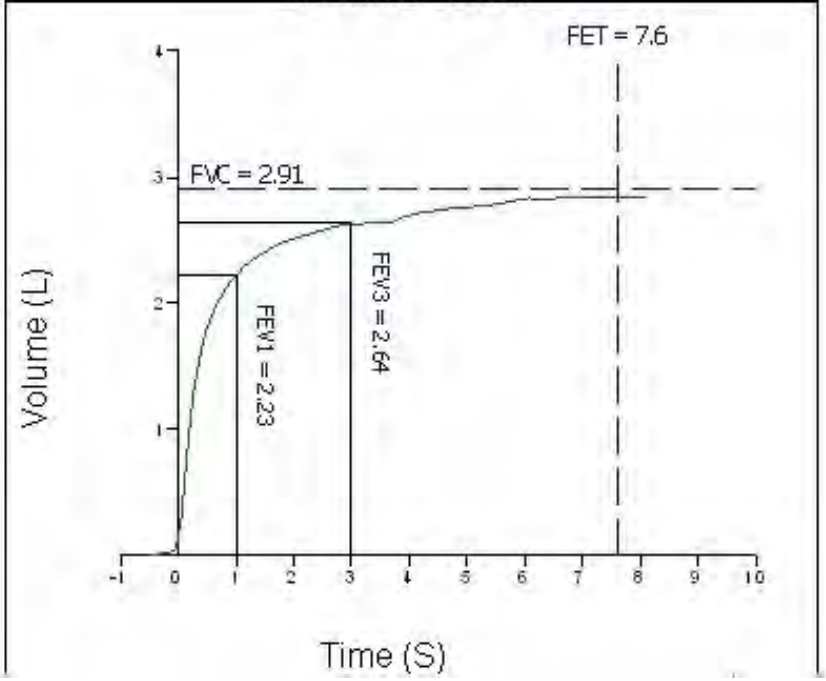
## Spirometry

| | | Predicted Range | | Pre Bronchodilator | |
|---|---|---|---|---|---|
| | | Mean | 95% | Actual | % Pred |
| FVC | L | 2.88 | 2.14 | **2.91** | 101 |
| $FEV_1$ | L | 2.15 | 1.52 | **2.23** | 104 |
| $FEV_1$ / FVC | % | 74 | 64 | **77** | 104 |
| $FEF_{25-75}$ | L/s | 1.53 | 0.21 | **1.87** | 122 |
| PEFR | L/s | 5.13 | 3.30 | **5.96** | 116 |
| SVC | L | 2.88 | 2.14 | ---- | ---- |
| IC | L | 2.36 | ---- | ---- | ---- |

**Flow Volume**




**Volume Time**



# Spirometry utilization for COPD Dx

Han et al. Chest 2007;132(2):403

Retrospective study of patients in 5 health insurance plans

n = 5,039 patients with a new diagnosis of COPD

primary outcome: % patients with spirometry 2 years before or 6 months after diagnosis.

32%

# This Drives Me CRAZY!!

# PFTs? I’ve got a stethoscope!

# wheeze

King et al Ann Intern Med 1989;110:451

44 adult patients methacholine challenge

14 patients + MCT

8/14 57% + wheezing

# wheeze

Wilson et al. Eur Respir J. 1995;8(3):364-370.

30 5-year-old patients with a hx of asthma given a methacholine challenge

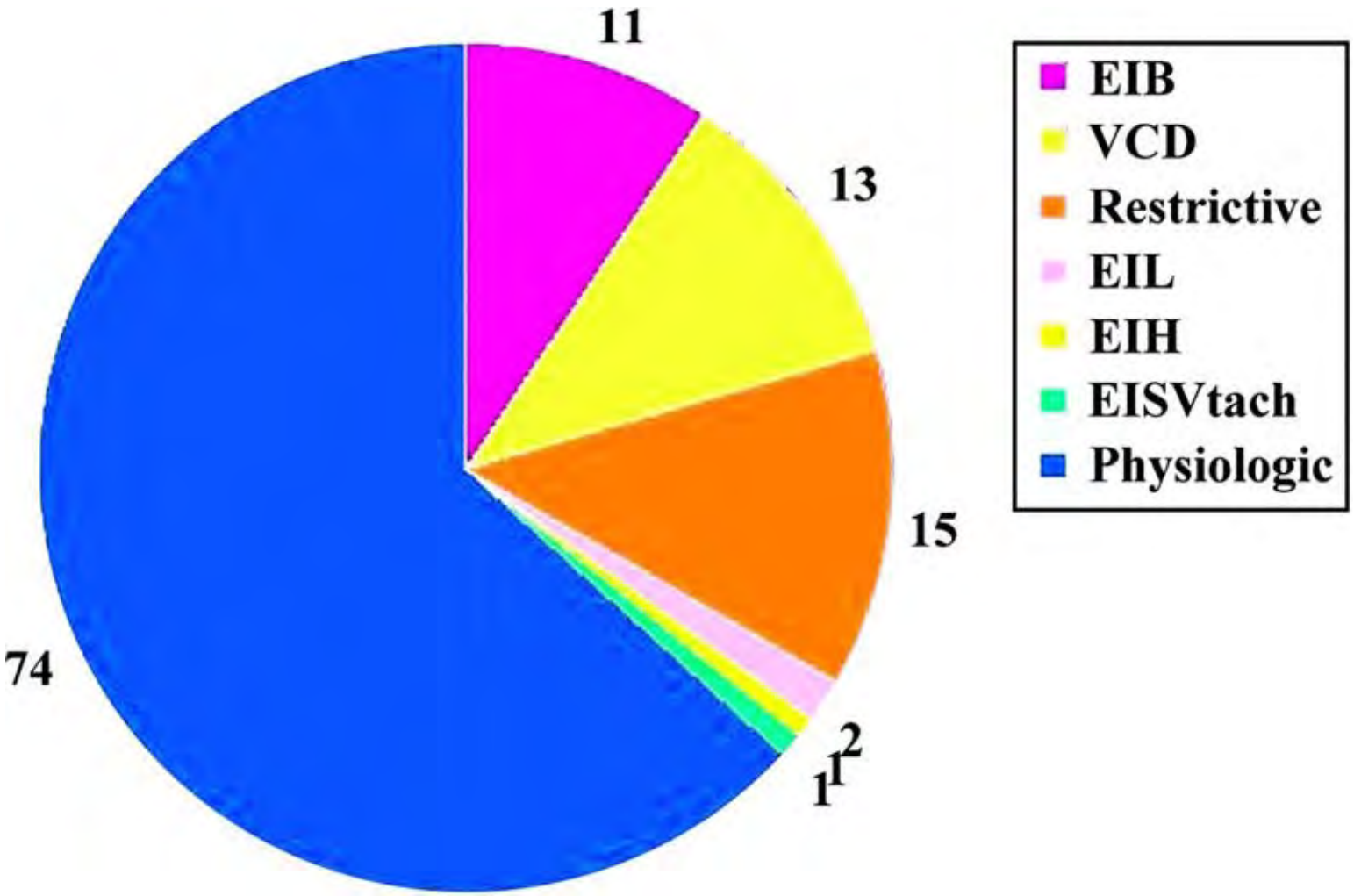
25 patients + MCT

4/25 16% + wheezing

# "Dyspnea in kids is usually asthma"

117 Children with dyspnea undergoing exercise treadmill testing

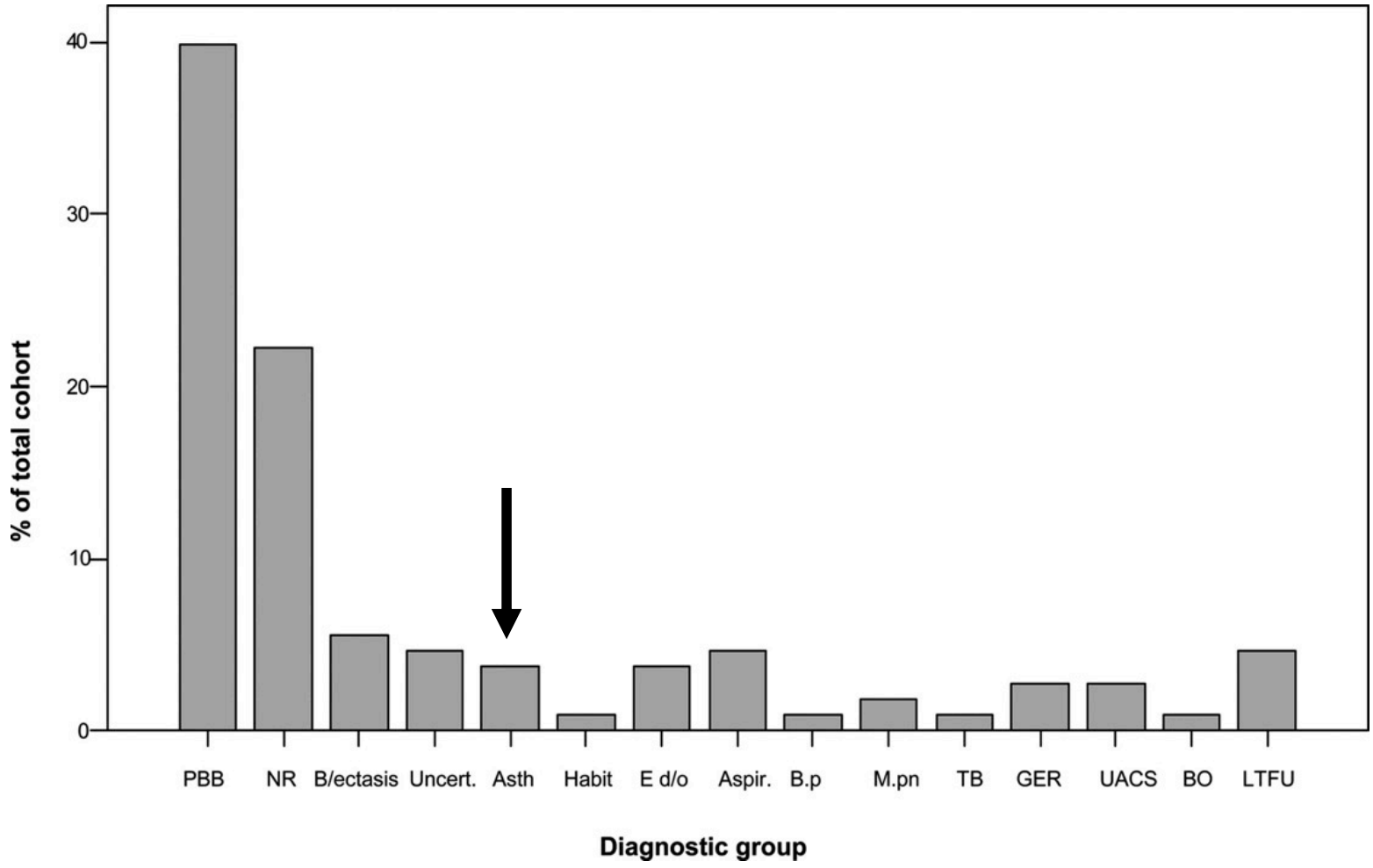
Abu-Hasan et al Ann Allergy Asthma Immunol.2005;94:366.



# “Coughing in kids is usually asthma”

108 children ages 1-7 undergoing BAL

Marchant JM.. Chest. 2006;129(5):1132-1141.



# PFTs? “Here try this”

# Dx by Rx

- placebo effect

49 asthmatics stable on inhaled steroids

randomized to 50 mcg salmeterol vs. placebo for 1 month

<u>self-reported symptom-free days (% increase)</u>

| | |
|---|---|
| salmeterol | 40% |
| placebo | 10% |

Langley et al. Eur Respir J. 1998;11:1081.

# Dx by Rx

Shrestha Am J Emerg Med. 1996;14:380.

- 125 patients asthma, ED
- MDI technique divided into 7 steps
- 21% performed correctly
- 100% performed correctly after teaching
- mean teaching time for success: 8 minutes

# Dx by Rx

Simmons Chest. 2000;118:290

- compliance & deception

- 101 patients with moderate airflow obstruction enrolled in the Lung Health Study
- MDI equipped with a monitoring device
- Asked to bring their MDI with them for follow-up inspection

- 30% actuated their MDI 100 times 3 hours prior to their appointment

~~PFTs? We don't need no stinking PFTs!~~

If you're not testing,
you're just guessing!

# Let’s Start From the Very Beginning

# Patient Instructions for PFTs

- ☐ **Establish Diagnosis**
  - **DO NOT take Albuterol (ventolin, proair, proventil) or Maxair 8 hours before testing unless you are experiencing difficulty breathing**
  - **DO NOT take Combivent, DuoNeb, Atrovent, or Xopenex 24 hours before testing unless you are experiencing difficulty breathing**
  - **DO NOT take Advair, Symbicort, Dulera, Brovana, Perforomist Serevent, Foradil, Singulair, Tudorza, Breo, Anoro or Spiriva 48 hours before testing unless you are experiencing difficulty breathing**
  - ***Limit* caffeine on the day of testing (morning coffee/tea is permitted)**

- ☐ **Additional Instructions For Methacholine/Mannitol/Exercise Challenges**
  **(check if applicable)**
  - **NO exercise on the day of testing**
  - ***Limit* caffeine on the day of testing (morning coffee/tea is permitted)**
  - **NO smoking on the day of testing**
  - **NO antihistamines 48 hours before methacholine testing**
  - **NO antihistamines 72 hours before mannitol testing**
  - **Inhaled or oral steroids can reduce responsiveness to methacholine and mannitol and may need to be withheld for at least one week before testing. Products containing inhaled steroids include Flovent, Advair, Symbicort, Breo, Pulmicort (budesonide), Aerobid, Alvesco, Dulera, Asmanex, Azmacort, QVar, Prednisone, Medrol, and Methylprednisolone.**
  - **Patients should not undergo methacholine or mannitol challenge testing within 6 weeks of a chest infection since false positive results can occur.**

- ☐ **Assess Functionality/Treatment Response (Dx already established)**
  - **Take all of your prescribed medicines as ordered, including the day of the test**

# No Caffeine!

# No Caffeine?

Yurach et al. Respir Med 2011;105;1606

- 16 asthmatic patients
- Randomized single-blind crossover trial of 16 oz. coffee and 16 oz. decaffeinated coffee on separate days
- $FE_{NO}$ and $FEV_1$ pre & 1 hour post coffee
  MCT performed 1 hour after coffee

# No Caffeine?

## Yurach et al. Respir Med 2011;105;1606

| | Decaffeinated | |
|---|---|---|
| | Pre | Post |
| $FEV_1$ (L) | 3.31 ± 0.69 | 3.31 ± 0.76 |
| eNO (ppb) | 35.7 ± 23.5 | 33.6 ± 22.2[a] |
| Serum Caffeine (μg/mL) | | 1.39 ± 1.18 |
| log $PC_{20}$ | | 0.132 ± 0.48 |
| Geometric Mean $PC_{20}$ (mg/mL) | | 1.36 |

| | Caffeinated | |
|---|---|---|
| | Pre | Post |
| $FEV_1$ (L) | 3.31 ± 0.75 | 3.36 ± 0.74 |
| eNO (ppb) | 31.2 ± 19.6 | 31.5 ± 20.4 |
| Serum Caffeine (μg/mL) | | 4.33 ± 1.6 |
| log $PC_{20}$ | | 0.129 ± 0.45 |
| Geometric Mean $PC_{20}$ (mg/mL) | | 1.35 |


DUNKIN'
DONUTS
AMERICA RUNS ON DUNKIN'


I will be amused AFTER my coffee
Limit caffeine on the day of testing

# Withhold all medications before your PFT!

# “I can’t take my inhalers?”

57-year-old female, severe emphysema

Alerted that my next patient has arrived and is in bad shape

Withheld all Rx for 24 hours: SOB, wheezing,

Test had been rescheduled for violating this rule!

| | |
|---|---|
| FVC | 1.48 L |
| $FEV_1$ | .33 L |
| $FEV_1/FVC$ | 22% |
| DLCO | 4.5 ml/min/mmHg |

# Don’t take your cardiac meds on the morning of your stress test

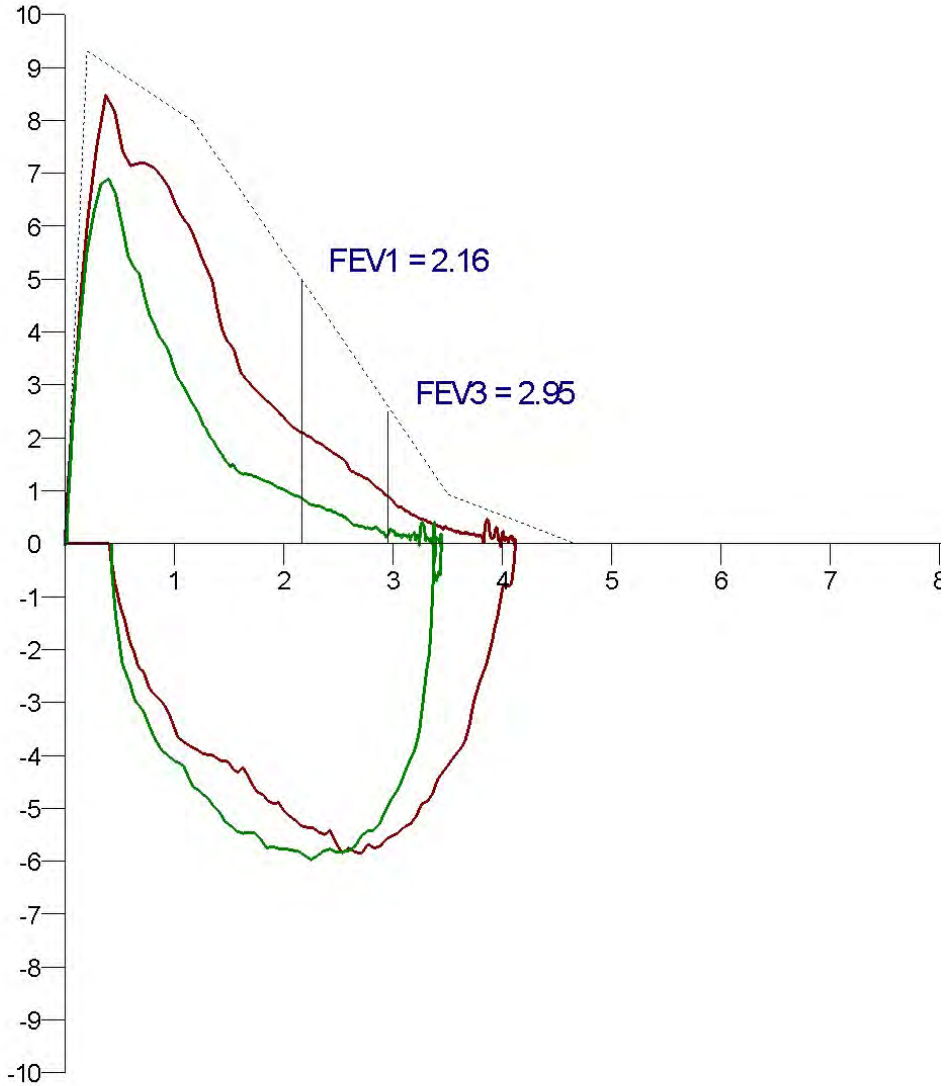
# Patient Instructions for Dx

- ☐ **Establish Diagnosis**
  - **DO NOT take Albuterol (ventolin, proair, proventil) or Maxair 8 hours before testing unless you are experiencing difficulty breathing**
  - **DO NOT take Combivent, DuoNeb, Atrovent, or Xopenex 24 hours before testing unless you are experiencing difficulty breathing**
  - **DO NOT take Advair, Symbicort, Dulera, Brovana, Perforomist Serevent, Foradil, Singulair, Tudorza, Breo, Anoro or Spiriva 48 hours before testing unless you are experiencing difficulty breathing**
  - ***Limit* caffeine on the day of testing (morning coffee/tea is permitted)**

- ☐ **Additional Instructions For Methacholine/Mannitol/Exercise Challenges**
  **(check if applicable)**
  - **NO exercise on the day of testing**
  - ***Limit* caffeine on the day of testing (morning coffee/tea is permitted)**
  - **NO smoking on the day of testing**
  - **NO antihistamines 48 hours before methacholine testing**
  - **NO antihistamines 72 hours before mannitol testing**
  - **Inhaled or oral steroids can reduce responsiveness to methacholine and mannitol and may need to be withheld for at least one week before testing. Products containing inhaled steroids include Flovent, Advair, Symbicort, Breo, Pulmicort (budesonide), Aerobid, Alvesco, Dulera, Asmanex, Azmacort, QVar, Prednisone, Medrol, and Methylprednisolone.**
  - **Patients should not undergo methacholine or mannitol challenge testing within 6 weeks of a chest infection since false positive results can occur.**

- ☐ **Assess Functionality/Treatment Response (Dx already established)**
  - **Take all of your prescribed medicines as ordered, including the day of the test**

# What about BD response?



# Acute BD Response on maintenance therapy

Positive Response

- Is the maintenance program inadequate?
- Is the patient taking their medications correctly?
- Is the patient taking them at all?

Negative Response

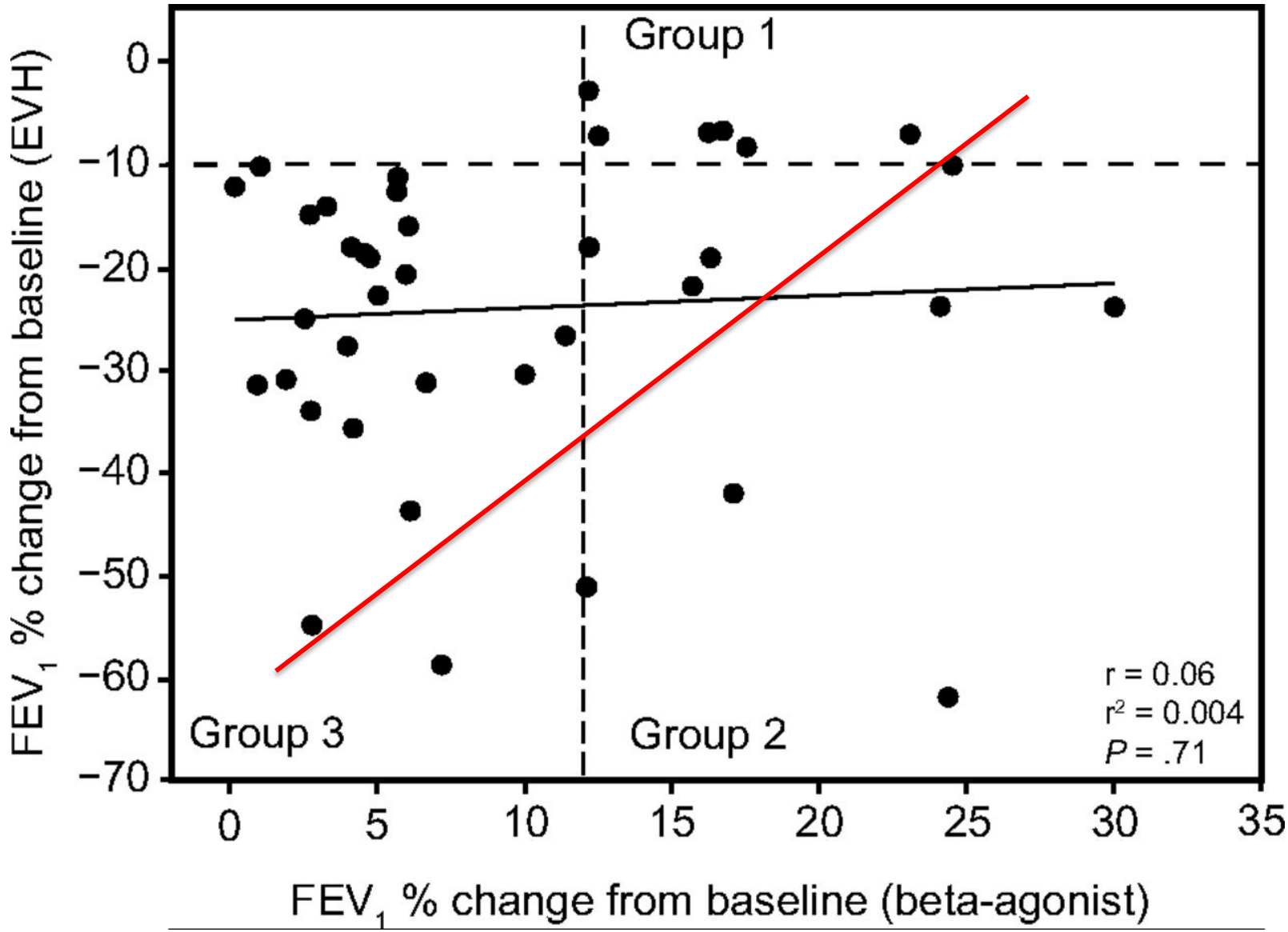
- Maximum benefit has been achieved (?)

# BD Response what does it mean?

“Bronchodilator responsiveness testing can determine whether or not you have asthma?

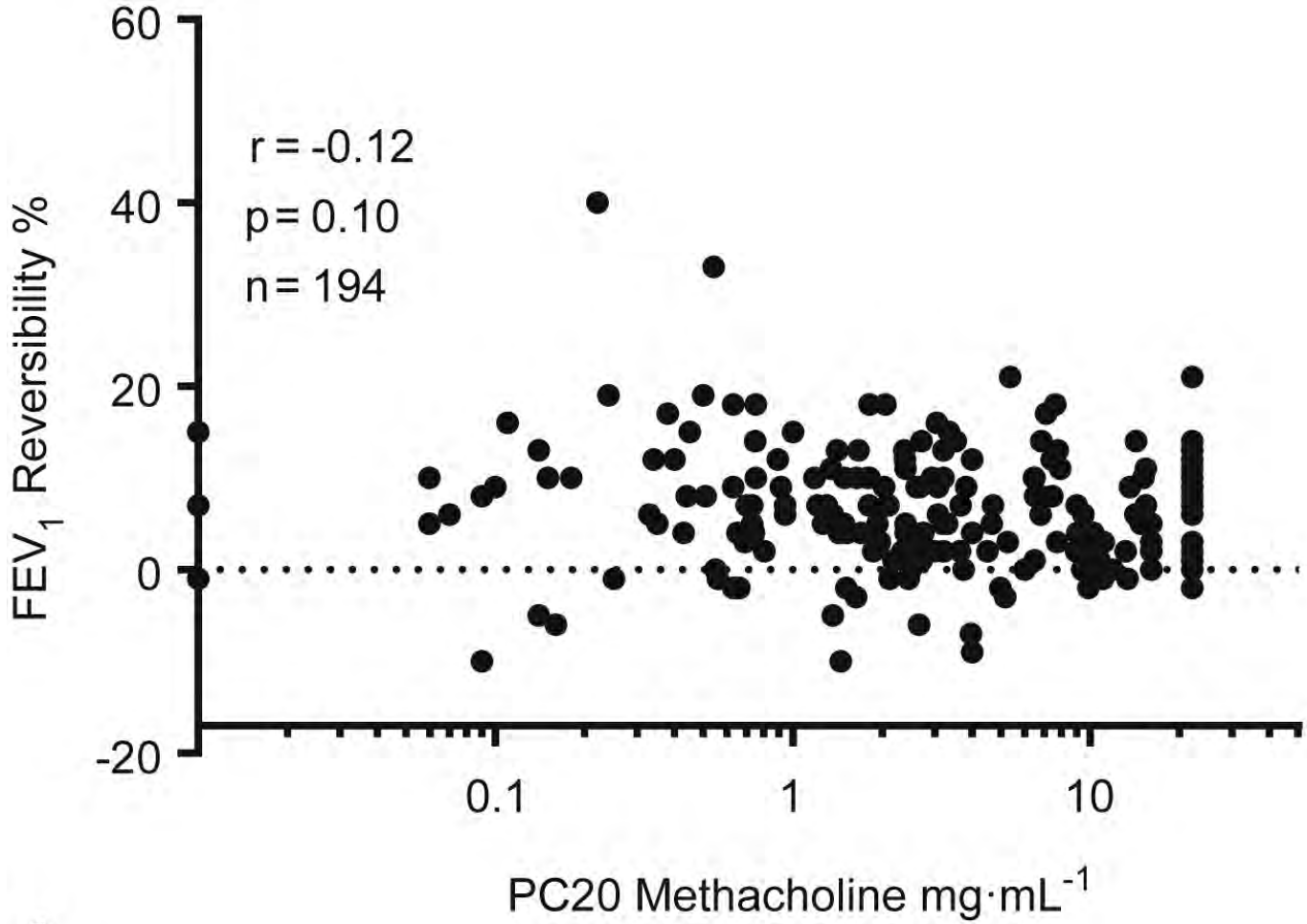
# Spirometric Response to Bronchodilator and Eucapnic Voluntary Hyperpnea in Adults With Asthma

Hans Christian Haverkamp, David A Kaminsky, Sterling M McPherson, and Charles G Irvin



# Bronchodilation Test with Inhaled Salbutamol Versus Bronchial Methacholine Challenge to Make an Asthma Diagnosis: Do They Provide the Same Information?

Renaud Louis, MD, PhD, Nicolas Bougard, MD, Françoise Guissard, MHS, Virginie Paulus, BS, Monique Henket, BS, and Florence Schleich, MD, PhD *Liege, Belgium*

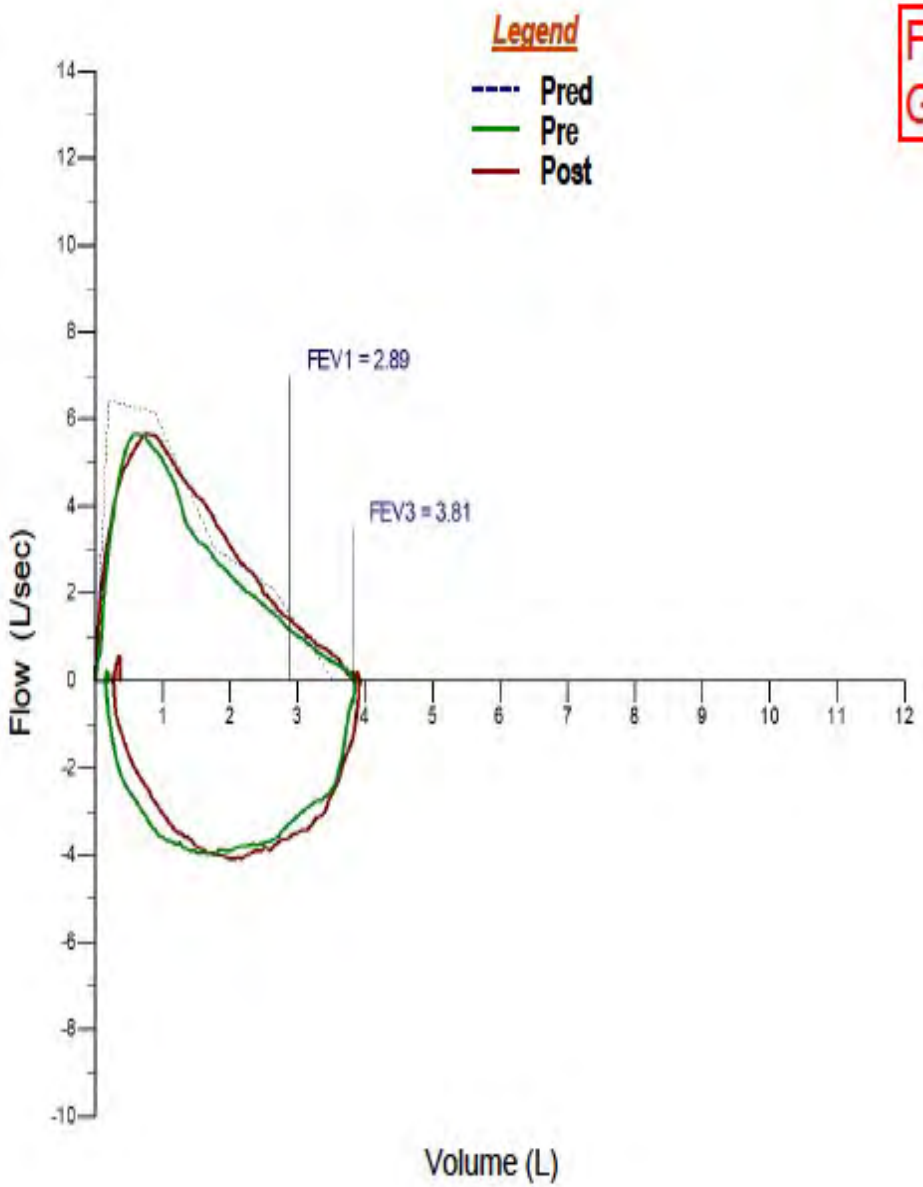



The Journal of Allergy and Clinical Immunology: In Practice
Volume 8, Issue 2, February 2020, Pages 618-625.e8

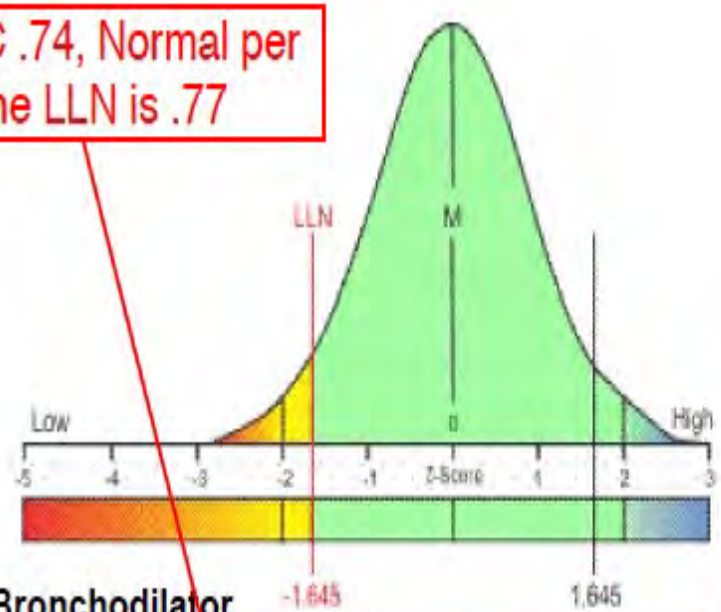
# Maybe we're using the wrong tool?

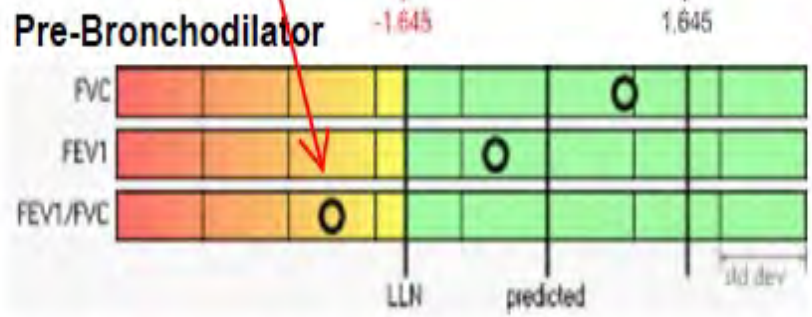
# "The $FEV_1$ didn't change, the bronchodilators don't work"

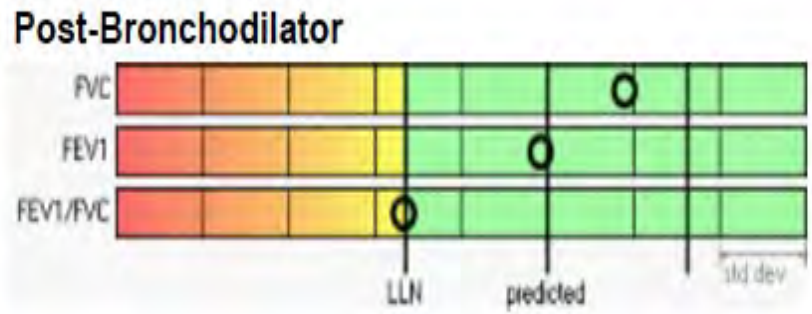
| *Spirometry (BTPS)* | | Pre Bronchodilator | | | | | | Post Bronchodilator | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Actual | LLN | ULN | Predicted | % Pred | Z-score | Actual | % Pred | Abs Chg | % Change | Z-score |
| StartTime | | 13:14 | ---- | ---- | ---- | ---- | ---- | 13:34 | ---- | ---- | -- | ---- |
| FVC | L | 3.92 | 2.83 | 4.27 | 3.53 | 111 | 0.87 | 3.92 | 111 | ---- | 0 | 0.87 |
| $FEV_1$ | L | 2.89 | 2.51 | 3.70 | 3.11 | 93 | -0.61 | 3.08 | 99 | 190 mL | 7 | -0.09 |
| $FEV_1$ / FVC | % | 74 | 77 | 97 | 89 | 83 | -2.00 | 79 | 89 | ---- | 7 | -1.41 |
| $FEF_{25-75}$ | L/s | 2.15 | 2.51 | 5.17 | 3.76 | 57 | -2.16 | 2.75 | 73 | 0.60 L/s | 28 | -1.31 |
| PEFR | L/s | 5.66 | 4.80 | 8.04 | 6.42 | 88 | ---- | 5.67 | 88 | 0.01 L/s | 0 | ---- |
| MVV | L/m | ---- | 59.6 | 161.6 | 110.6 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| SVC | L | ---- | 2.83 | 4.27 | 3.53 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| ERV | L | ---- | 0.71 | 1.43 | 1.07 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| IC | L | ---- | 1.40 | 3.52 | 2.46 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| CPF | L/s | ---- | 6.65 | 10.65 | 8.13 | ---- | ---- | ---- | ---- | ---- | -- | ---- |




FEV1/FVC .74, Normal per GOLD. The LLN is .77



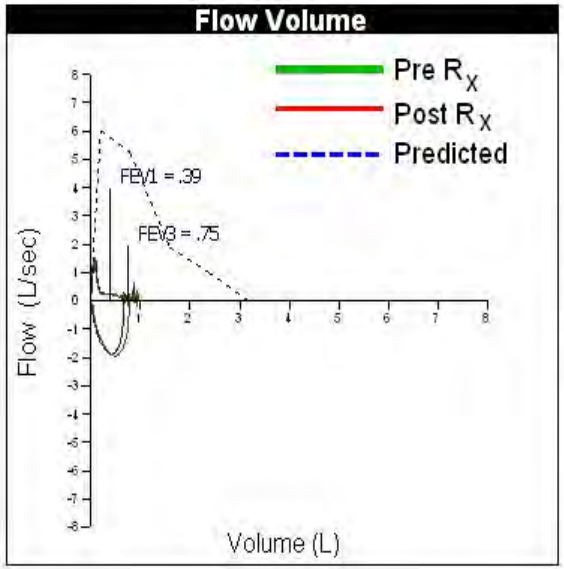
# "The $FEV_1$ didn't change, the bronchodilators don't work"

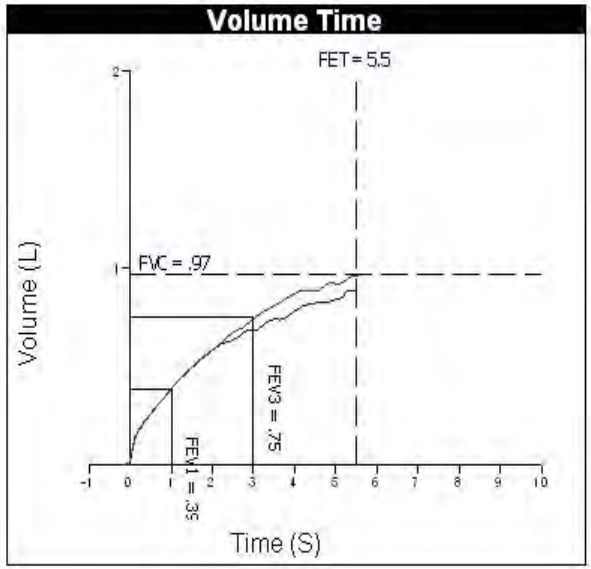
| Spirometry (BTPS) | | Pre Bronchodilator | | | | | | Post Bronchodilator | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Actual | LLN | ULN | Predicted | % Pred | Z-score | Actual | % Pred | Abs Chg | % Change | Z-score |
| StartTime | | 13:14 | ---- | ---- | ---- | ---- | ---- | 13:34 | ---- | ---- | -- | ---- |
| FVC | L | 3.92 | 2.83 | 4.27 | 3.53 | 111 | 0.87 | 3.92 | 111 | ---- | 0 | 0.87 |
| $FEV_1$ | L | 2.89 | 2.51 | 3.70 | 3.11 | 93 | -0.61 | 3.08 | 99 | 190 mL | 7 | -0.09 |
| $FEV_1$ / FVC | % | 74 | 77 | 97 | 89 | 83 | -2.00 | 79 | 89 | ---- | 7 | -1.41 |
| $FEF_{25-75}$ | L/s | 2.15 | 2.51 | 5.17 | 3.76 | 57 | -2.16 | 2.75 | 73 | 0.60 L/s | 28 | -1.31 |
| PEFR | L/s | 5.66 | 4.80 | 8.04 | 6.42 | 88 | ---- | 5.67 | 88 | 0.01 L/s | 0 | ---- |
| MVV | L/m | ---- | 59.6 | 161.6 | 110.6 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| SVC | L | ---- | 2.83 | 4.27 | 3.53 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| ERV | L | ---- | 0.71 | 1.43 | 1.07 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| IC | L | ---- | 1.40 | 3.52 | 2.46 | ---- | ---- | ---- | ---- | ---- | -- | ---- |
| CPF | L/s | ---- | 6.65 | 10.65 | 8.13 | ---- | ---- | ---- | ---- | ---- | -- | ---- |

| Resistance | | Pre Bronchodilator | | | | | Post Bronchodilator | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Actual | LLN | ULN | Predicted | % Pred | Actual | % Pred | % Change |
| sGaw | L/s/cmH2O/L | 0.09 | 0.11 | 0.40 | 0.26 | 35 | 0.19 | 73 | 111 |
| Raw | cmH2O/L/s | 3.36 | 0.60 | 2.80 | 1.70 | 198 | 1.53 | 90 | -54 |

# "The $FEV_1$ didn't change, the bronchodilators don't work"

| Spirometry | | Predicted Range | | Pre Bronchodilator | | Post Bronchodilator | |
|---|---|---|---|---|---|---|---|
| | | Mean | 95% | Actual | % Pred | Actual | % Pred |
| FVC | L | 3.18 | 2.49 | 0.97 | 31 | 0.89 | 28 |
| $FEV_1$ | L | 2.43 | 1.85 | 0.39 | 16 | 0.39 | 16 |
| $FEV_1$ / FVC | % | 77 | 67 | 40 | 52 | 44 | 57 |
| $FEF_{25-75}$ | L/s | 2.14 | 0.90 | 0.20 | 9 | 0.19 | 9 |
| PEFR | L/s | 6.02 | 4.30 | 1.63 | 27 | 1.41 | 23 |
| SVC | L | 3.18 | 2.49 | ---- | ---- | ---- | ---- |
| IC | L | 2.45 | ---- | ---- | ---- | ---- | ---- |



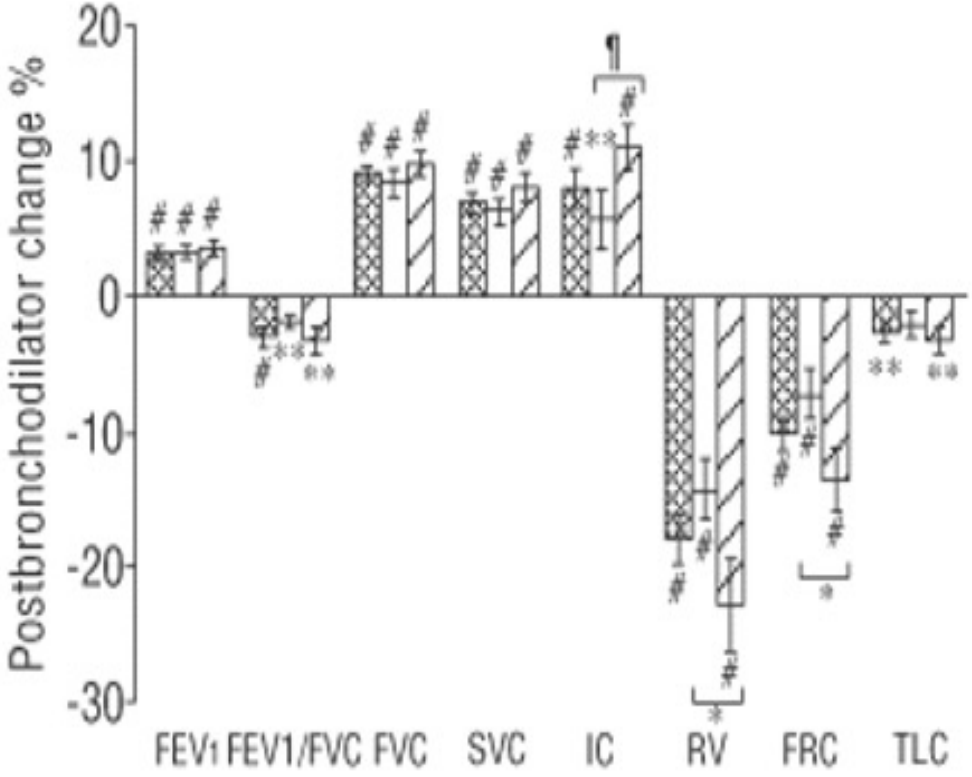
# Lung Volumes to Assess BD Response

O'Donnell Eur Respir J 2001;18:914

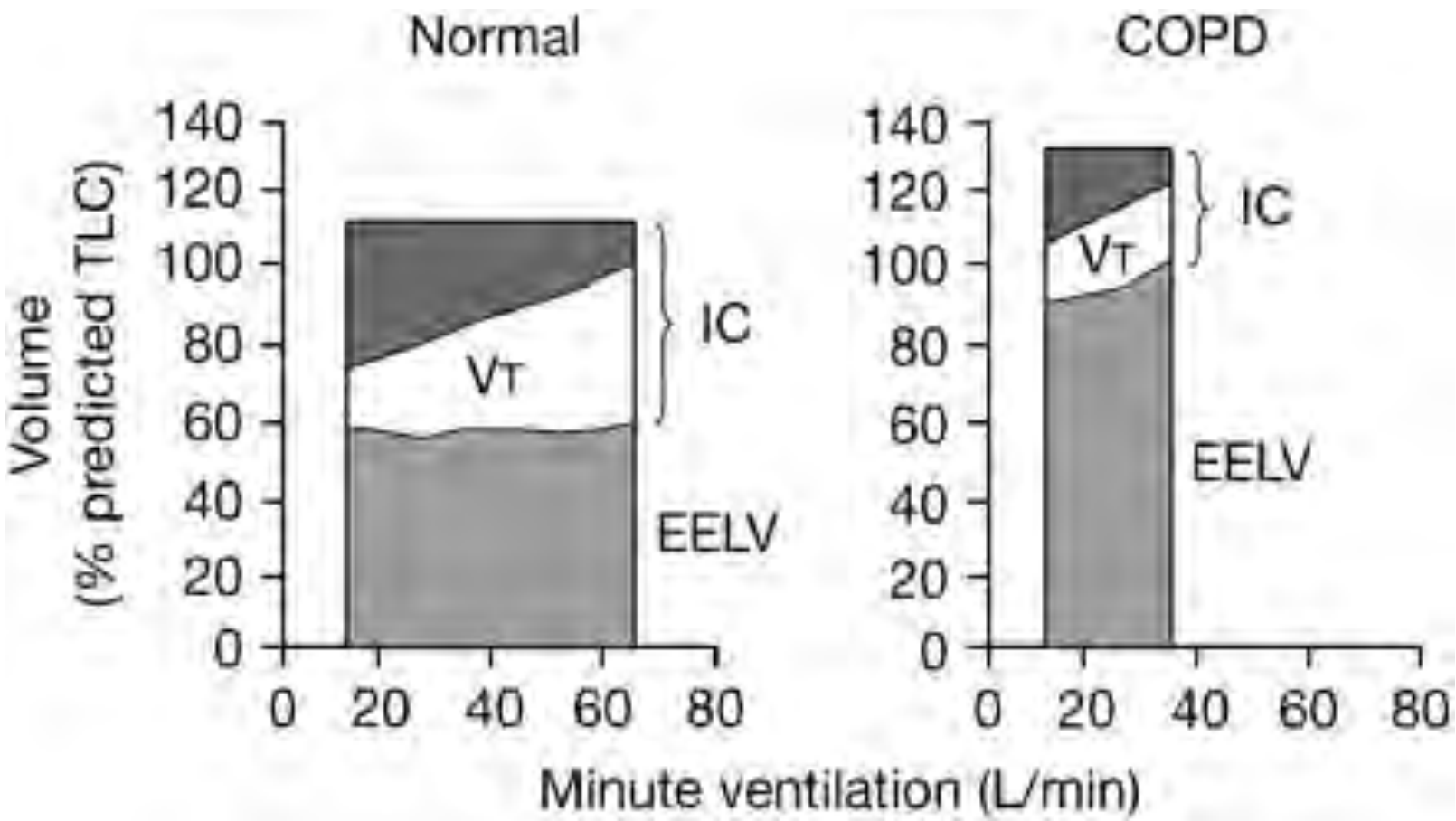
n = 84

Mean $FEV_1$ 32%

Change from bronchodilator <10%



# Dynamic Hyperinflation



# Overreliance on $FEV_1$

Patient:

"I feel much better after the nebulizer"

Us:

"I think its all in your head, the $FEV_1$ didn't change"

# So where do myths and dogma in pulmonary diagnostics originate?

AMERICAN THORACIC SOCIETY DOCUMENTS

**Standardization of Spirometry 2019 Update**

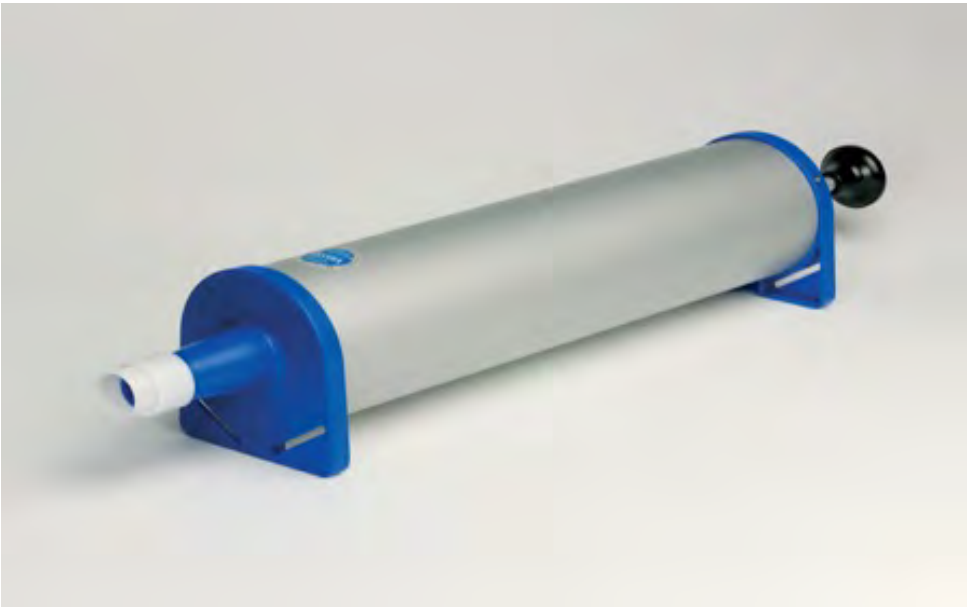
An Official American Thoracic Society and European Respiratory Society Technical Statement

Brian L. Graham, Irene Steenbruggen, Martin R. Miller, Igor Z. Barjaktarevic, Brendan G. Cooper, Graham L. Hall, Teal S. Hallstrand, David A. Kaminsky, Kevin McCarthy, Meredith C. McCormack, Cristine E. Oropez, Margaret Rosenfeld, Sanja Stanojevic, Maureen P. Swanney†, and Bruce R. Thompson; on behalf of the American Thoracic Society and the European Respiratory Society

THIS OFFICIAL TECHNICAL STATEMENT WAS APPROVED BY THE AMERICAN THORACIC SOCIETY AND THE EUROPEAN RESPIRATORY SOCIETY SEPTEMBER 2019

# Calibration Verification

- 3L syringe
- ~~gain +/-3.5%~~
- ~~2.9-3.1 liters~~
- gain +/- 3%
- 2.91-3.09 liters
- 0.5-6 sec strokes
- Inspiratory and expiratory strokes
- Use a filter (?)
- Don't hold the syringe (?)



# A bit of a stretch….

"If an in-line filter is used in spirometry testing, then it must also be used during recalibration and verification"

American Journal of Respiratory and Critical Care Medicine

## Calibration Myths in the 2019 American Thoracic Society/European Respiratory Society Spirometry Technical Standards

Jeffrey M. Haynes, Gregg L. Ruppel, and Matthew J. O'Brien

Filter vs. No Filter at low, mid, and fast speeds

4 pressure differential pneumotachs
-(2 metal screens,1 Fleisch,1 Pitot tube)
1 Heated wire pneumotach
1 Dry rolling seal spirometer

The largest difference we found was 20 ml (0.7%)

# A bit of a stretch….

"Holding the syringe during calibration can raise its temperature and contribute to measurement error"

American Journal of Respiratory and Critical Care Medicine

## Calibration Myths in the 2019 American Thoracic Society/European Respiratory Society Spirometry Technical Standards

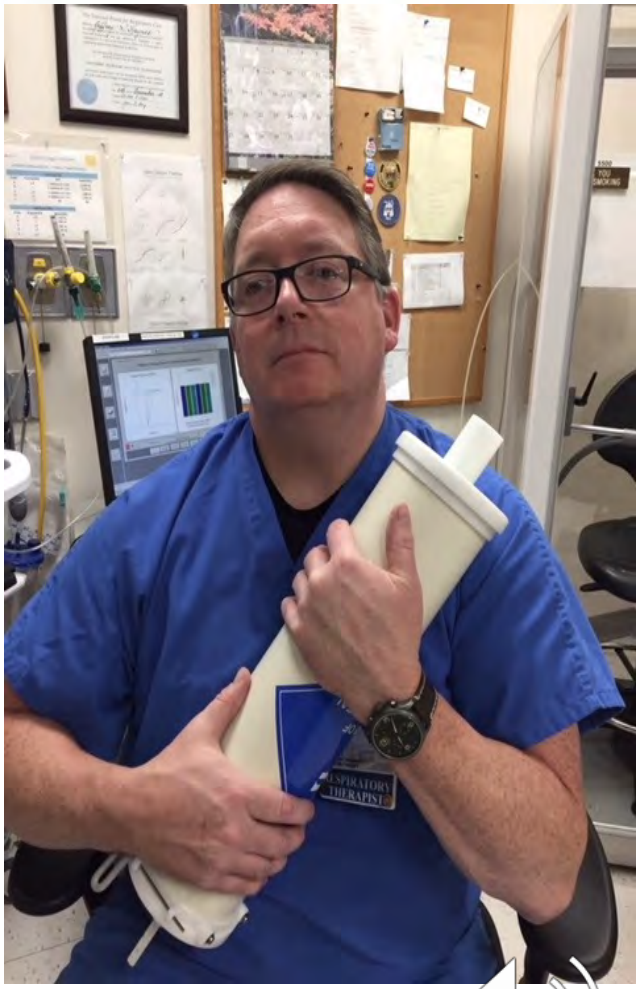
Jeffrey M. Haynes, Gregg L. Ruppel, and Matthew J. O'Brien

Calibration differences after a 1-minute bear hug

Low flow: +20 ml (0.7%)
Mid flow: 0 ml
High flow: +10 ml (0.3%

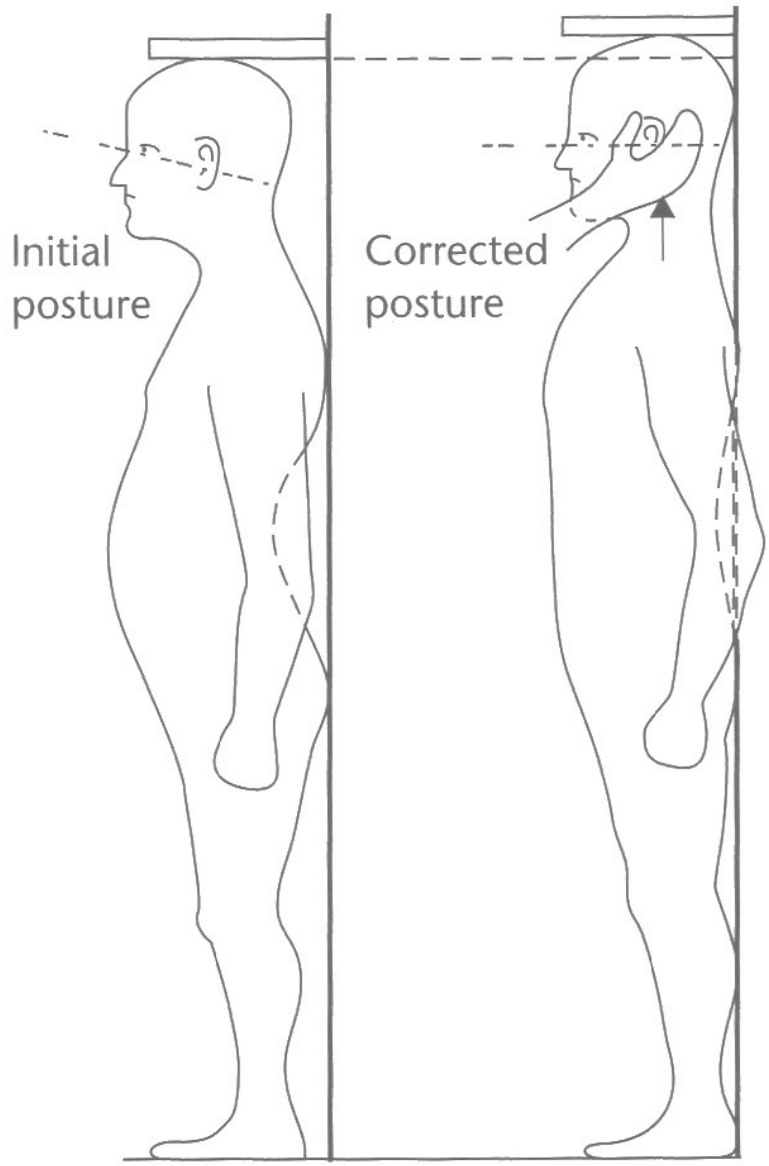
Calibration differences after 10 minutes at 96ºF

Low flow: +30 ml (1%)
Mid flow: 0 ml
High flow: +10 ml (0.3%

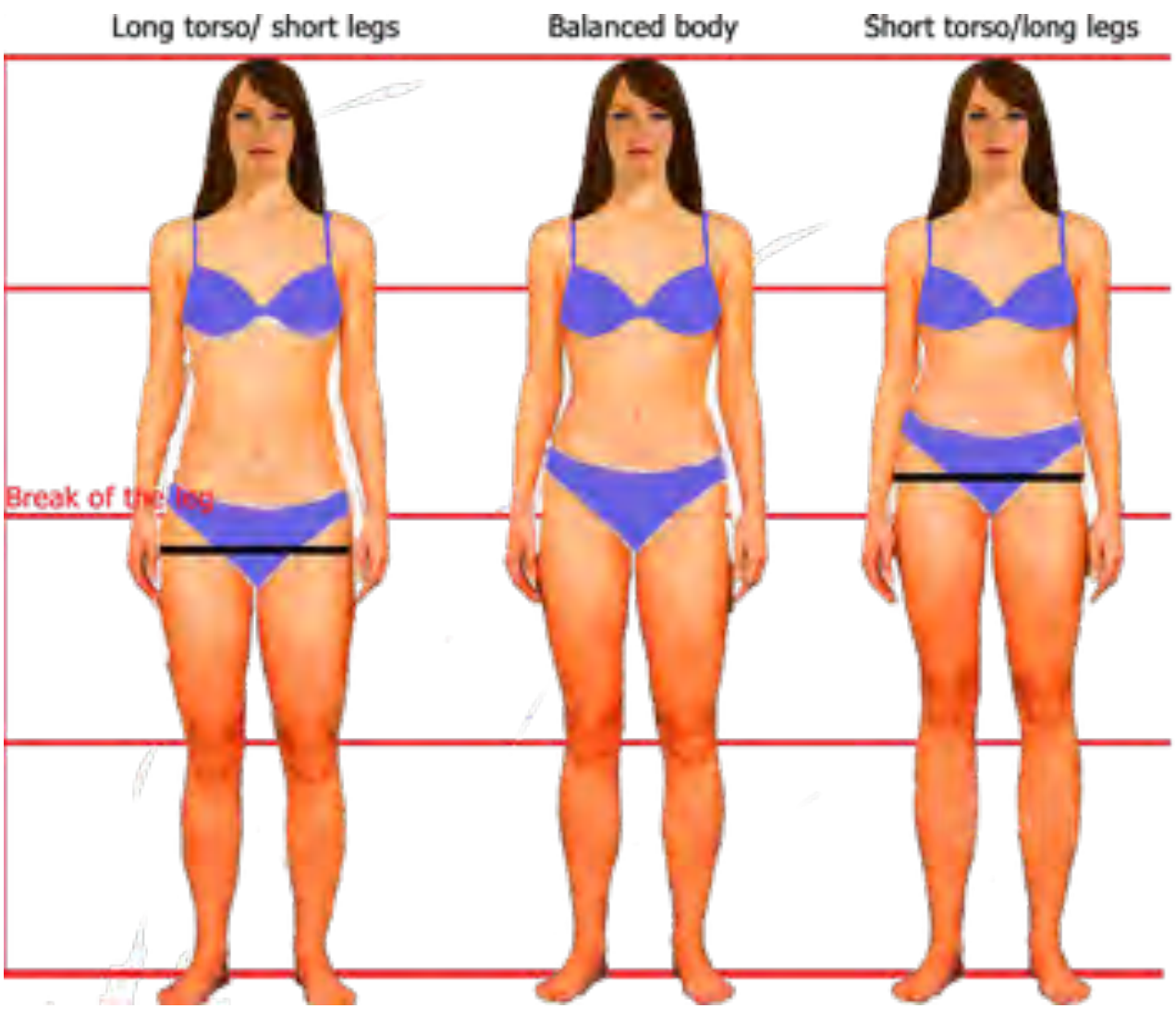


# Height determines lung size

# Height determines lung size



# Is Height a Reliable Proxy for Thorax Size?




+ bias

- bias

# Is Height a Reliable Proxy for Thorax Size?



- bias

+ bias

# Is Height a Reliable Proxy for Thorax Size?

**TABLE 4. THE EFFECT SIZE* OF SITTING HEIGHT, POVERTY INDEX, EDUCATION, BMI ON THE FVC RACE DIFFERENCE IN NONSMOKING ASYMPTOMATIC WOMEN**

| Age Coefficient (p Value) | Standing Height Coefficient (p Value) | Sitting Height Coefficient (p Value) | Poverty Index Coefficient (p Value) | Education Coefficient (p Value) | BMI Coefficient (p Value) | Adjusted Racial Difference† (p Value) | $R^2$ |
|---|---|---|---|---|---|---|---|
| −18.9 (0.0001) | 50.9 (0.0001) | — | — | — | — | −611.1 (0.0001) | 0.58 |
| −17.2 (0.0001) | — | 91.9 (0.0001) | — | — | — | −383.5 (0.0001) | 0.57 |
| −17.4 (0.0001) | — | 89.5 (0.0001) | 37.2 (0.0001) | — | — | −335.9 (0.0001) | 0.58 |
| −16.6 (0.0001) | — | 91.5 (0.0001) | 33.3 (0.0001) | — | −7.4 (0.0002) | −311.0 (0.0001) | 0.58 |
| −16.7 (0.0001) | — | 90.7 (0.0001) | — | 85.0 (0.0007) | — | −371.4 (0.0001) | 0.58 |
| −16.0 (0.0001) | — | 92.7 (0.0001) | — | 70.0 (0.0057) | −8.0 (0.0001) | −341.5 (0.0001) | 0.58 |

*Definition of abbreviations*: BMI = body mass index; education = (≤ high school = 0, > high school = 1); poverty index = the ratio of family income in the last 12 mo to the federal poverty line; thus a higher poverty index indicates a higher socioeconomic status.

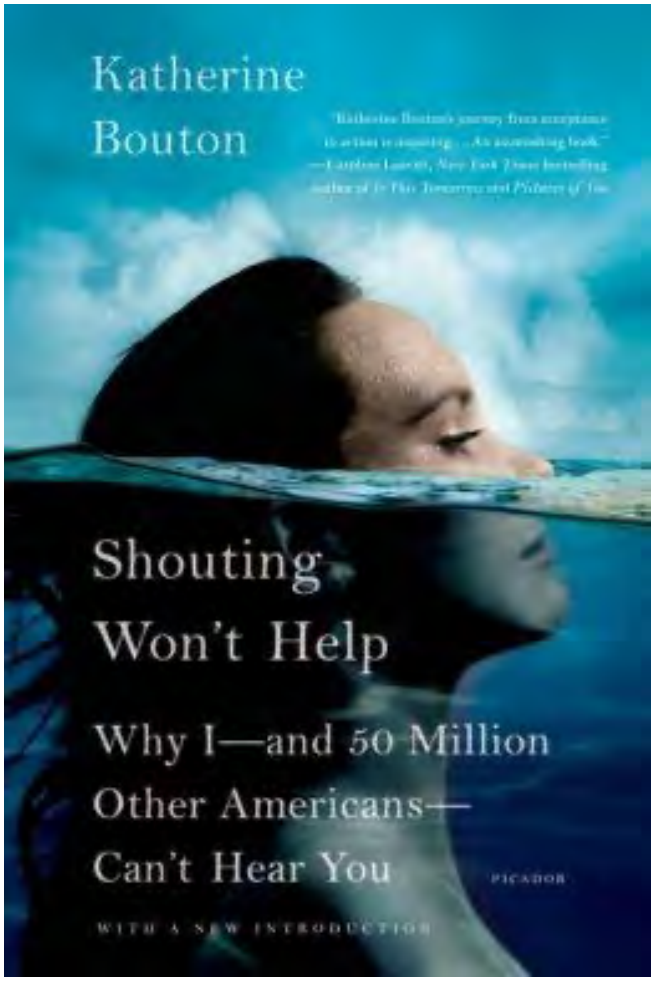
* Parameter coefficients in regression model with FVC as dependent variable.

† Adjusted racial difference (ml) between 806 non-Hispanic white women and 696 non-Hispanic African-American women as defined in METHODS.

# Patient Instruction/Coaching

# You must scream to get results!

# Shouting won't help-Katherine Bouton


"talk as clearly and distinctly as possible — facing the speaker."

# “Blast the air out of your lungs as hard as you can until I tell you to stop”

# Trial of Standard versus Modified Expiration to Achieve End-of-Test Spirometry Criteria

JAMES K. STOLLER, STEPHEN BASHEDA, DANIEL LASKOWSKI, MARLENE GOORMASTIC, and KEVIN MCCARTHY

Departments of Pulmonary and Critical Care Medicine and Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, Ohio

TABLE 3

LARGEST VALUES* OF FORCED EXPIRATORY TIME (FET) USING STANDARD VERSUS MODIFIED EXPIRATORY TECHNIQUE

| Group No. | $FEV_1/FVC$ Strata | Patients (*n*) | FET (*s*) | | |
|---|---|---|---|---|---|
| | | | Standard | Modified | p Value† |
| 1 | < 0.45 | 12 | 13.75 ± 2.47 | 18.56 ± 4.42 | 0.002 |
| 2 | 0.45–0.60 | 11 | 14.02 ± 4.48 | 22.11 ± 6.94 | 0.001 |
| 3 | 0.61–0.74 | 16 | 13.32 ± 3.26 | 20.12 ± 3.60 | 0.0001 |
| 4 | ⩾ 0.75 | 9 | 11.67 ± 2.20 | 17.35 ± 5.39 | 0.008 |
| Total | | 48 | | | |

# Trial of Standard versus Modified Expiration to Achieve End-of-Test Spirometry Criteria

JAMES K. STOLLER, STEPHEN BASHEDA, DANIEL LASKOWSKI, MARLENE GOORMASTIC, and KEVIN MCCARTHY

Departments of Pulmonary and Critical Care Medicine and Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, Ohio

TABLE 5

LARGEST VALUES* OF FVC USING STANDARD VERSUS MODIFIED EXPIRATORY TECHNIQUE

| Group No. | $FEV_1$/FVC Strata | Patients (*n*) | FVC (*L*) | | |
|---|---|---|---|---|---|
| | | | Standard | Modified | p Value† |
| 1 | < 0.45 | 12 | 2.29 ± 0.72 | 2.62 ± 0.76 | 0.007 |
| 2 | 0.45–0.60 | 11 | 2.86 ± 1.06 | 3.13 ± 1.25 | 0.02 |
| 3 | 0.61–0.74 | 16 | 3.75 ± 1.13 | 3.83 ± 1.19 | 0.01 |
| 4 | ⩾ 0.75 | 9 | 3.87 ± 1.23 | 3.93 ± 1.16 | 0.15 |
| Total | | 48 | | | |

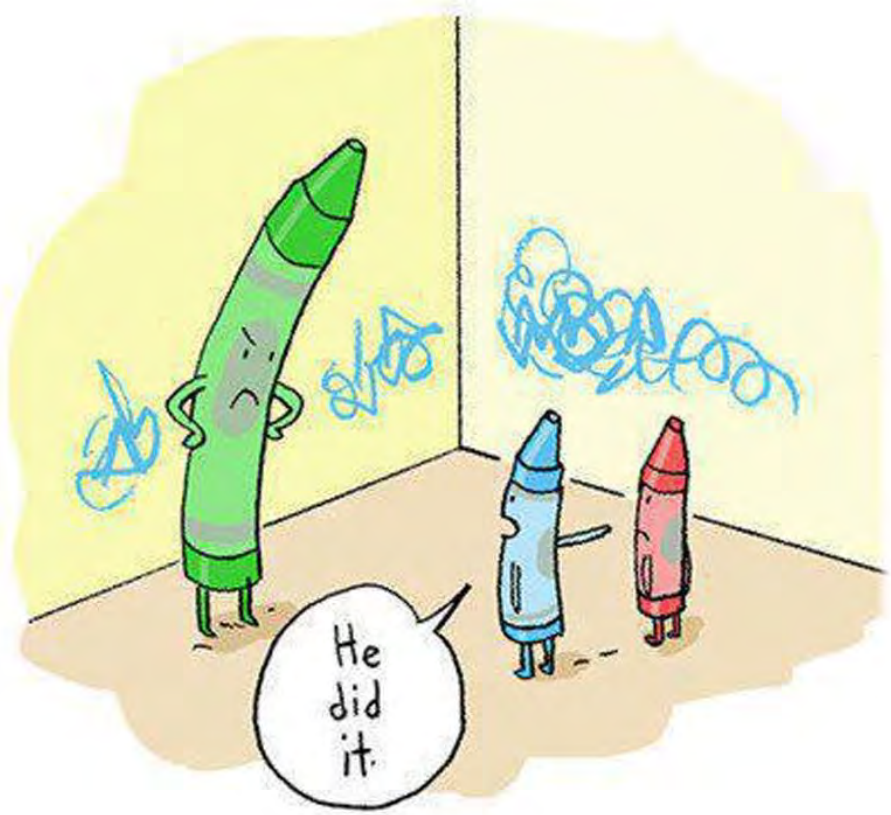
# Trial of Standard versus Modified Expiration to Achieve End-of-Test Spirometry Criteria

JAMES K. STOLLER, STEPHEN BASHEDA, DANIEL LASKOWSKI, MARLENE GOORMASTIC, and KEVIN MCCARTHY

Departments of Pulmonary and Critical Care Medicine and Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, Ohio

- Less patient discomfort
- Less lightheadedness

# Who’s to blame for poor quality data?



# It must be the patient’s fault

# “Older people can’t perform PFT correctly”

# Pulmonary Function Test Quality in the Elderly: A Comparison With Younger Adults

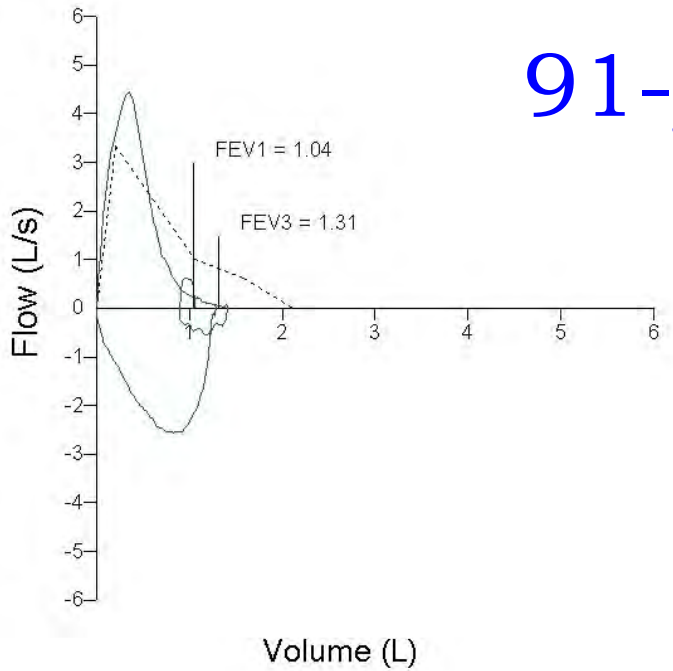
Jeffrey M Haynes RRT RPFT

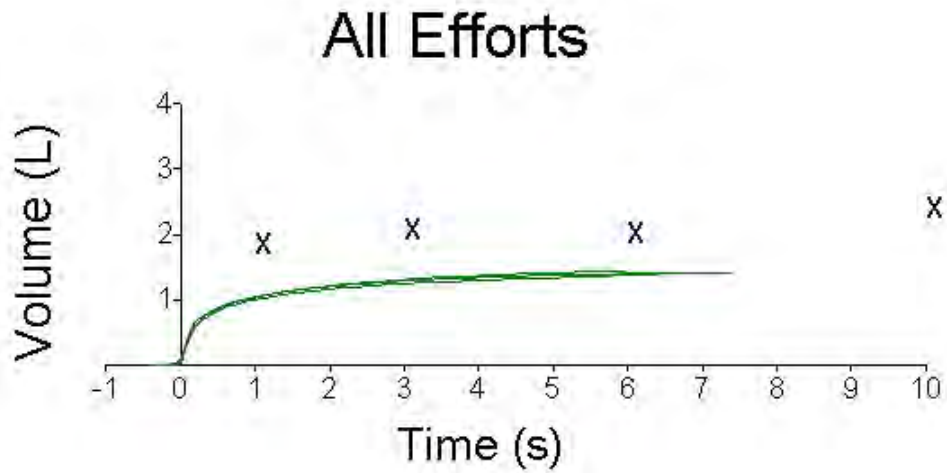
22 month sample of spirometry and DLCO quality (ATS/ERS)

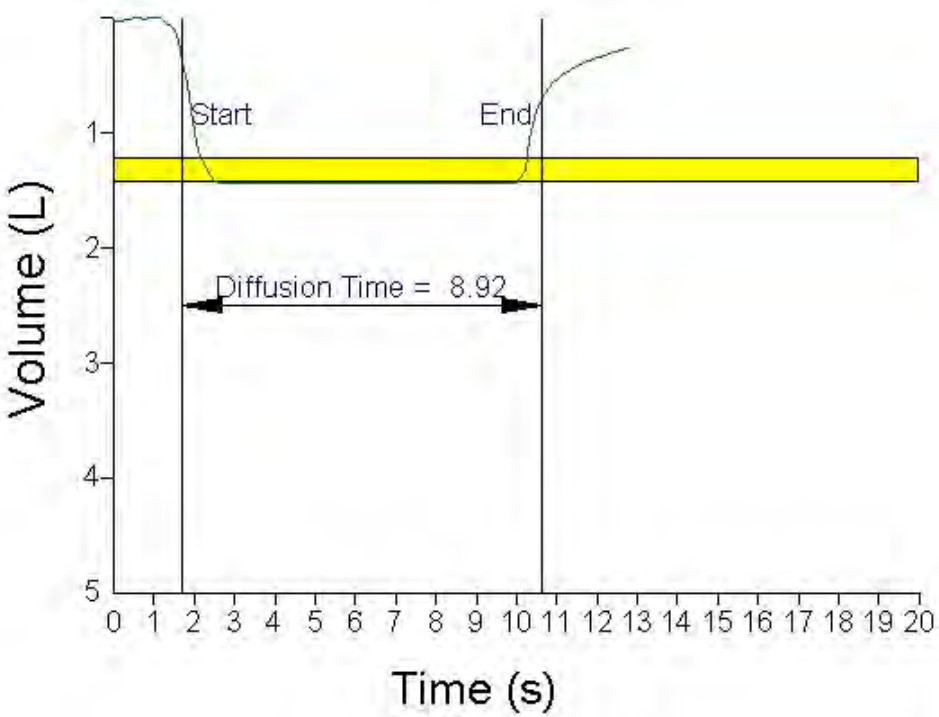
| | 80+ | 40-50 | p |
|---|---|---|---|
| Spirometry | 92.6% | 91.5% | 0.84 |
| DLCO | 84.9% | 88.5% | 0.45 |

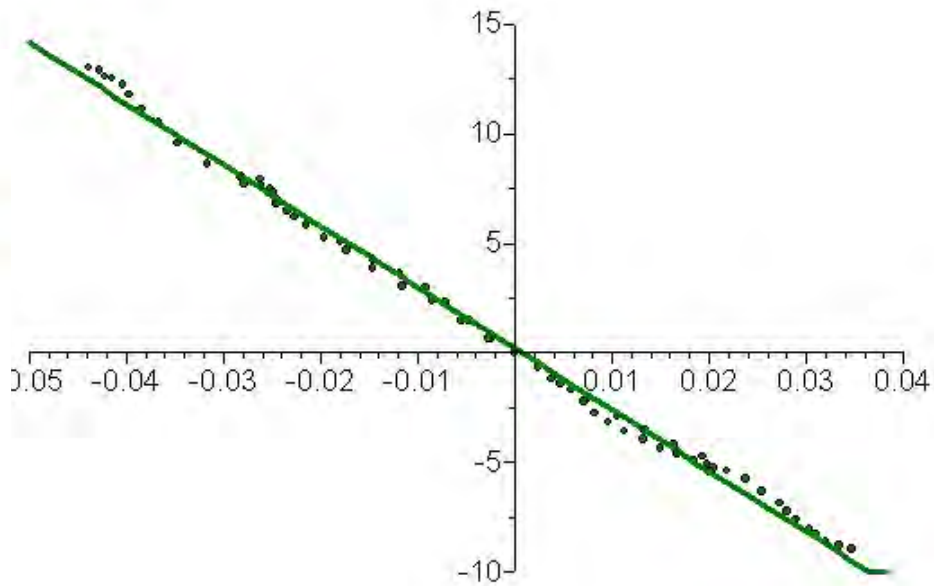
Haynes JM Respir Care 2014;59(1):16

# 91-year-old female

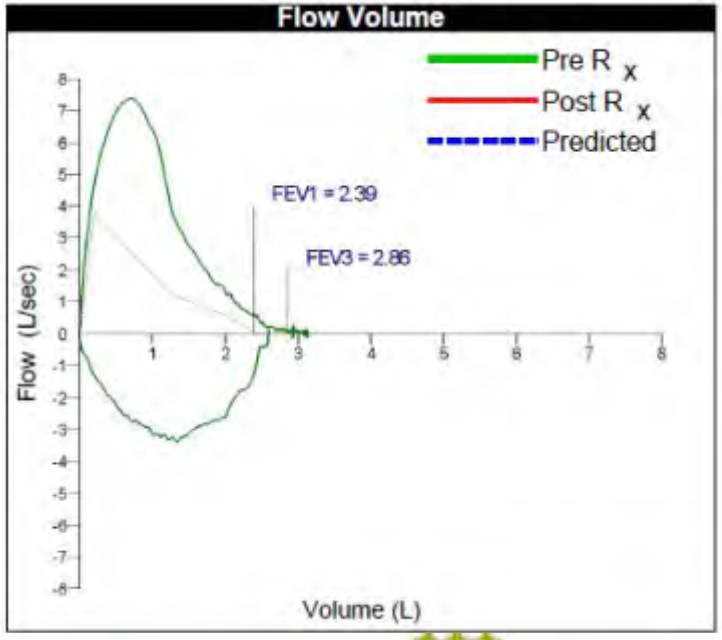


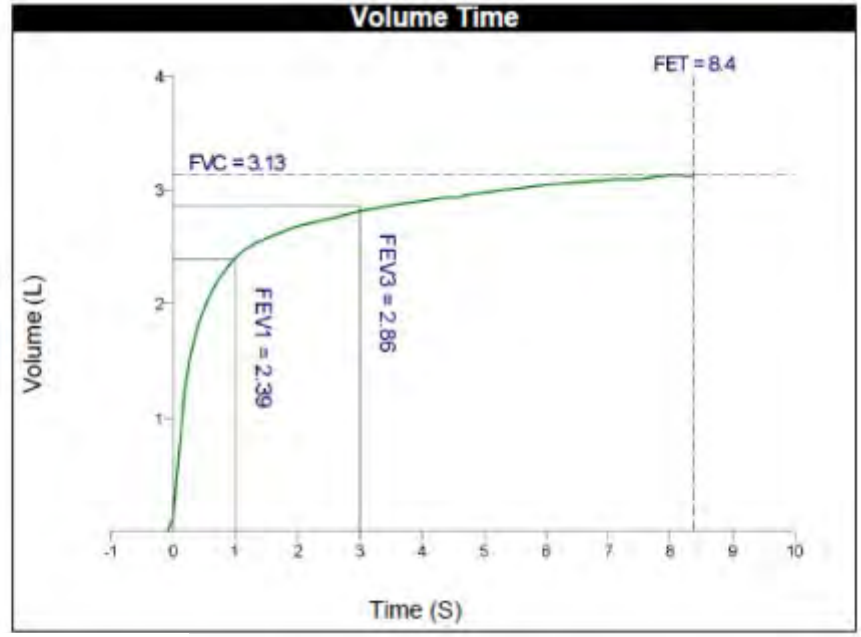



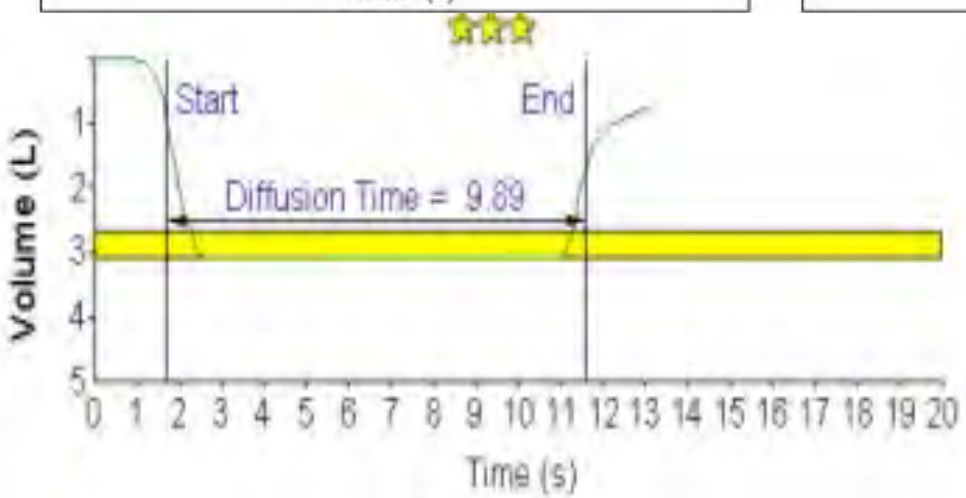



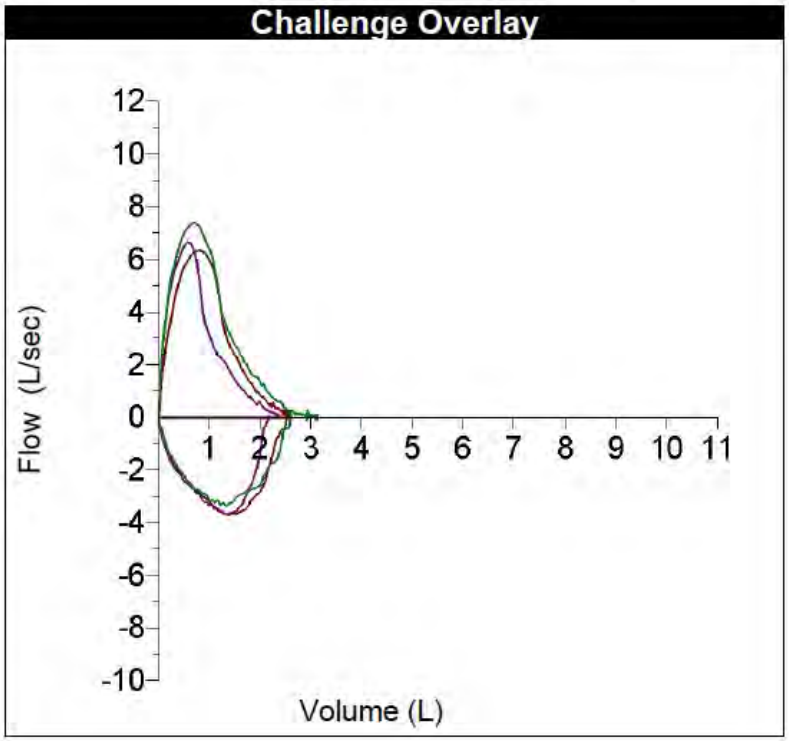
# 94-year-old female

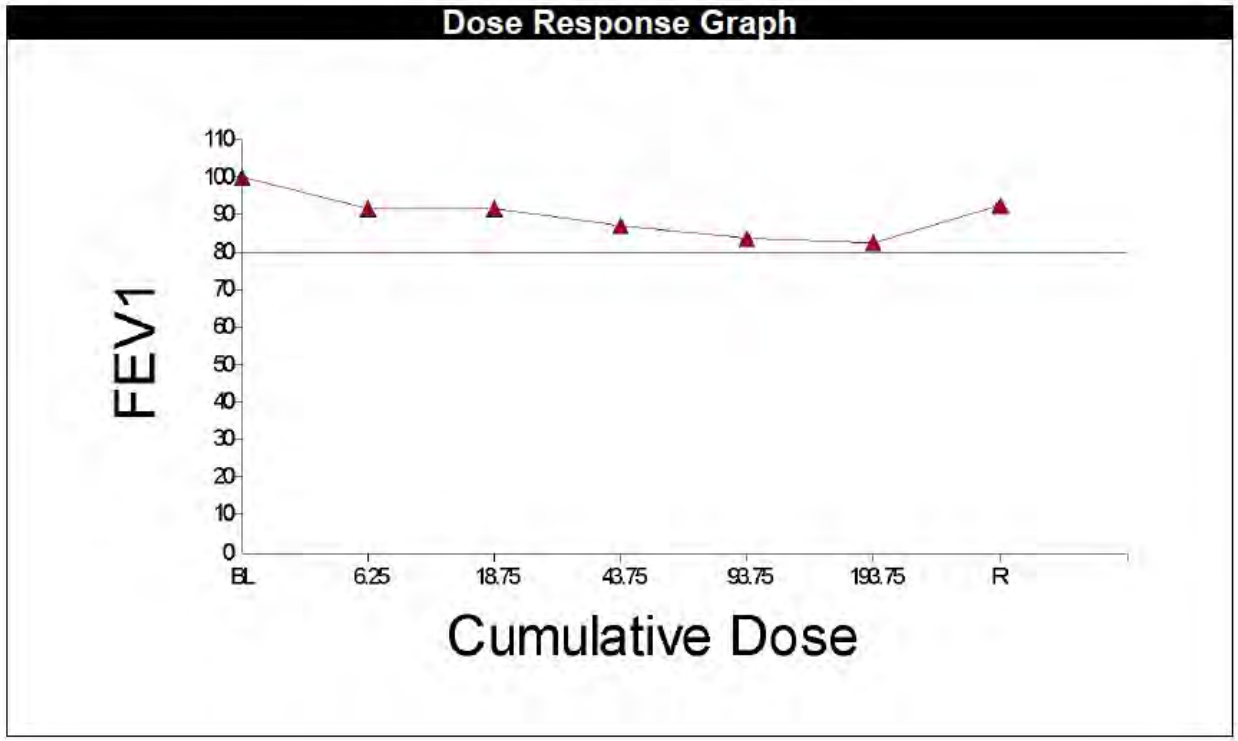


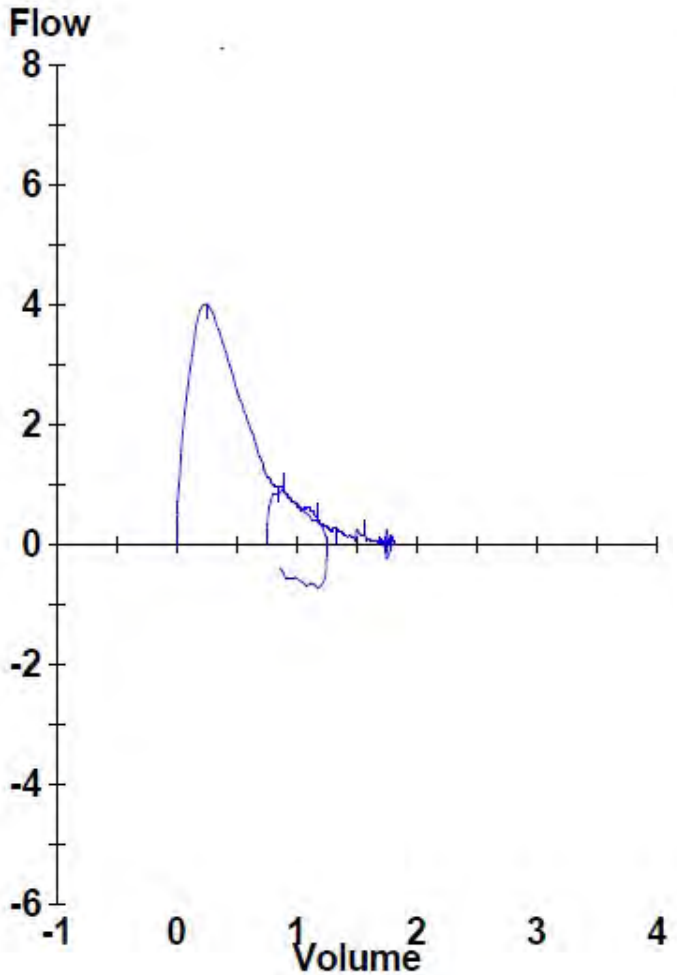



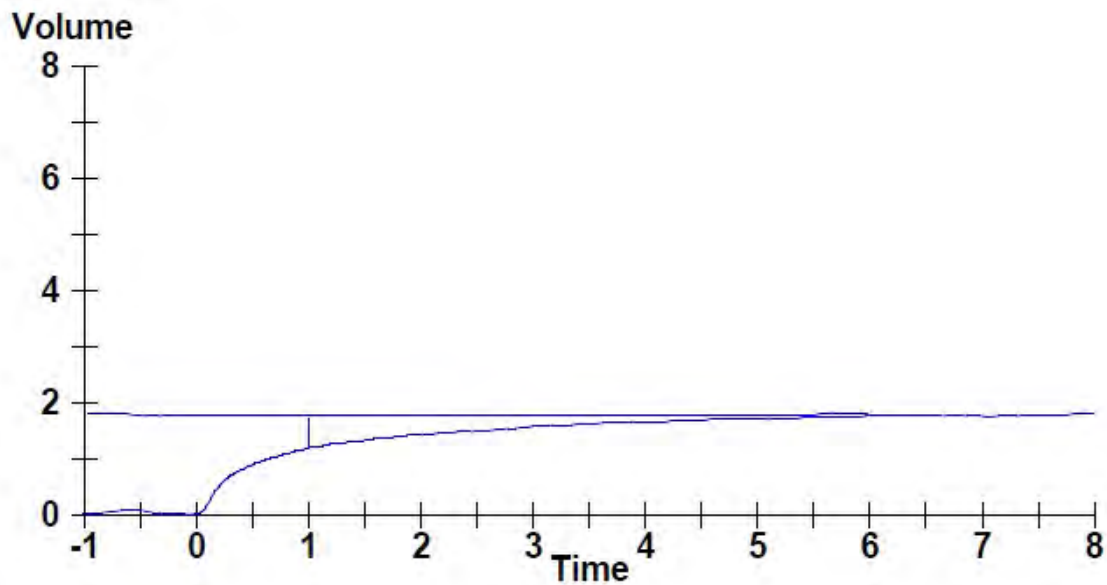

# 94-year-old female



# 101-year-old female

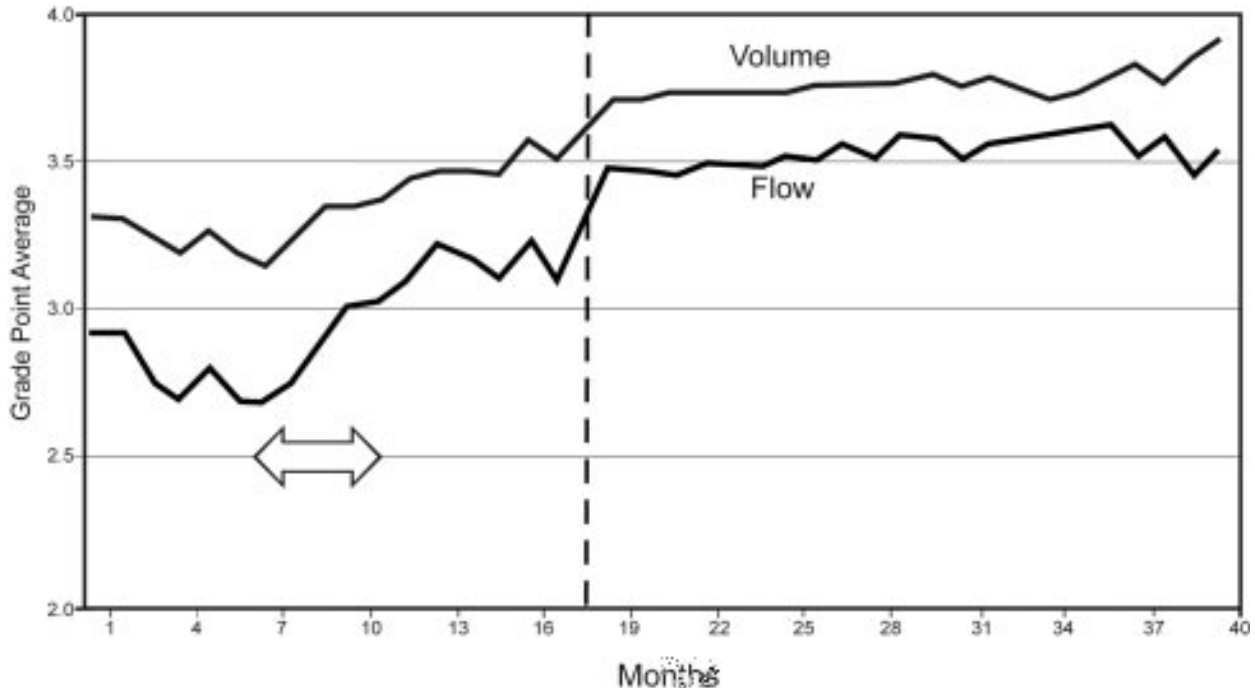



Courtesy of Eric Lindquist RRT CPFT


Who else could be responsible?

# Technologist Performance Monitoring & Feedback




Enright. Am Rev Respir Dis. 1990;143(6):1215.

# Technologist Performance Monitoring & Feedback

Borg et al. Respir Care 2012;57(12):2032

2 tertiary hospital PFT labs in Australia

Examined the quality of 100 consecutive spirometry tests each year between 2004-2008

Following the initial survey “Lab #1” implemented technologist monitoring & feedback program

“Lab #2” served as a control

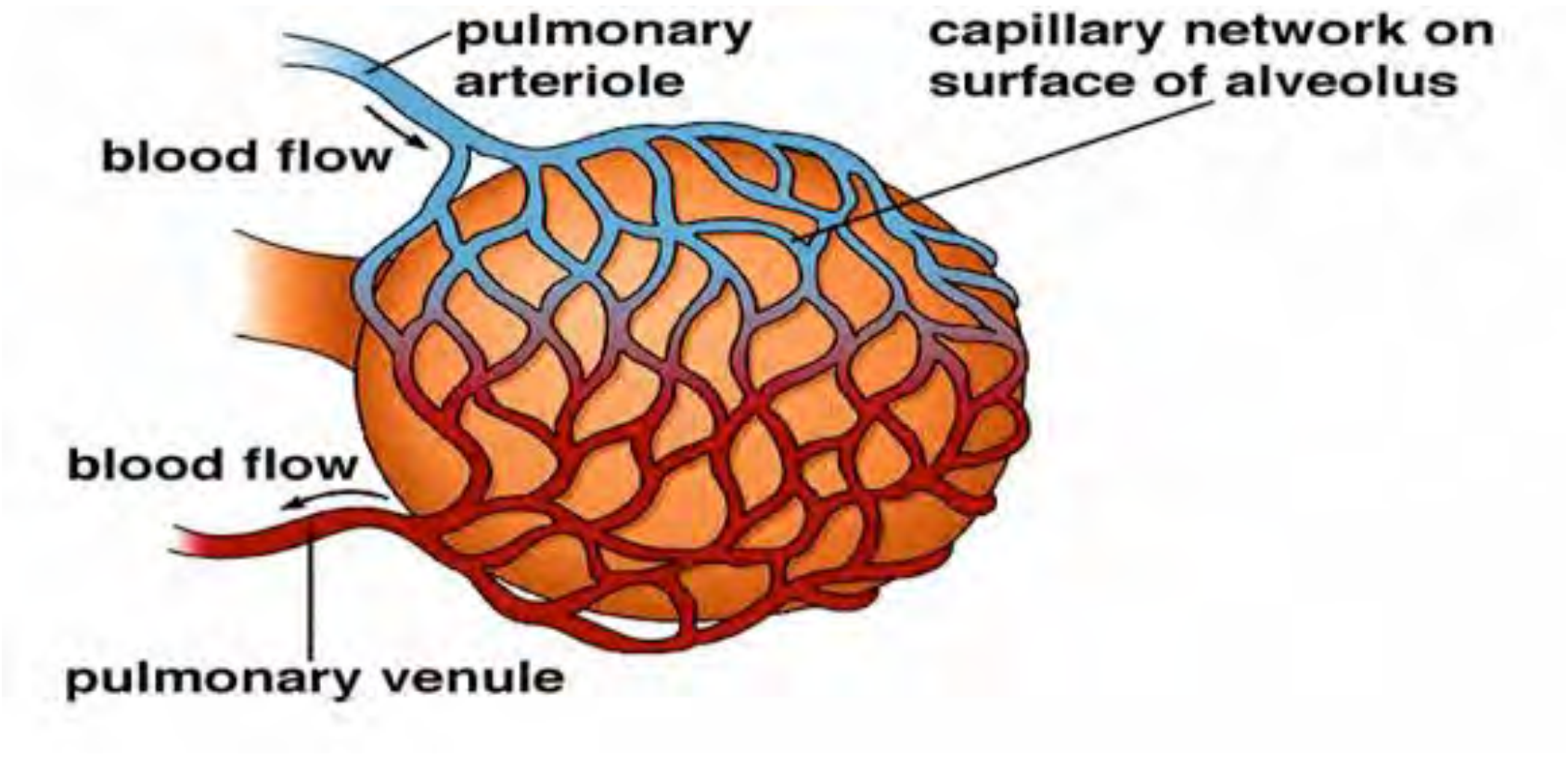
# Technologist Performance Monitoring & Feedback

% tests satisfying ATS/ERS acceptability & reproducibility standards

| | Lab #1 | Lab #2 | p |
|---|---|---|---|
| 2004 | 61% | 59% | .89 |
| 2008 | 92% | 65% | < .001 |

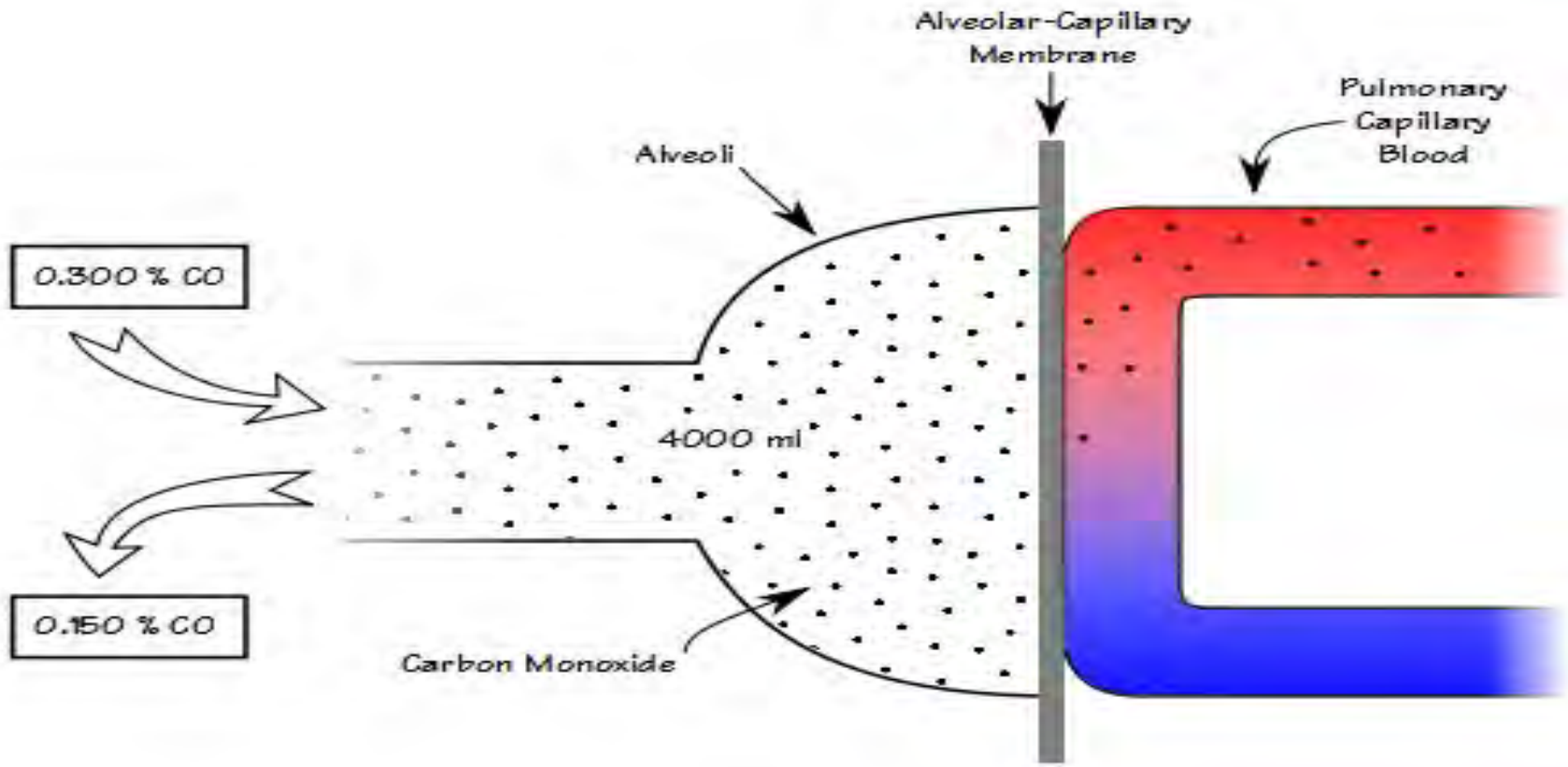
The Thoracic Society of Australia & New Zealand
LEADERS IN LUNG HEALTH

# DLCO


pulmonary arteriole
capillary network on surface of alveolus
blood flow
blood flow
pulmonary venule

# "The DLCO is normal when corrected for alveolar volume"

| ***Diffusion*** | | **Pre Bronchodilator** | | | | | |
|---|---|---|---|---|---|---|---|
| | | Actual | Range | | Predicted | % Pred | Z-score |
| DLCO | mL/min/mmHg | **10.52** | 17.61 | 32.00 | 24.15 | 44 | -3.93 |
| DLCO [Hb] | mL/min/mmHg | **10.52** | 17.61 | 32.00 | 24.15 | 44 | -3.93 |
| VA [BTPS] | L | **2.83** | 4.85 | 7.40 | 6.09 | 46 | -4.67 |
| KCO | mL/min/mmHg/L | **3.72** | 2.94 | 5.16 | 3.99 | 93 | -0.41 |

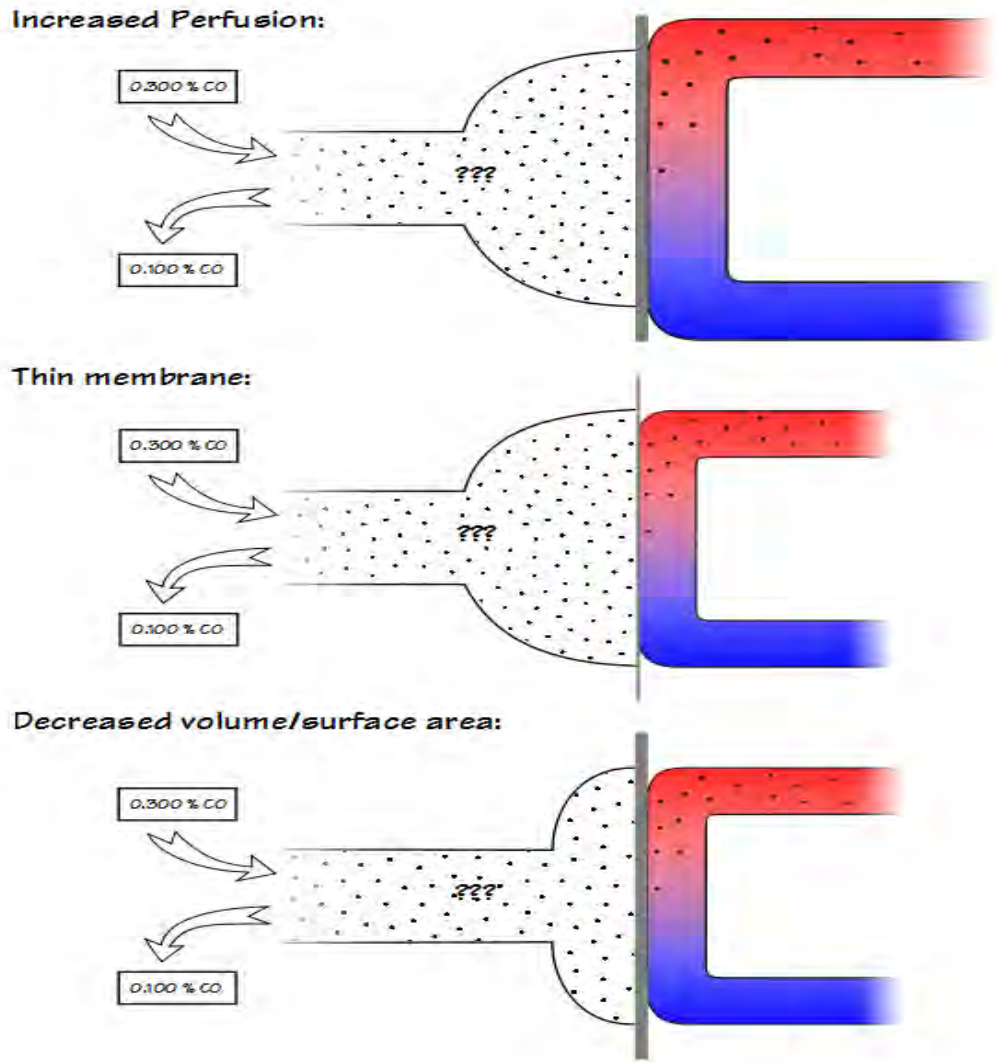



Images courtesy of Richard Johnston CPFT

# Correcting for volume?: "~~DLCO/$V_A$~~"

- DLCO/$V_A$ changed to KCO

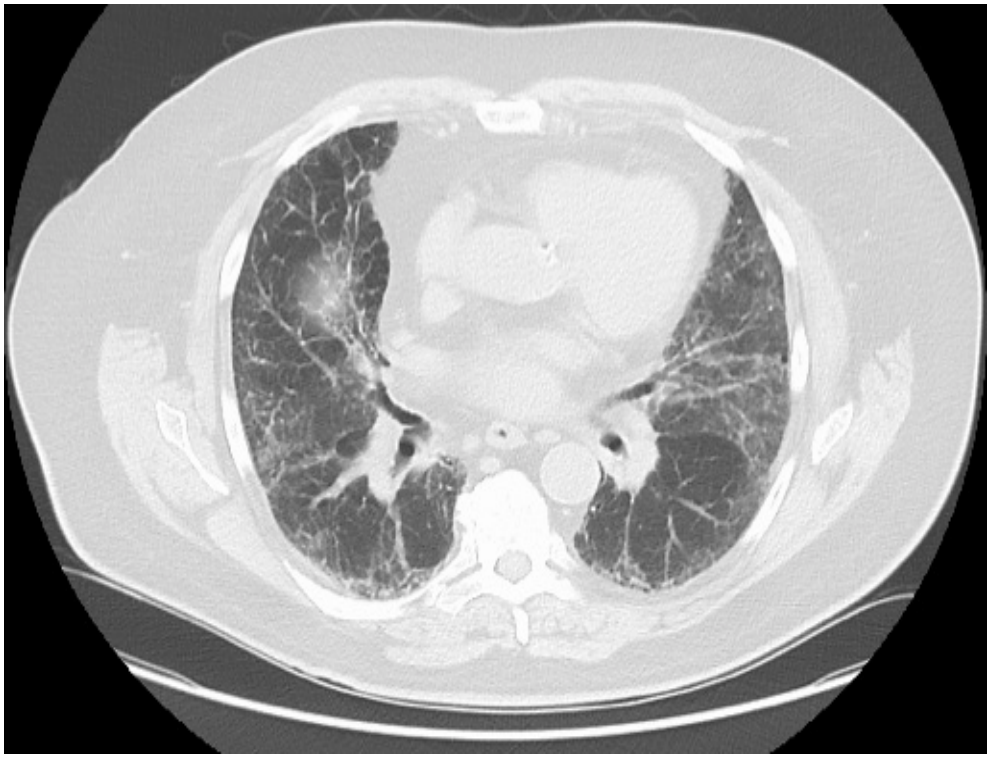
$$D_{\mathrm{LCO}} = \frac{V_{\mathrm{A}}}{t \cdot (P_{\mathrm{B}} - P_{\mathrm{H_2O}})} \cdot \ln\left(\frac{F_{\mathrm{ACO,0}}}{F_{\mathrm{ACO,t}}}\right)$$




# High KCO

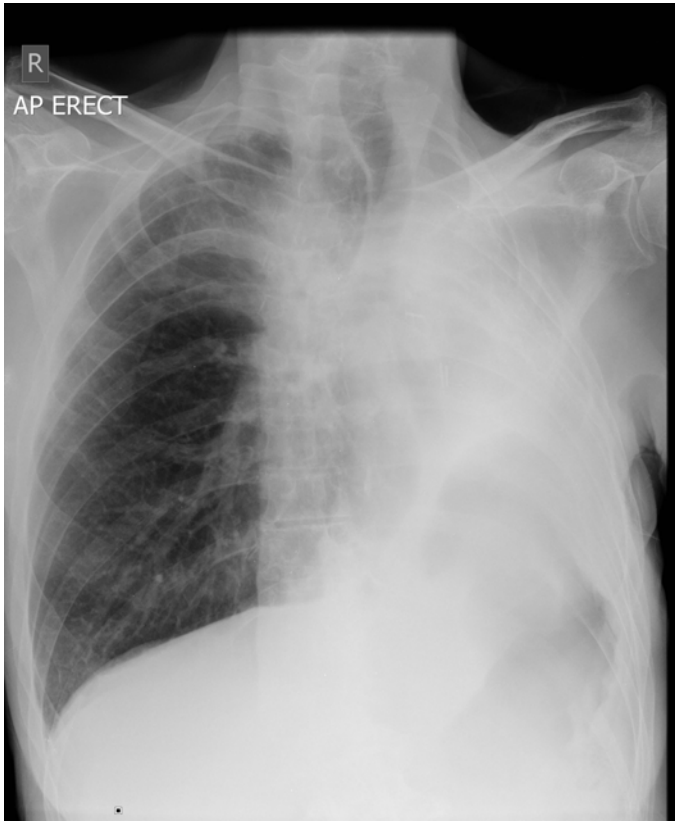
Images courtesy of Richard Johnston CPFT

“The DLCO is normal when corrected for alveolar volume”



THIS IS NOT NORMAL!!

"The DLCO is normal when corrected for alveolar volume"




THIS IS NOT NORMAL!!

“DLCO should always be adjusted for Hgb and COHb”

# DLCO Adjustments

- Adult males

$$D_{\mathrm{LCO}}[\text{predicted for Hb}] = D_{\mathrm{LCO}}[\text{predicted}] \cdot (1.7\mathrm{Hb}/(10.22 + \mathrm{Hb}))$$

- Females & <15 years

$$D_{\mathrm{LCO}}[\text{predicted for Hb}] = D_{\mathrm{LCO}}[\text{predicted}] \cdot (1.7\mathrm{Hb}/(9.38 + \mathrm{Hb}))$$

- Alternatively

$$D_{\mathrm{LCO}}[\text{predicted for Hb}] = D_{\mathrm{LCO}}[\text{predicted}] \cdot (1.7\mathrm{Hb}/(0.7\mathrm{Hb}_{\mathrm{ref}} + \mathrm{Hb}))$$

# Anemia example

71-year-old male

Predicted DLCO 22.78
Measured DLCO 14.36 63% predicted

Hgb: 6.6 g/dL

Adjusted predicted: 15.19
14.36 = 95% predicted

# DLCO Adjustments

1. CO back pressure
2. Anemia effect

$DL_{COpred}=DL_{COpred}$ x (102%-COHb%)

Predicted ↓ 1% every 1% COHb > 2%

RGA: $DL_{CO}$ corr = $DL_{CO}$ x $(1+F_{ACOb}/560)$

# COHB example

51-year-old female COHb: 15%
Predicted DLCO 22 ml/min/mmHg
Actual DLCO 17 ml/min/mm Hg (77% predicted)

22 x (1.02-.15)
22 x .87 = 19.14 corrected predicted

17 ml/min/mm Hg = 89% predicted

# What is the Impact of Hemoglobin & COHb Adjustment?

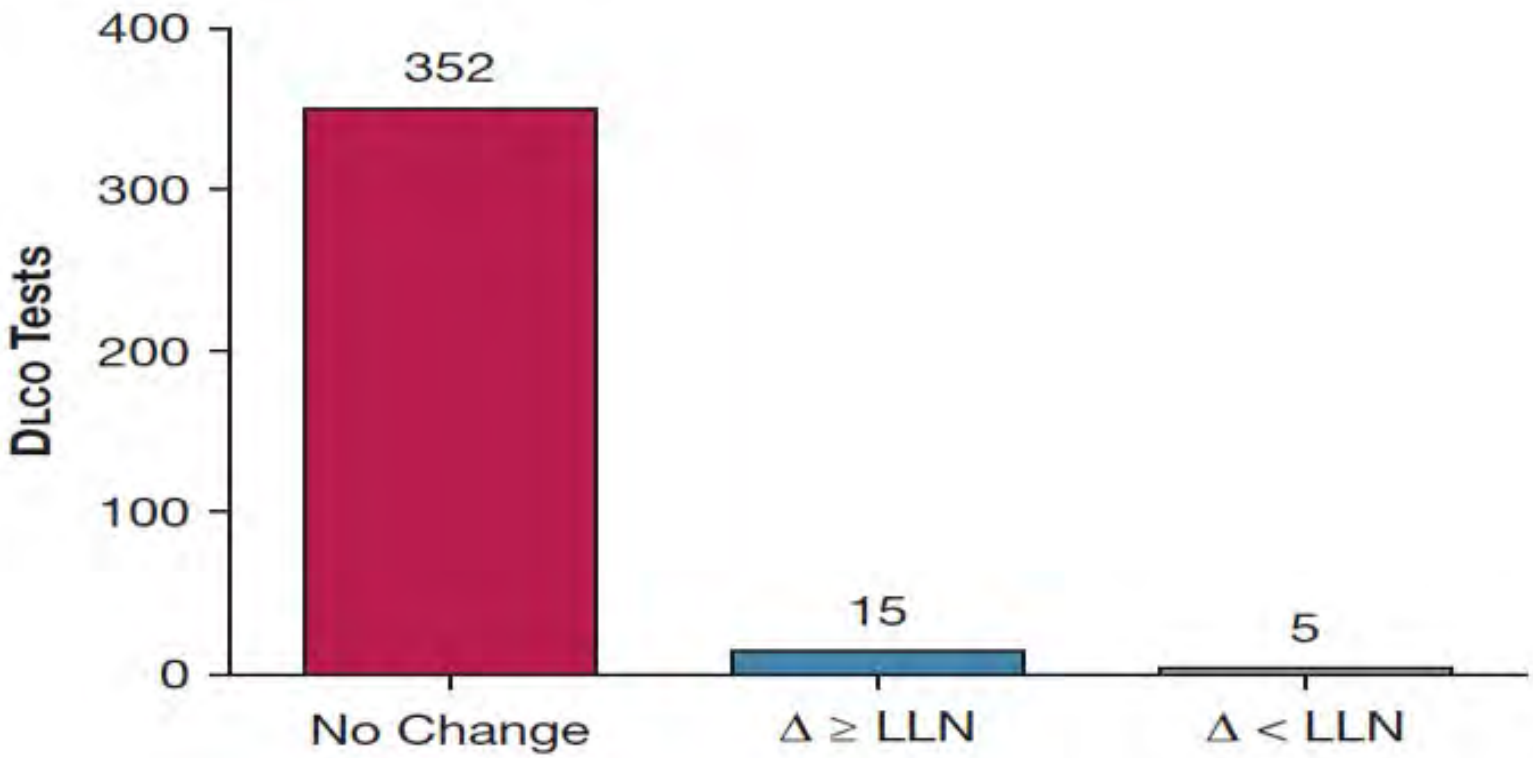
Haynes, Ruppel, Kaminsky Chest 2017;151(5):1188

n = 372 DLCO adjusted for hemoglobin and COHb ≥2%

| | |
|---|---|
| Change in normal vs. <LLN Status: | 5.4% |
| *with change > 3 ml/min/mmHg*: | *.05%* |
| Changed Severity Classification (<LLN): | 10.1% |
| *with change > 3 ml/min/mmHg*: | *.04%* |
| Changed > 3 ml/min/mmHg: | 1.3% |

# What is the Impact of Hemoglobin & COHb Adjustment?

Haynes, Ruppel, Kaminsky Chest 2017;151(5):1188



Plethysmography is more accurate than dilution in emphysema

CHEST

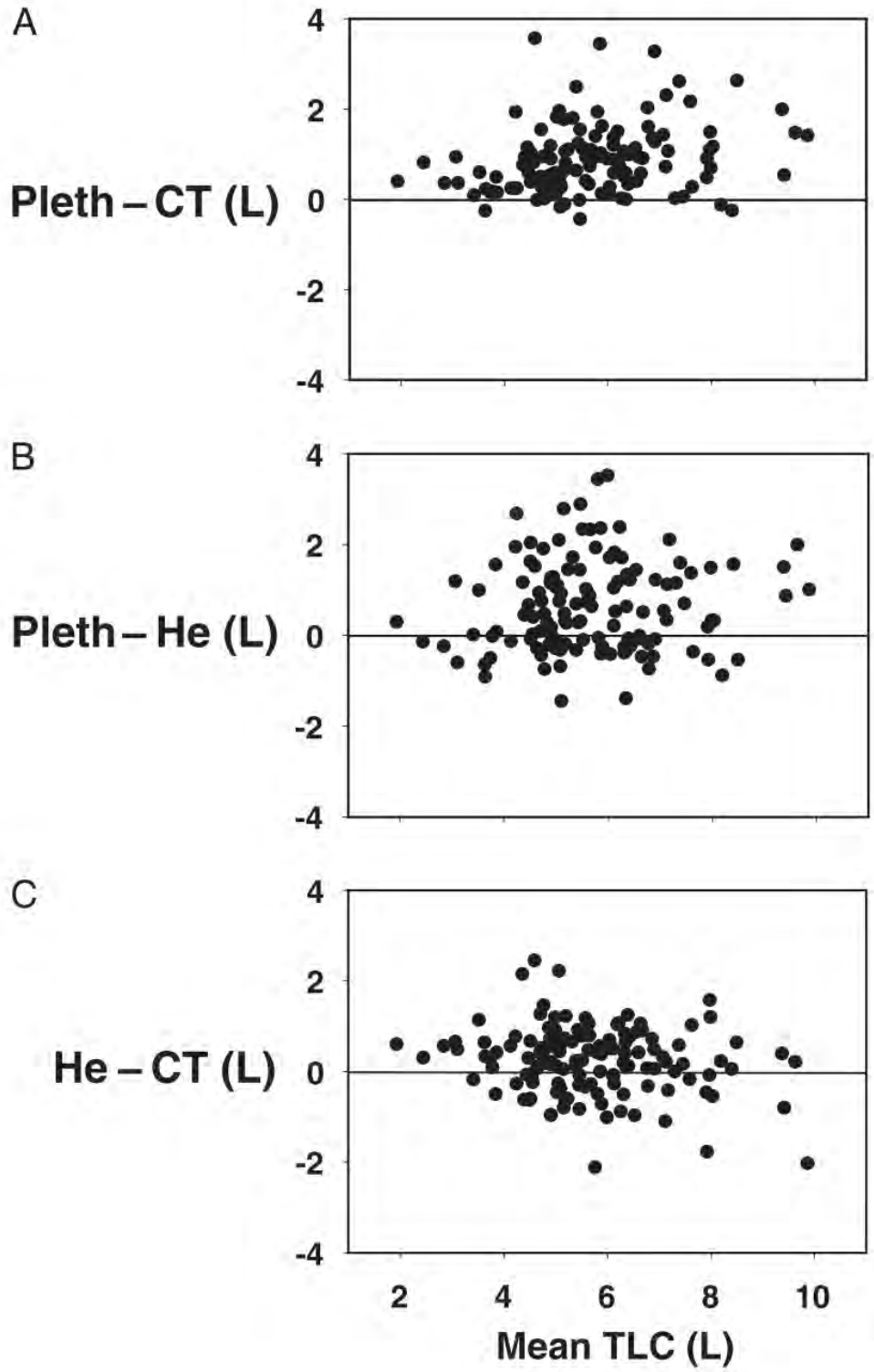
Original Research

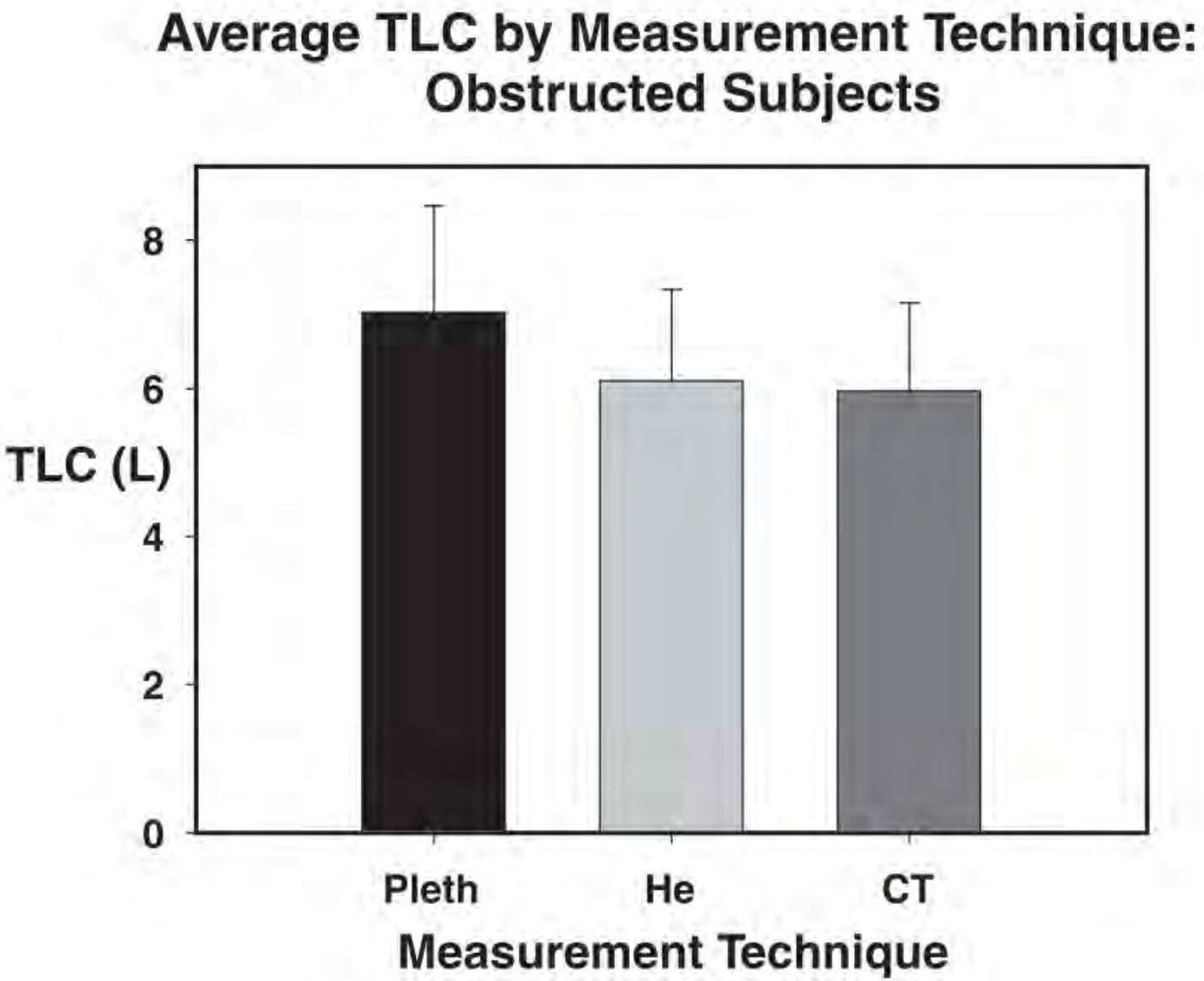
COPD

# Comparison of Plethysmographic and Helium Dilution Lung Volumes

## Which Is Best for COPD?

*Carl R. O'Donnell, ScD, MPH; Alexander A. Bankier, MD; Leopold Stiebellehner, MD; John J. Reilly, MD, FCCP; Robert Brown, MD; and Stephen H. Loring, MD*


A
Pleth – CT (L)
B
Pleth – He (L)
C
He – CT (L)
4
2
0
-2
-4
2
4
6
8
10
Mean TLC (L)


Average TLC by Measurement Technique:
Obstructed Subjects
TLC (L)
0
2
4
6
8
Pleth
He
CT
Measurement Technique

# Interpretation Myths

**Spirometry (BTPS)**

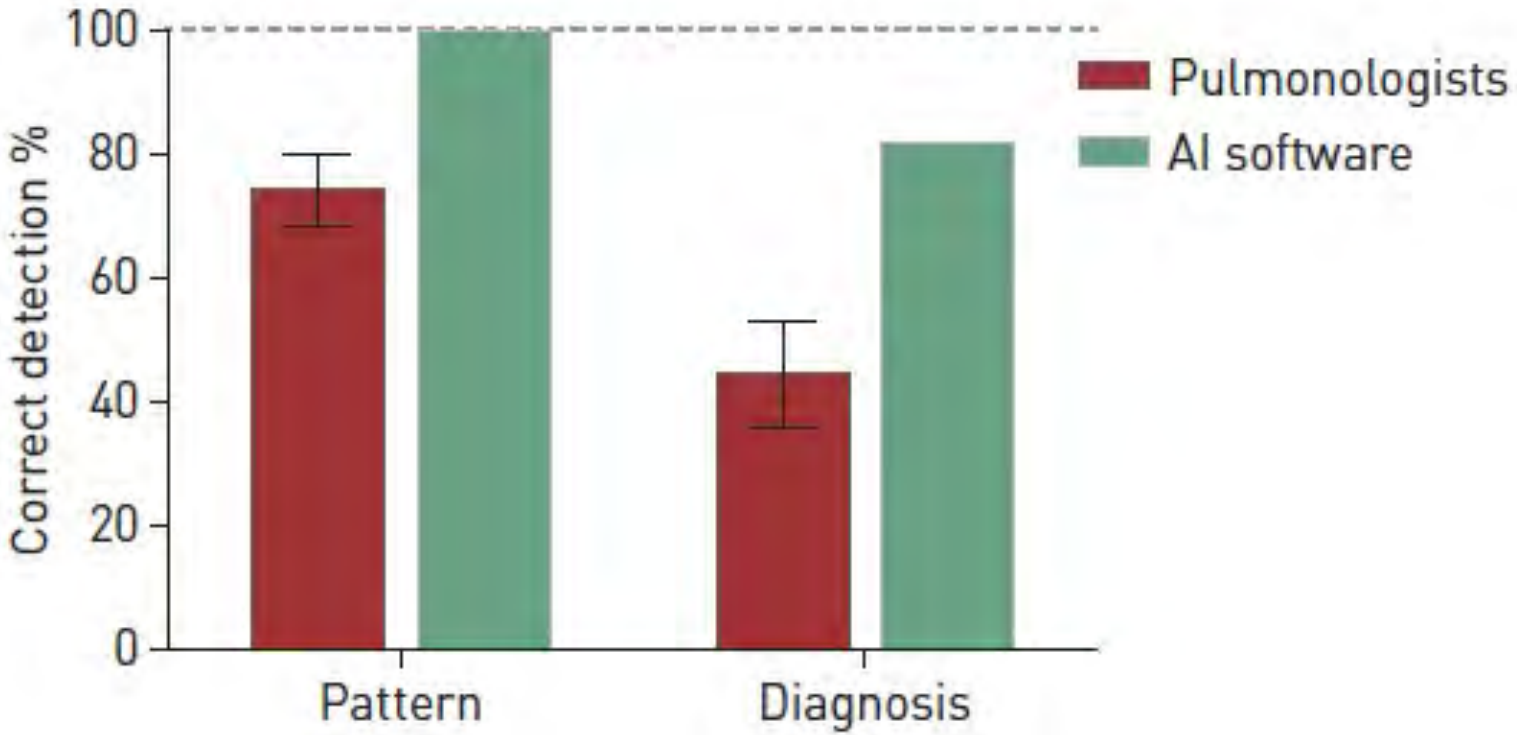
**Pre Bronchodilator**

| | | Actual | CI Range | | Predicted | % Pred | Z-score |
|---|---|---|---|---|---|---|---|
| StartTime | | **11:42** | ---- | ---- | ---- | ---- | ---- |
| FVC | L | **4.52** | 3.88 | 5.96 | 4.92 | 92 | -0.63 |
| $FEV_1$ | L | **3.59** | 3.09 | 4.75 | 3.92 | 92 | -0.67 |
| $FEV_1$ / FVC | % | **79** | 69 | 91 | 80 | 99 | -0.17 |
| $FEF_{25-75}$ | L/s | **3.10** | 2.08 | 5.36 | 3.72 | 83 | -0.54 |
| PEFR | L/s | **10.22** | 7.54 | ---- | 9.78 | 104 | ---- |

“Pulmonolgists are experts at PFT interpretation”

# Artificial intelligence outperforms pulmonologists in the interpretation of pulmonary function tests

Eur Respir J 2019; 53: 1801660



80% of predicted in the LLN

77 78 79 80 81 82

DISEASE NORMAL

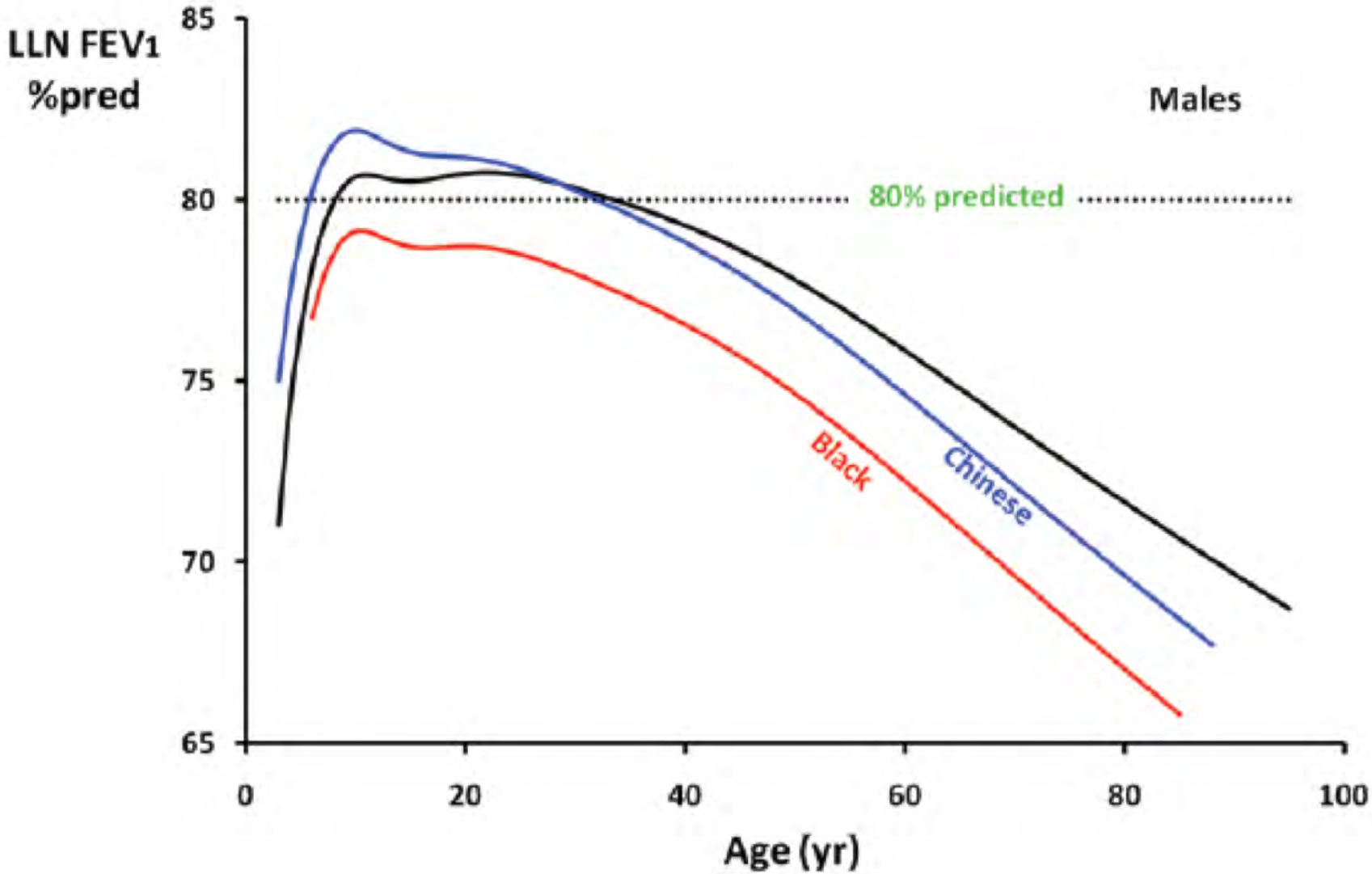
# Interpretation

$$80\% \neq \text{LLN}$$

# Global Lungs Initiative

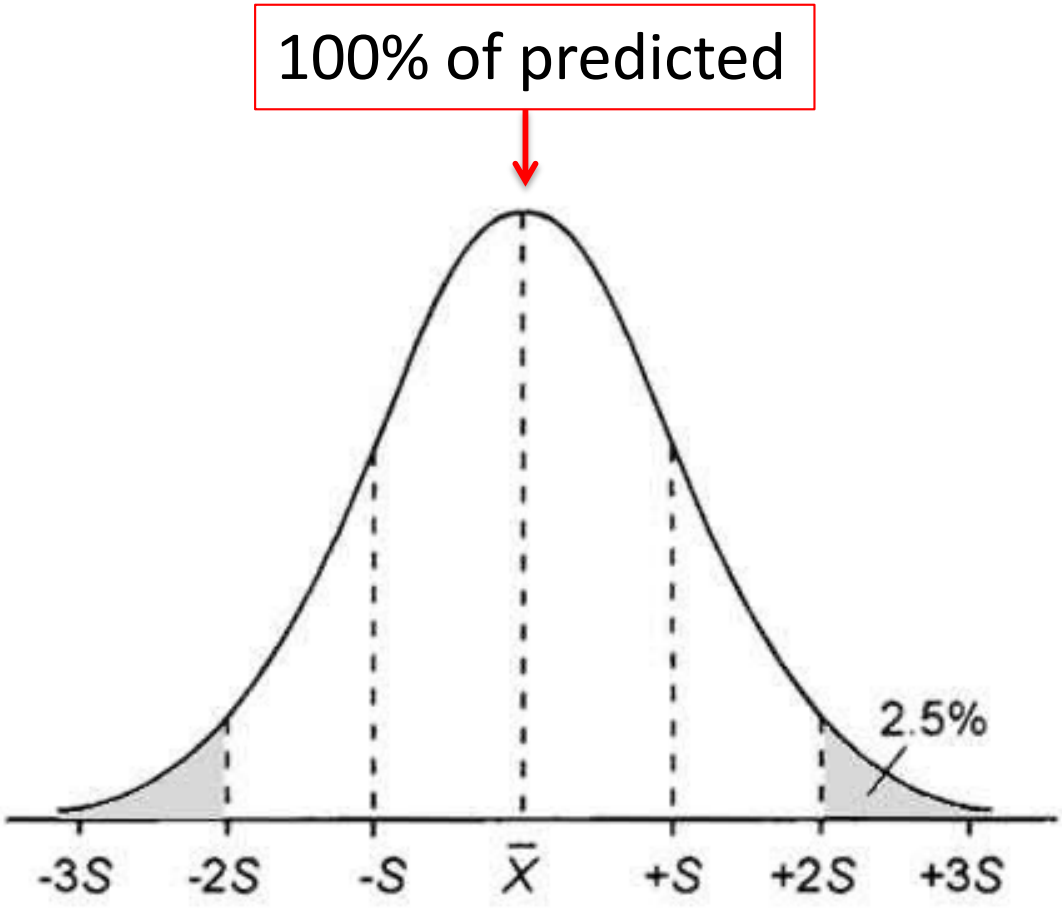
## Farewell to percent of predicted

"Nowhere else in medicine is such a naive view taken of the limit of normal." Sobol, Thorax, 1979

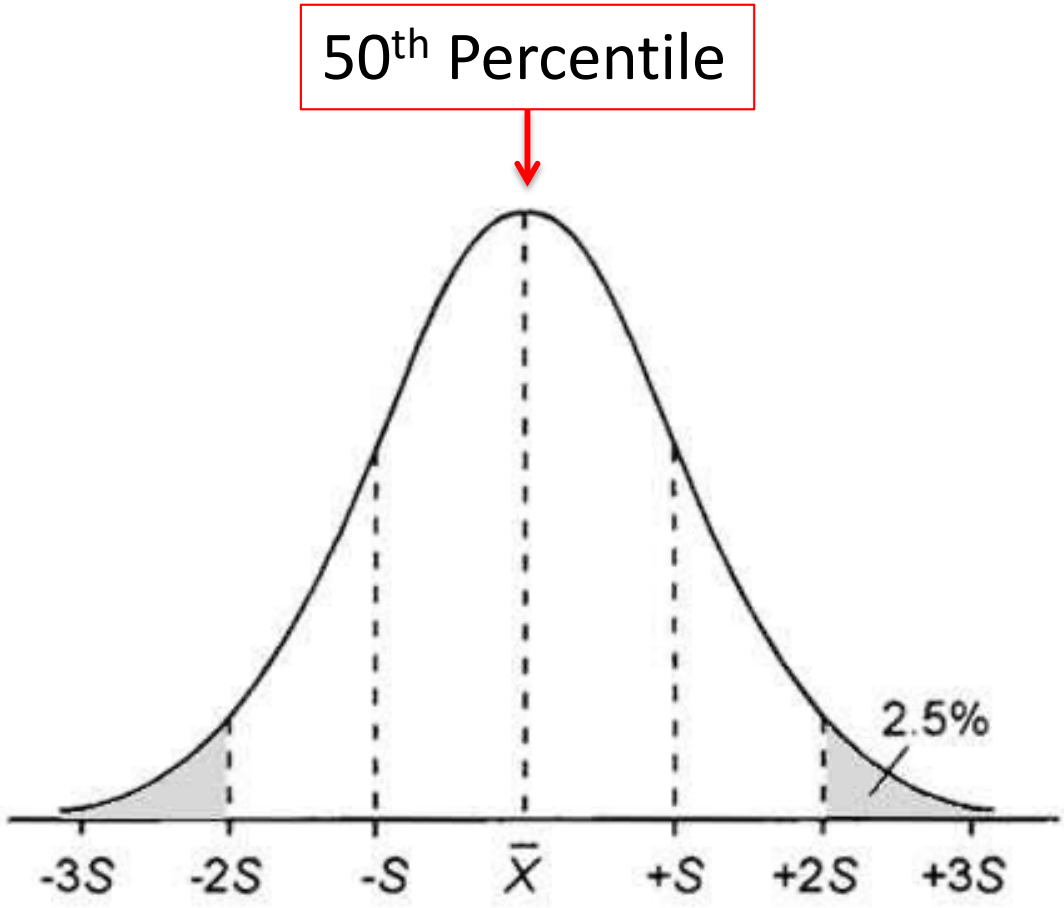


# How should we define normal?

# Normally Distributed Data

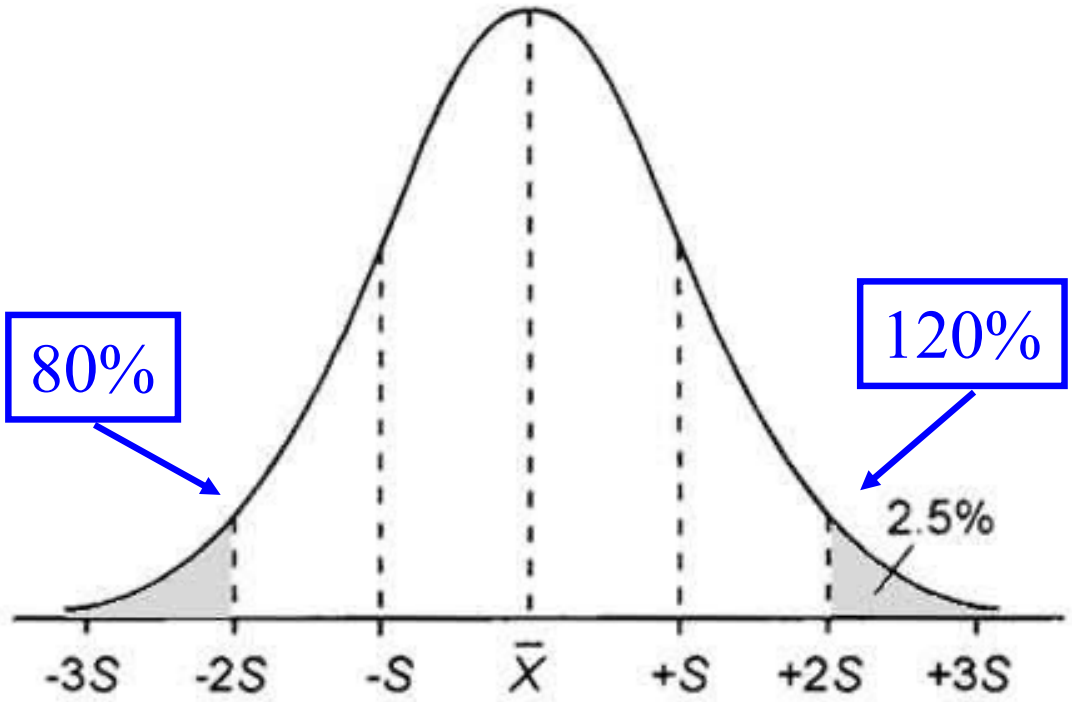


# Normally Distributed Data

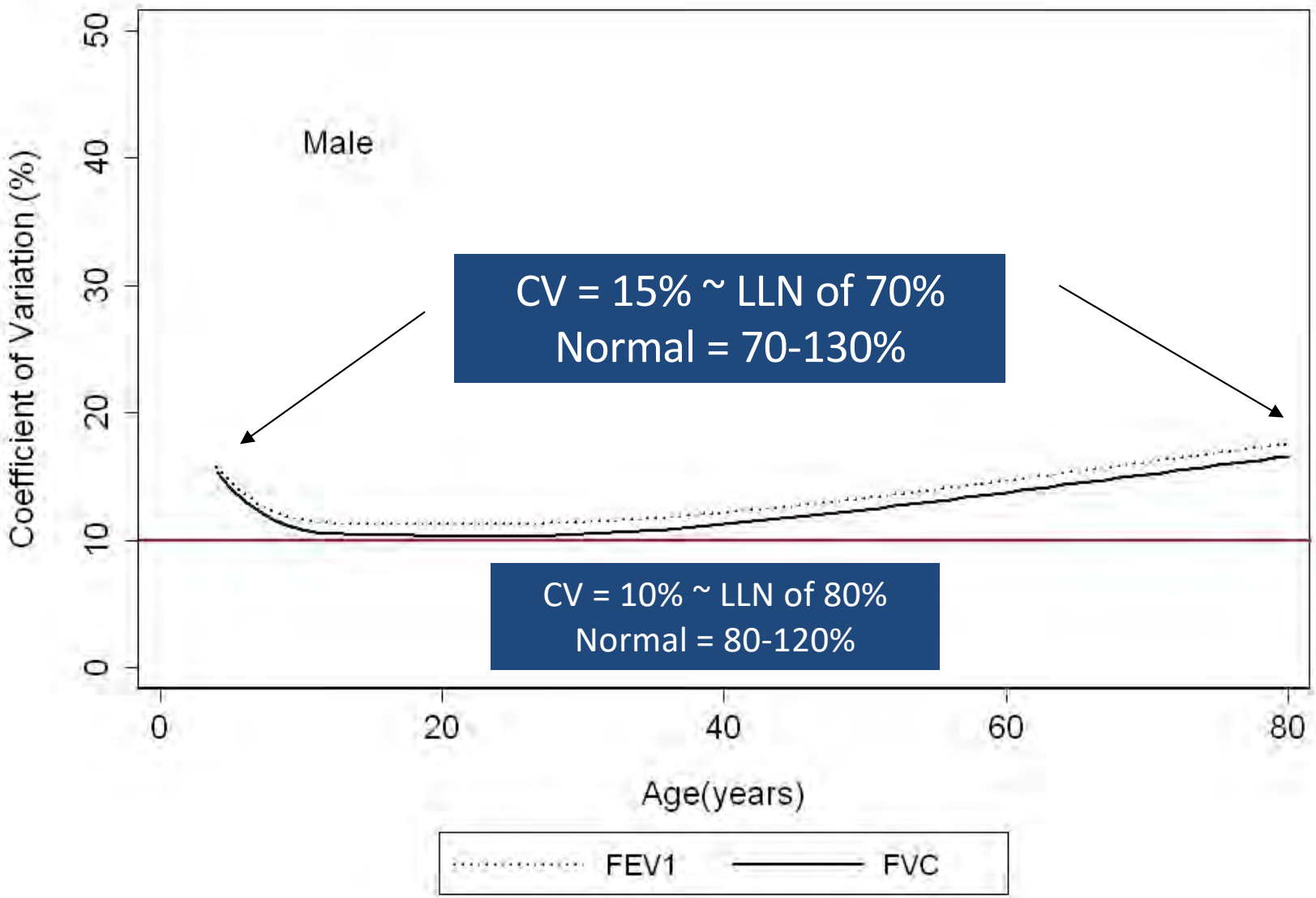


# Is 80% of predicted the LLN?

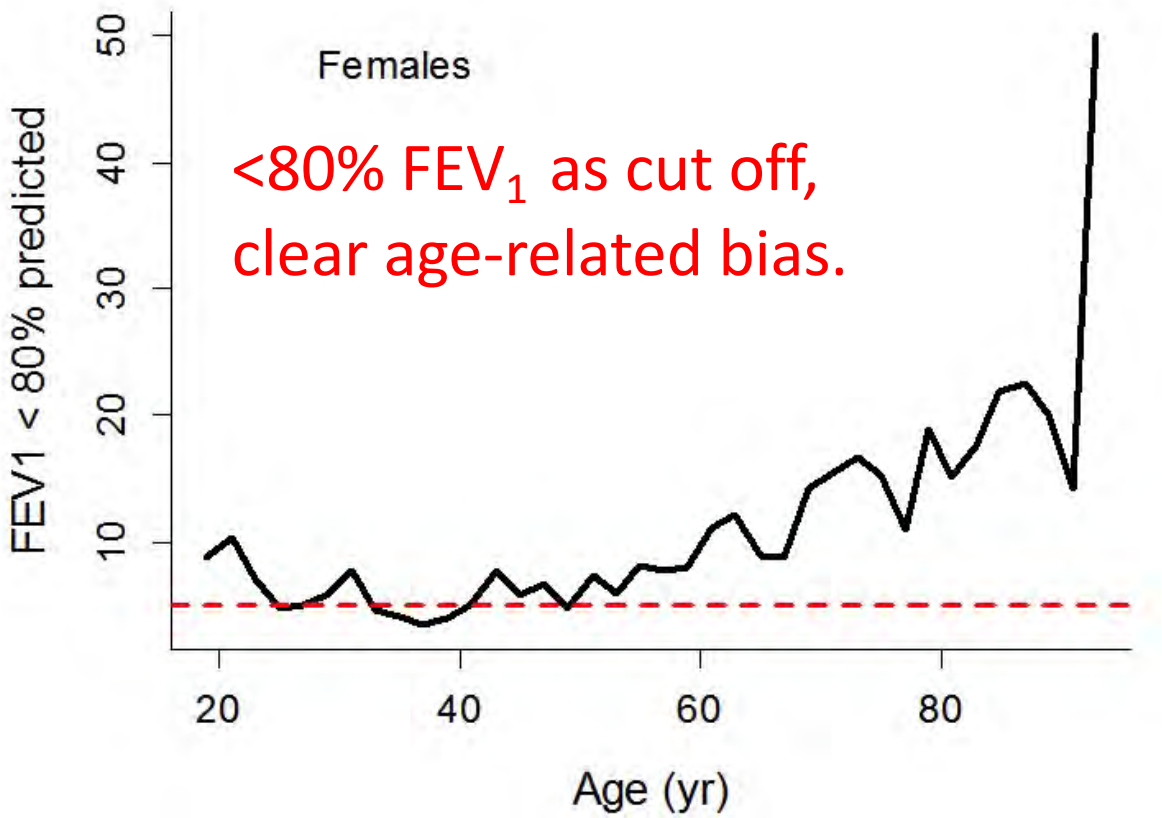
# Is 80% of average the LLN?




This assumes a CV of 10%

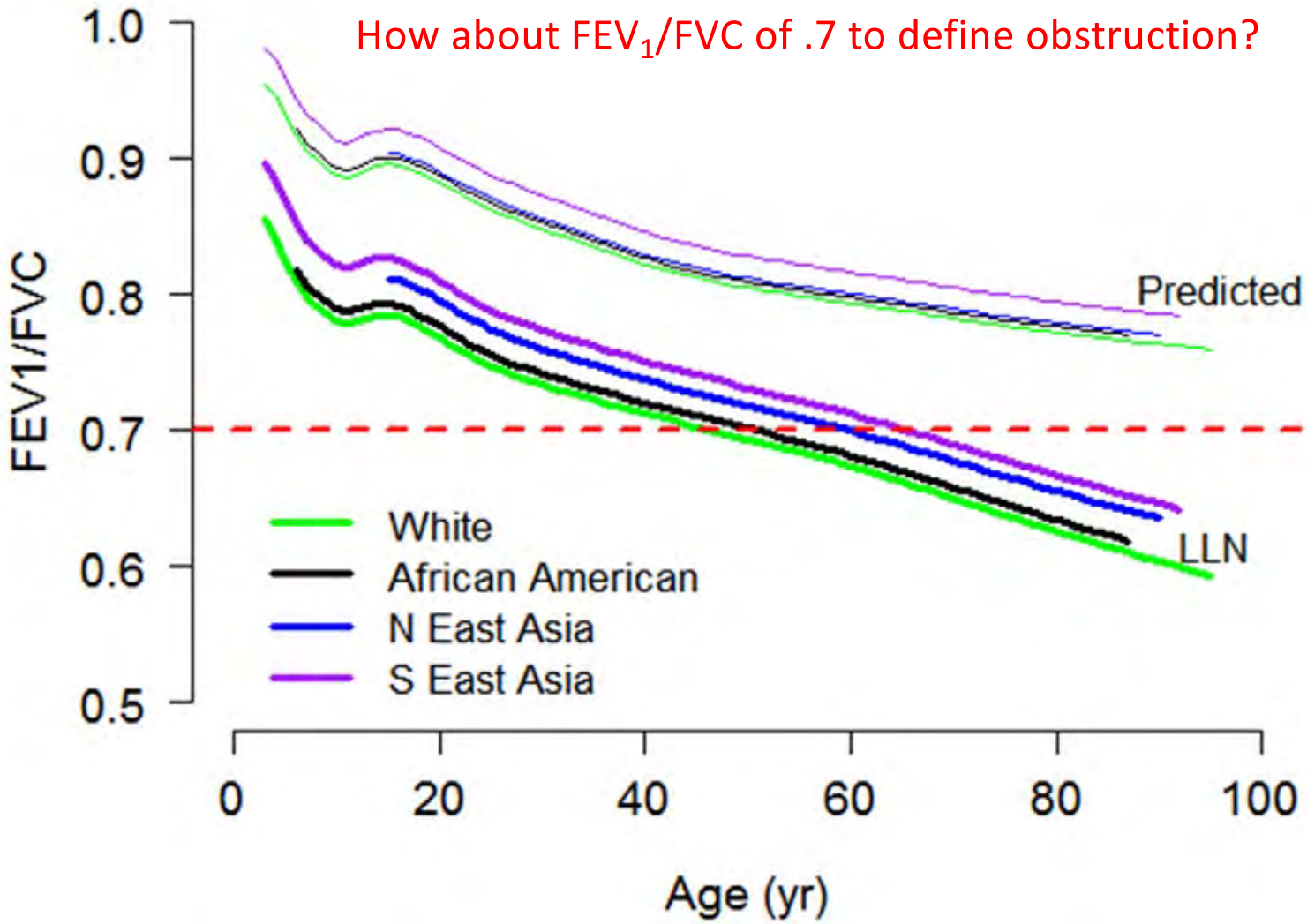

Male
CV = 15% ~ LLN of 70%
Normal = 70-130%
CV = 10% ~ LLN of 80%
Normal = 80-120%
Coefficient of Variation (%)
0
10
20
30
40
50
0
20
40
60
80
Age(years)
FEV1
FVC

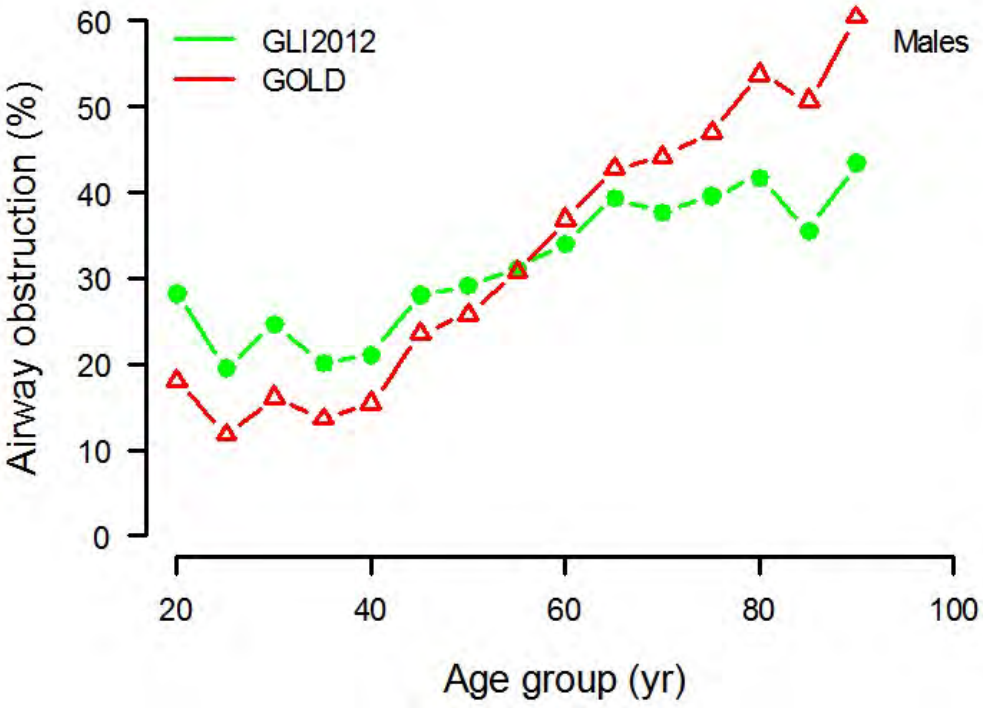
# Is 80% of predicted the LLN?

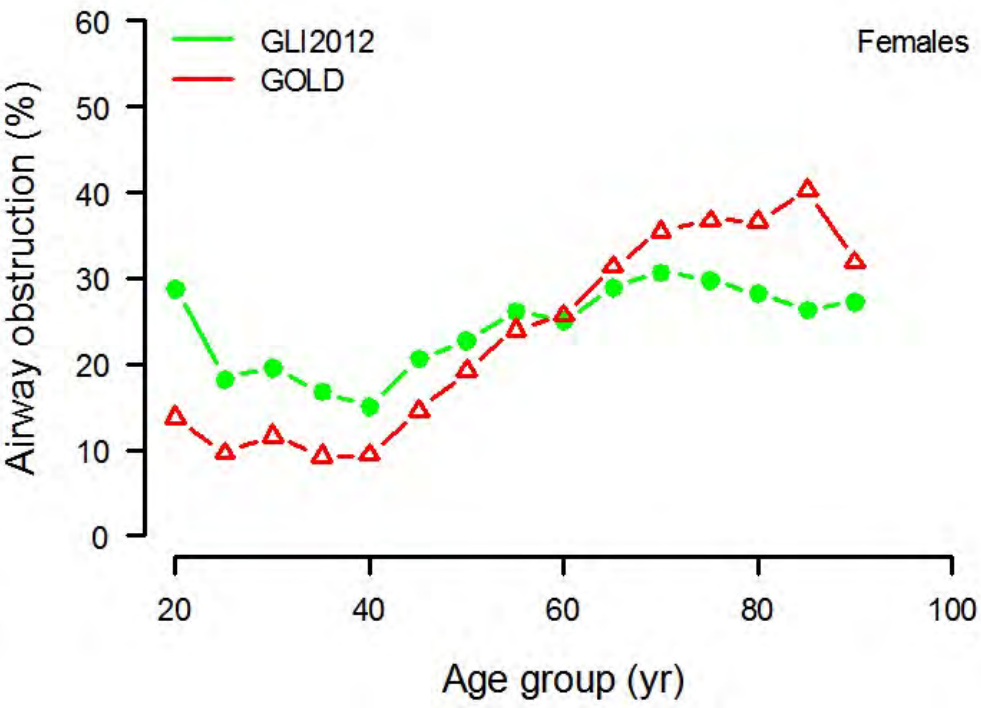



Only 5% of observations should be <LLN in population of healthy subjects.

# COPD (confusion over proper diagnosis) in the zone of maximum uncertainty




GLI2012
GOLD
Males
Airway obstruction (%)
Age group (yr)
0
10
20
30
40
50
60
20
40
60
80
100


GLI2012
GOLD
Females
Airway obstruction (%)
Age group (yr)
0
10
20
30
40
50
60
20
40
60
80
100

CHEST

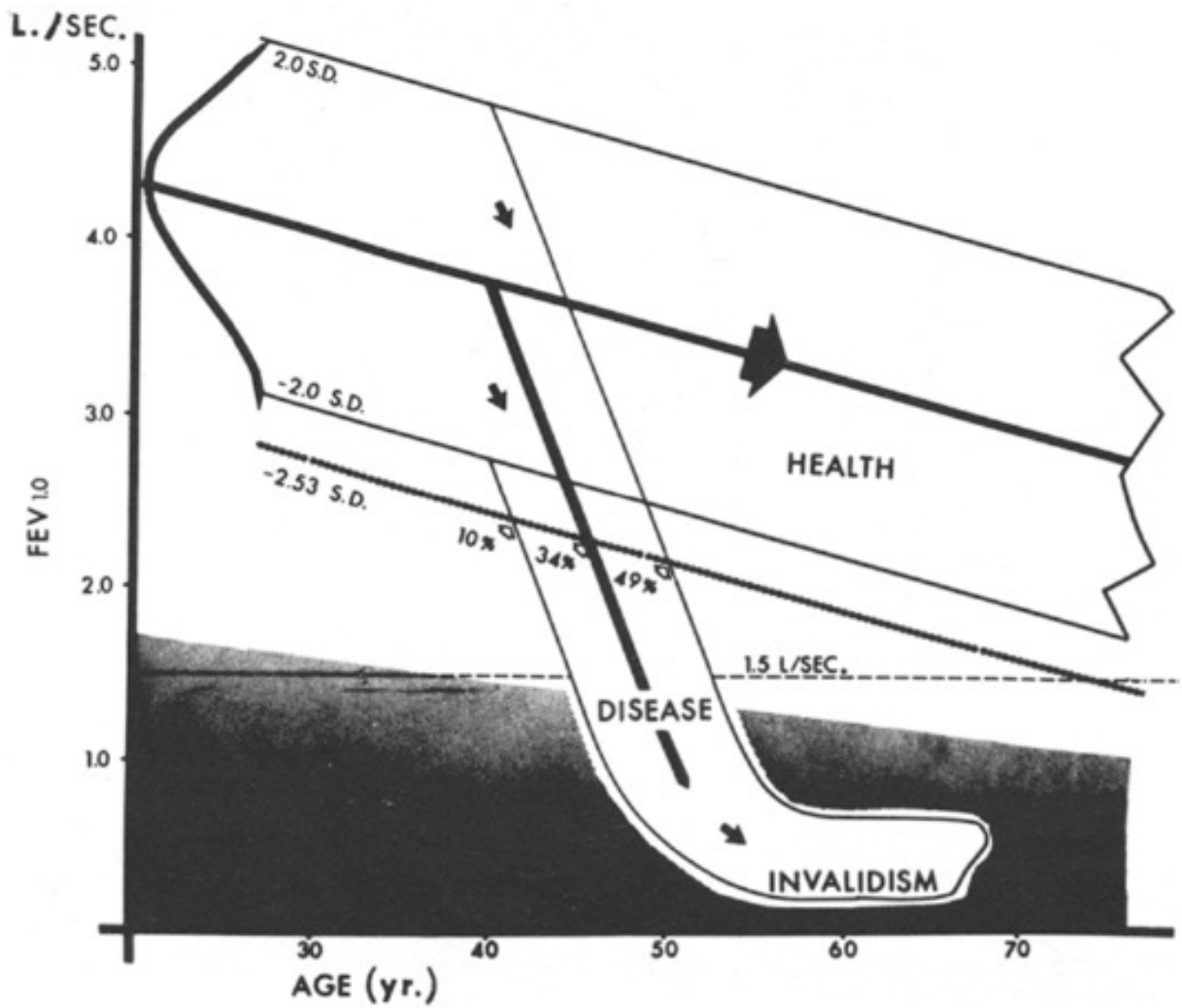
Original Research

PULMONARY PHYSIOLOGY

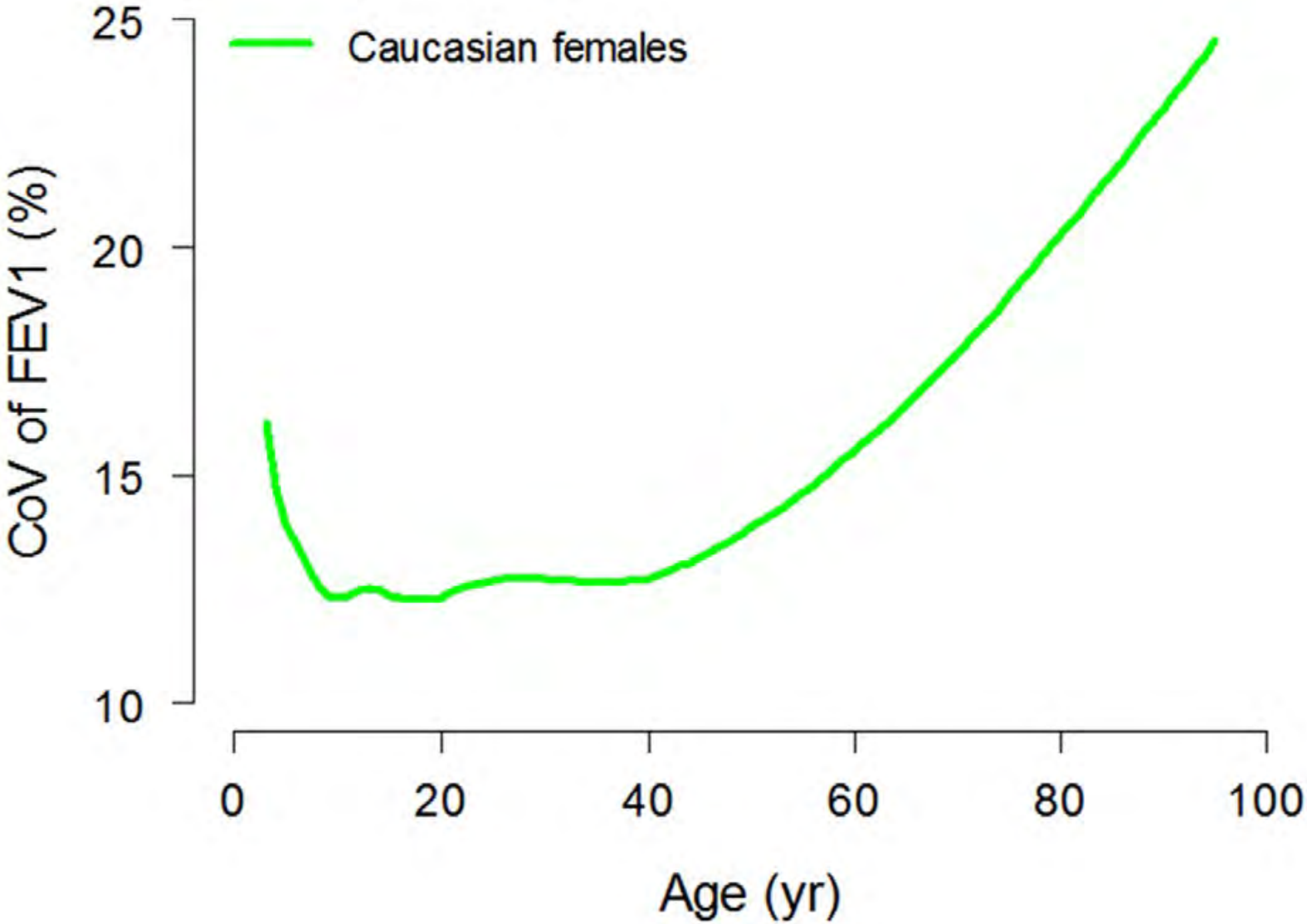
# Interpreting Lung Function Data Using 80% Predicted and Fixed Thresholds Misclassifies More Than 20% of Patients

*Martin R. Miller, MD; Philip H. Quanjer, MD, PhD; Maureen P. Swanney, PhD; Gregg Ruppel, MD; and Paul L. Enright, MD*

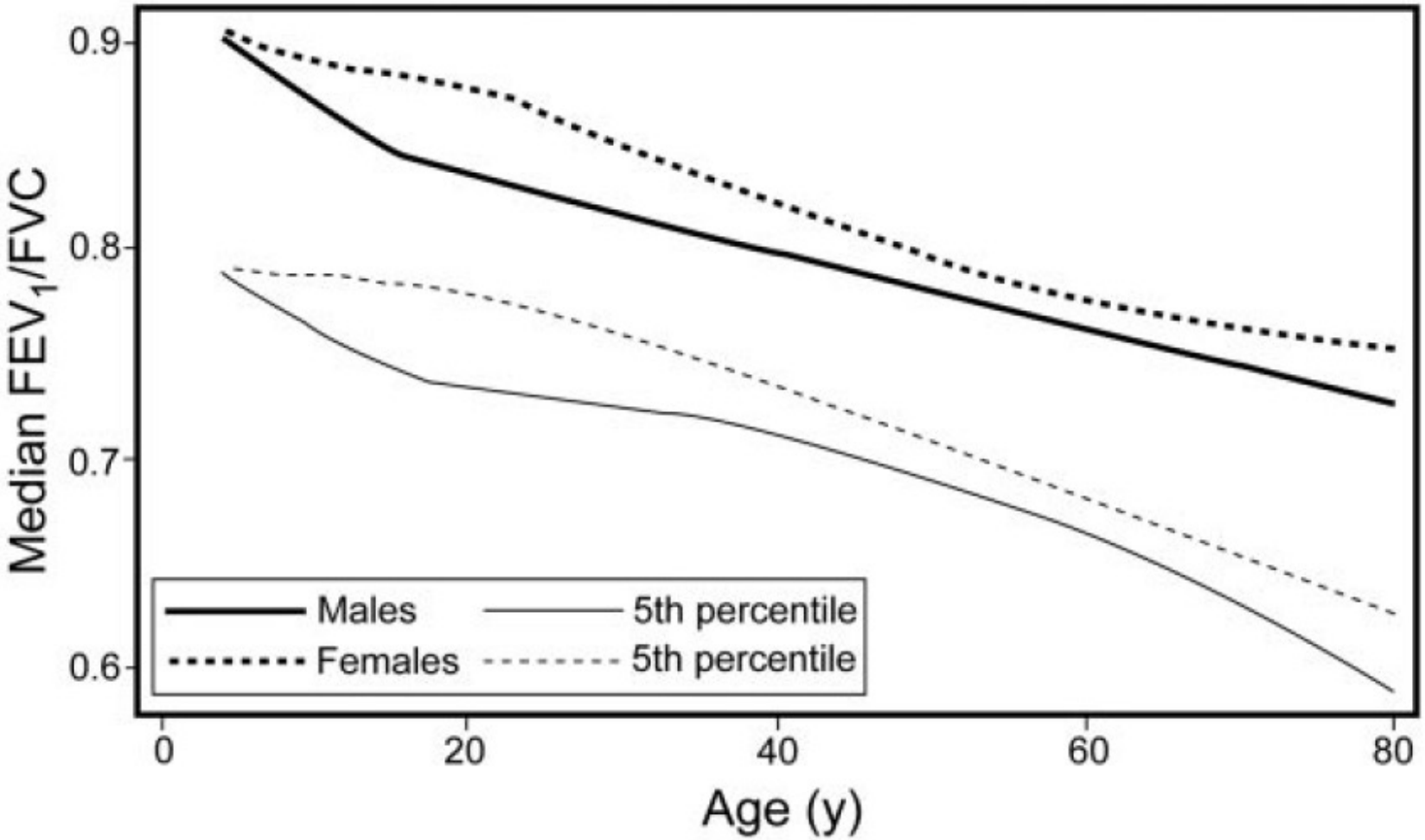
# Are pulmonary function values homoscedastic?

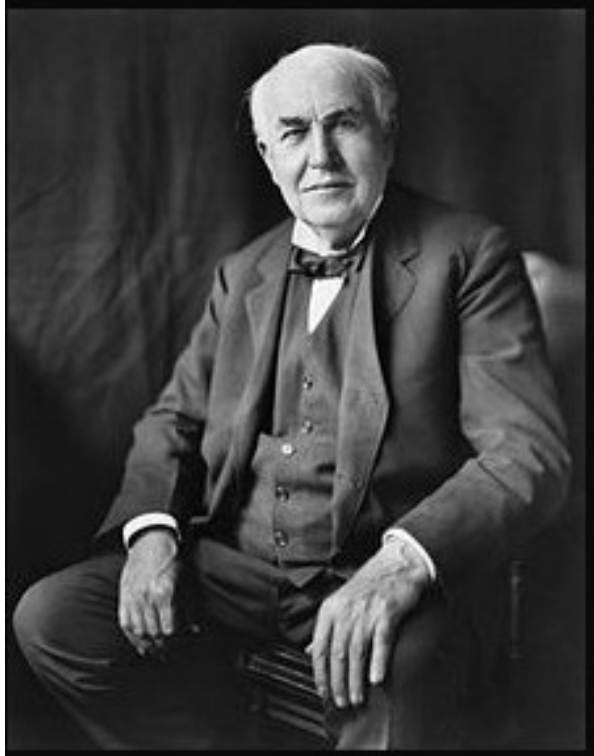


# Are pulmonary function ranges homoscedastic?



# Pulmonary function ranges are not homoscedastic





There's a way to do it better - find it.

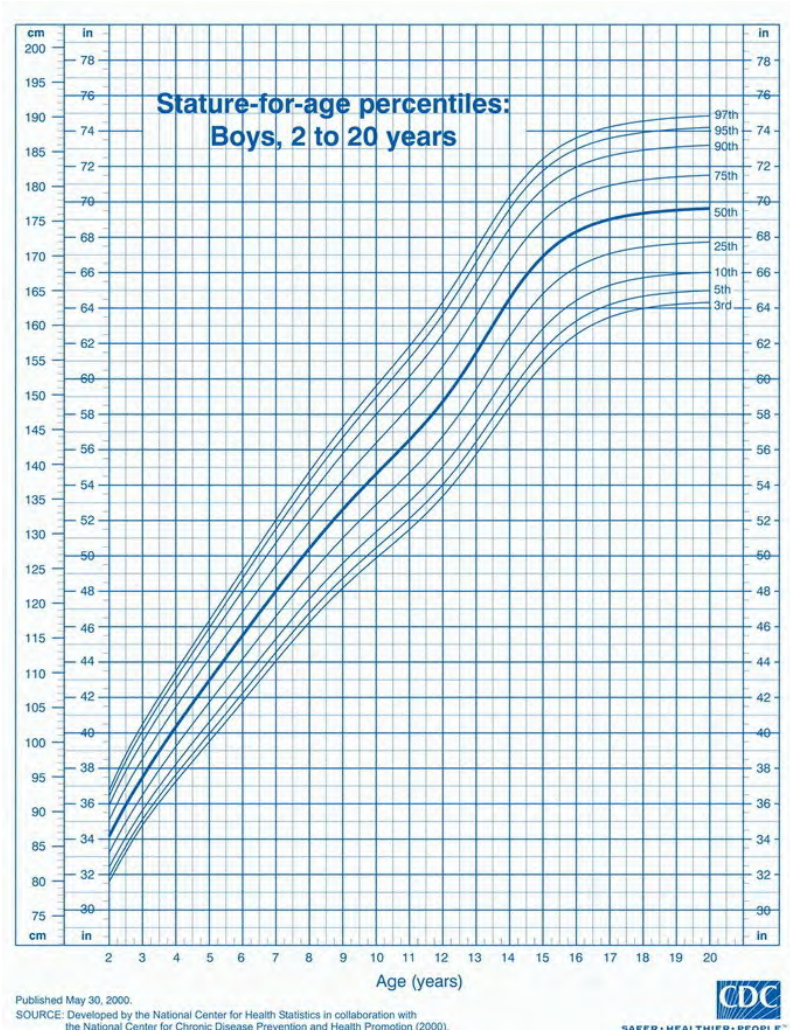
(Thomas Edison)

# Lambda Mu Sigma

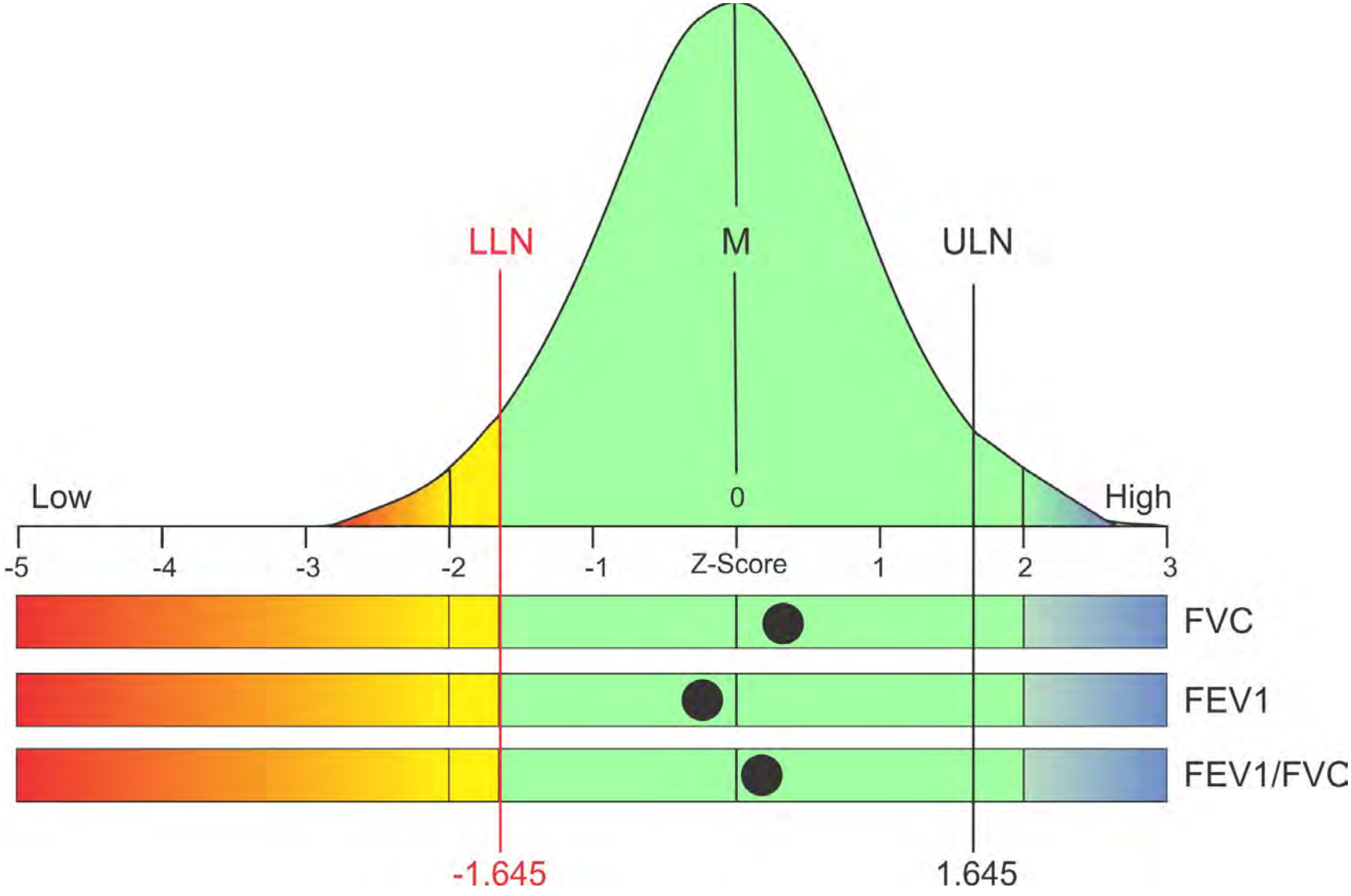
Lambda (skewness)
Mu (median)
Sigma (CV)

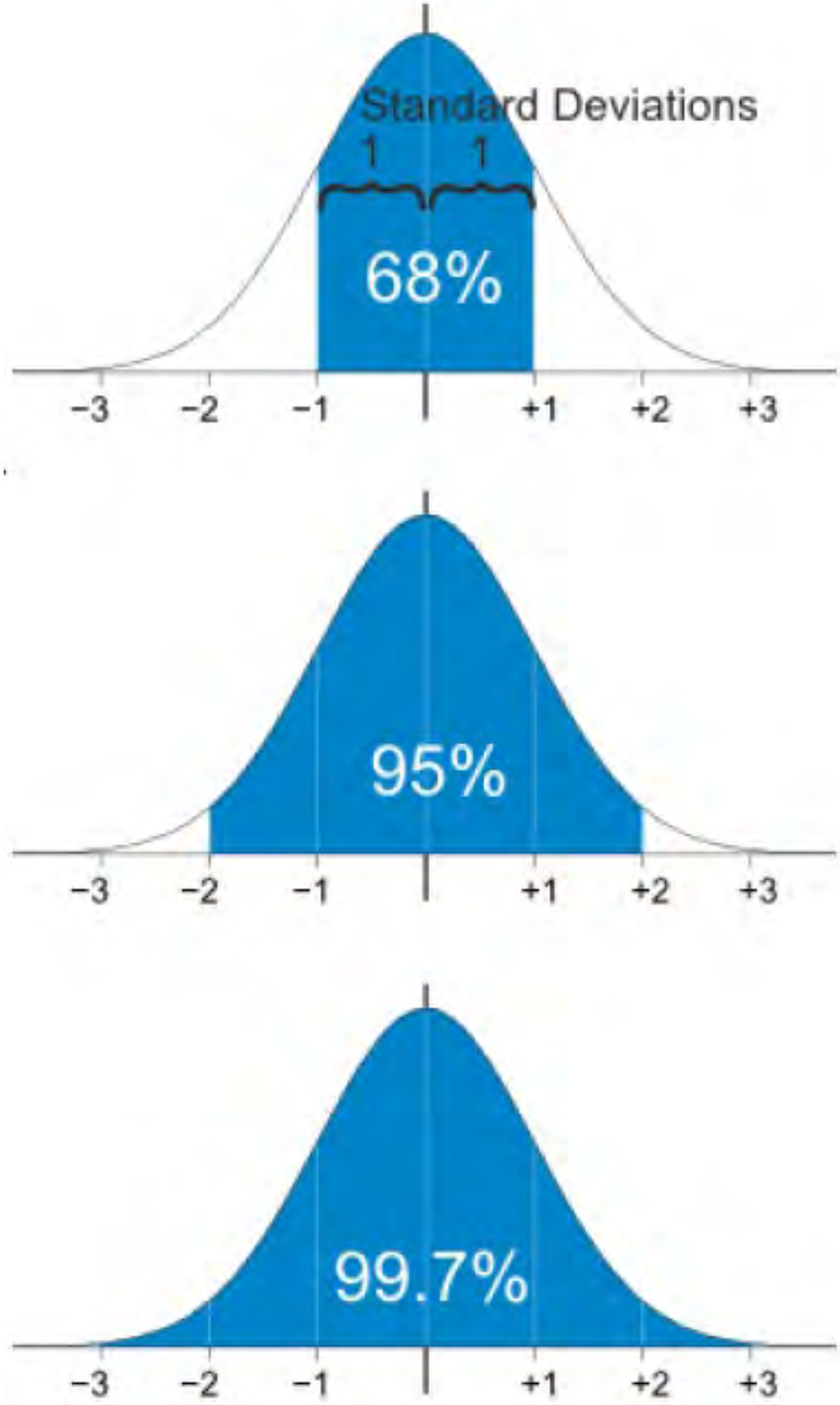
LLN = 5th percentile of z-scores

$$\text{Z score} = \frac{\text{observed} - \text{predicted}}{\text{RSD}}$$



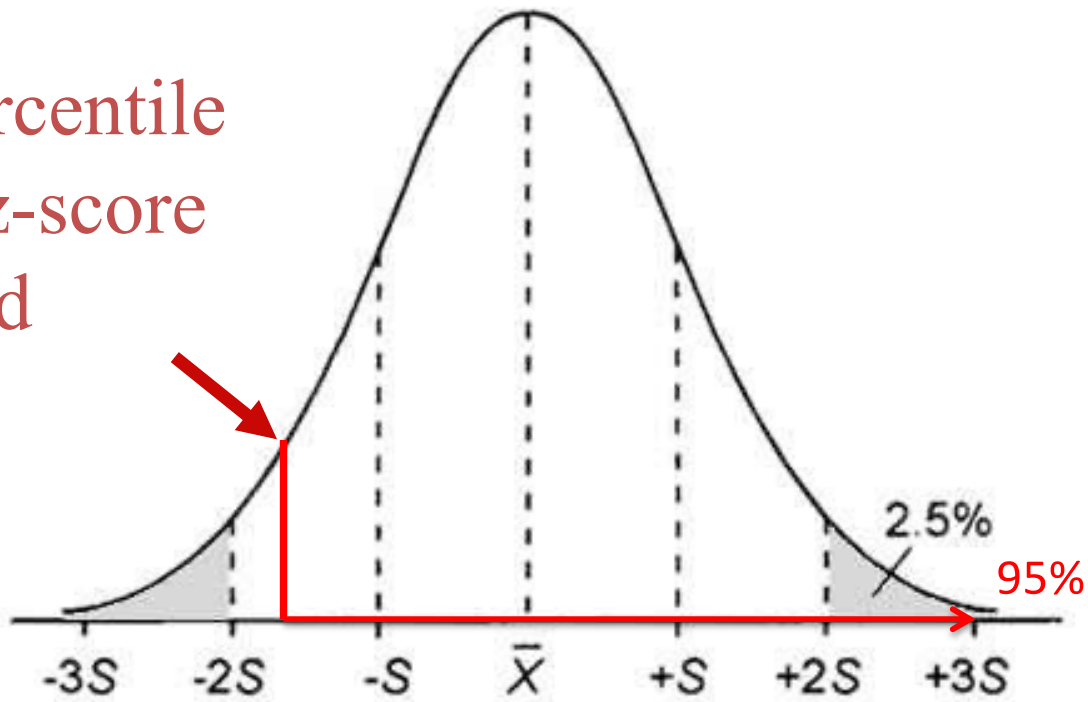
# Z-scores are EZ



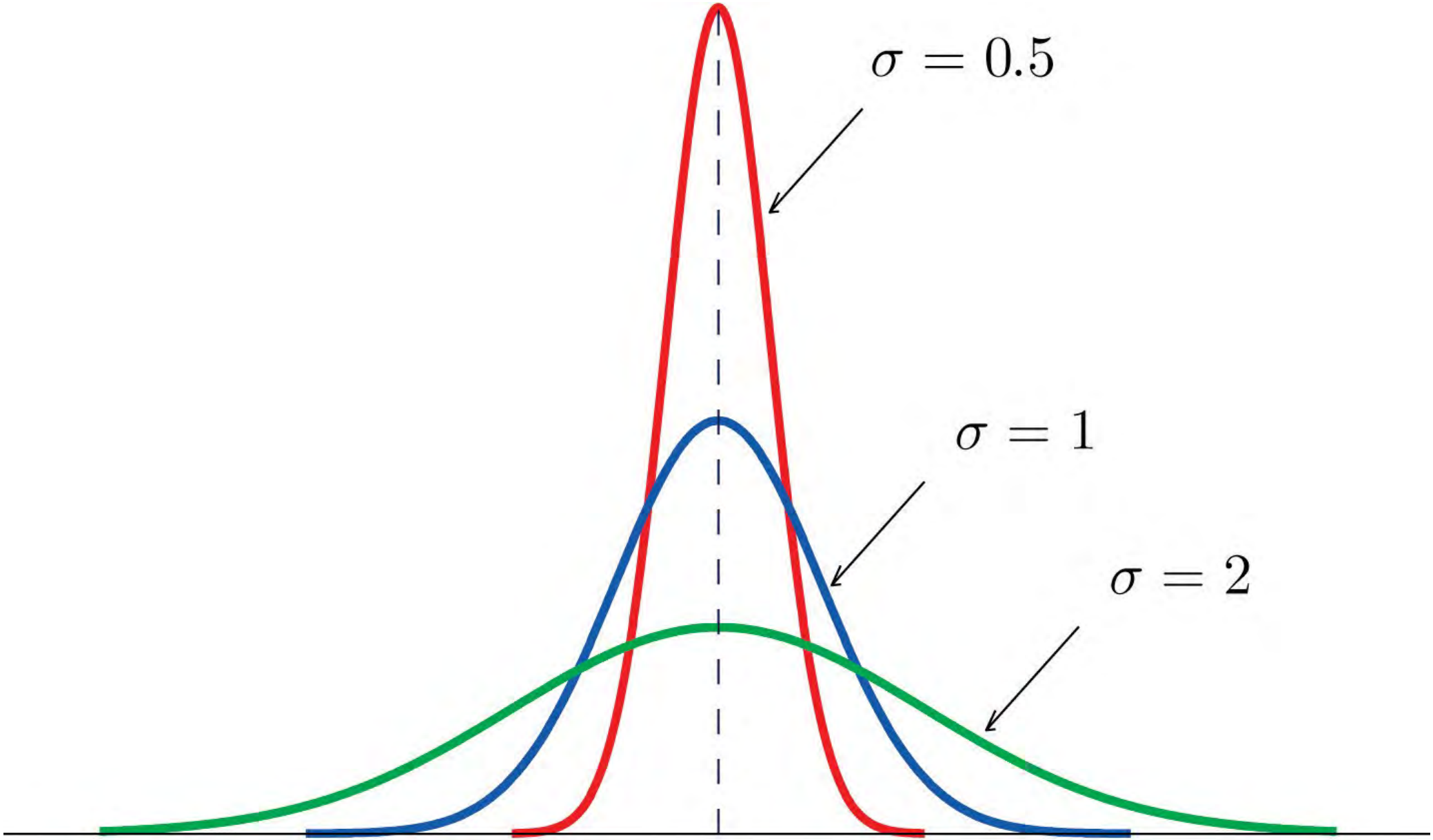

Standard Deviations
1
1
68%
−3
−2
−1
+1
+2
+3
95%
−3
−2
−1
+1
+2
+3
99.7%
−3
−2
−1
+1
+2
+3

# The ATS/ERS Recommends the 5th percentile as the LLN

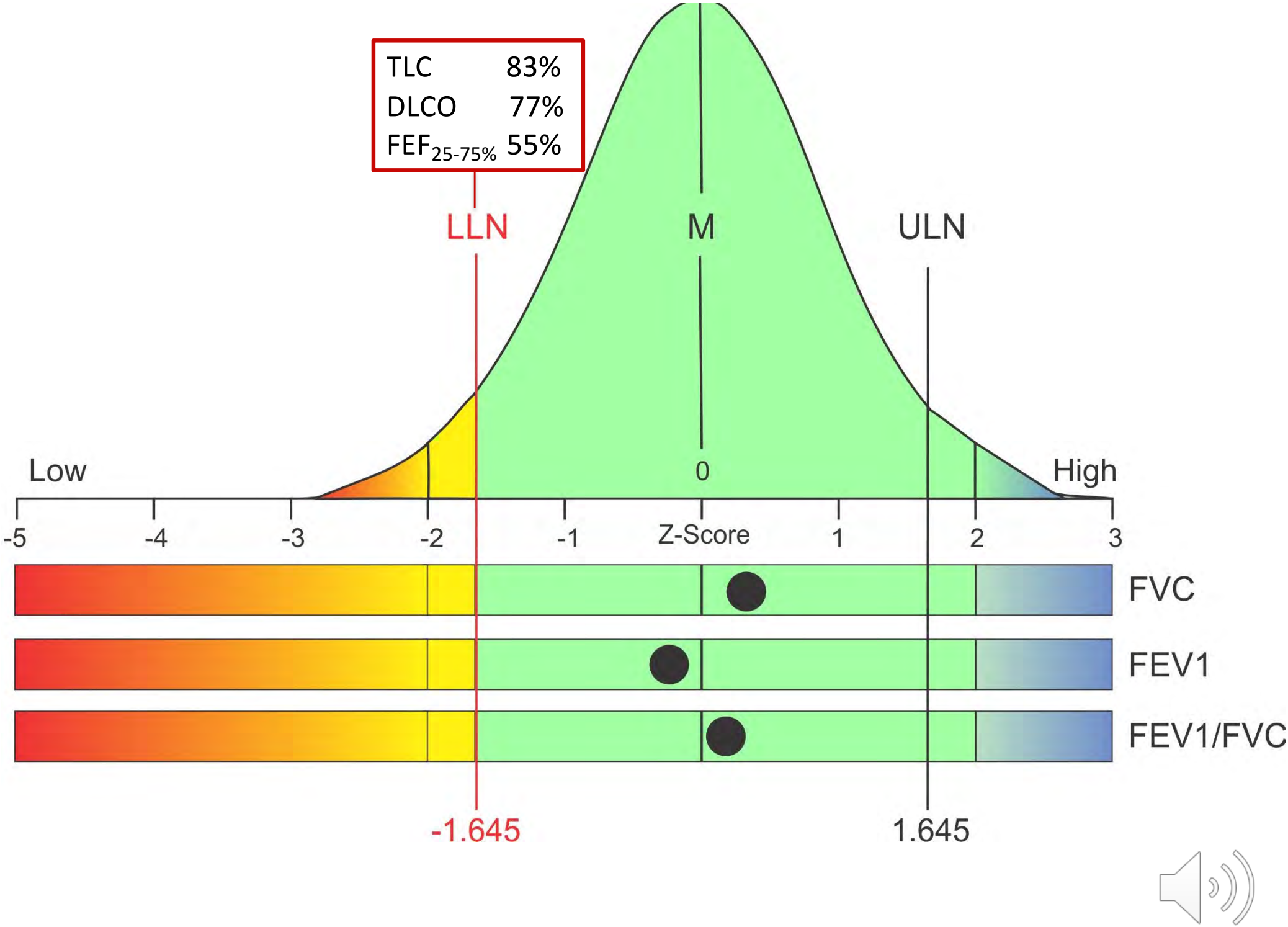
5th percentile
-1.64 z-score
1-tailed



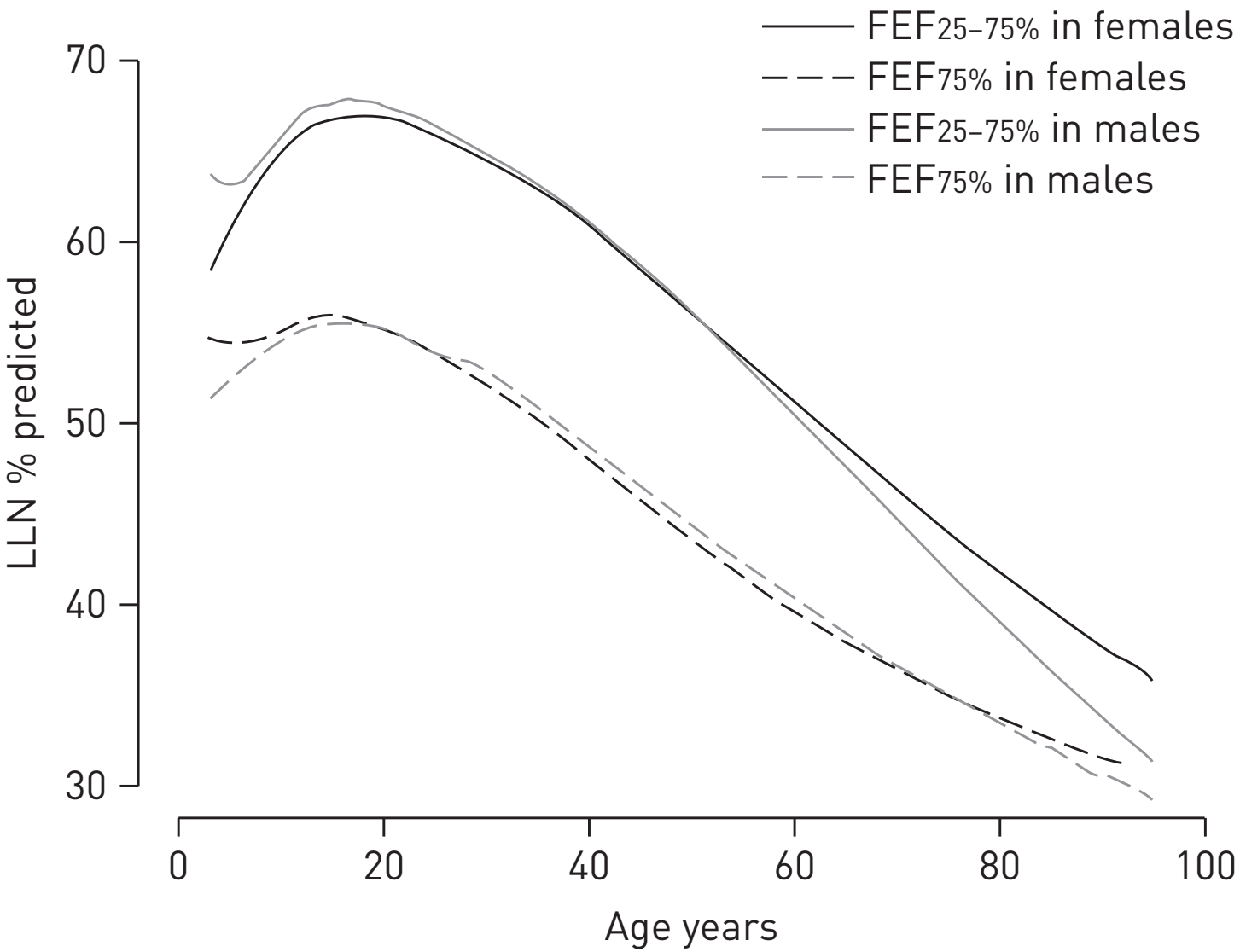

90% of values will fall between z-scores -1.64 to +1.64
5% of healthy subjects will have values below the 5th percentile




PFT values have different distribution

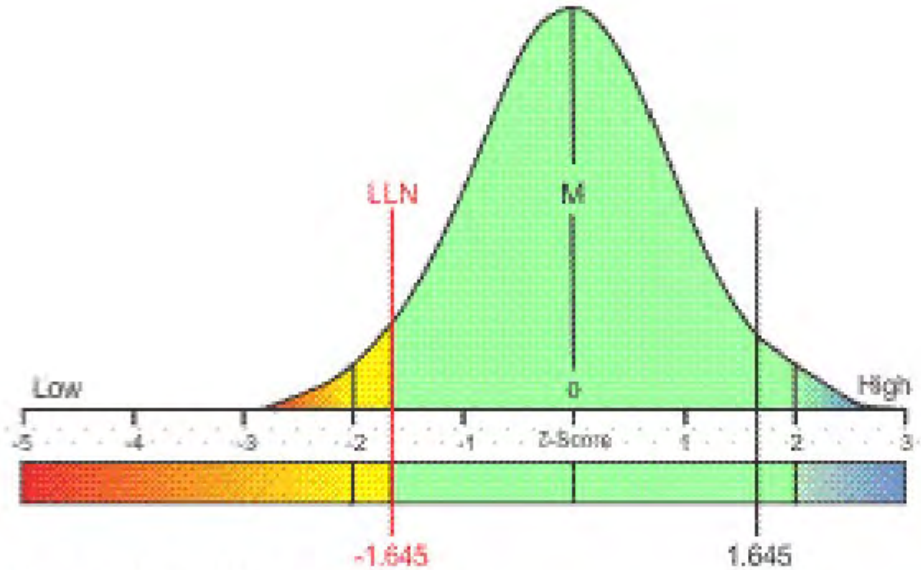

TLC 83%
DLCO 77%
FEF25-75% 55%
LLN
M
ULN
Low
High
0
-5
-4
-3
-2
-1
Z-Score
1
2
3
FVC
FEV1
FEV1/FVC
-1.645
1.645

# Quanjer Eur Respir J 2014;43:1051

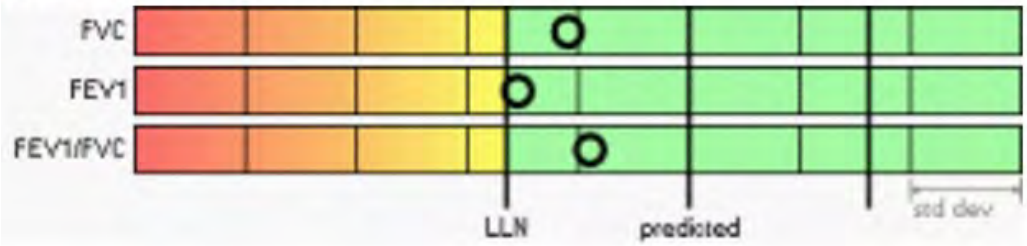


## *Spirometry (BTPS)*

| | | Pre Bronchodilator | | | | | |
|---|---|---|---|---|---|---|---|
| | | Actual | Range | | Predicted | % Pred | Z-score |
| StartTime | | 13:28 | ---- | ---- | ---- | ---- | ---- |
| FVC | L | 1.96 | 1.74 | 3.11 | 2.43 | 81 | -1.11 |
| $FEV_1$ | L | 1.39 | 1.34 | 2.41 | 1.88 | 74 | -1.51 |
| $FEV_1$ / FVC | % | 71 | 64 | 92 | 78 | 91 | -0.86 |
| $FEF_{25-75}$ | L/s | 0.79 | 0.71 | 2.50 | 1.61 | 49 | -1.46 |

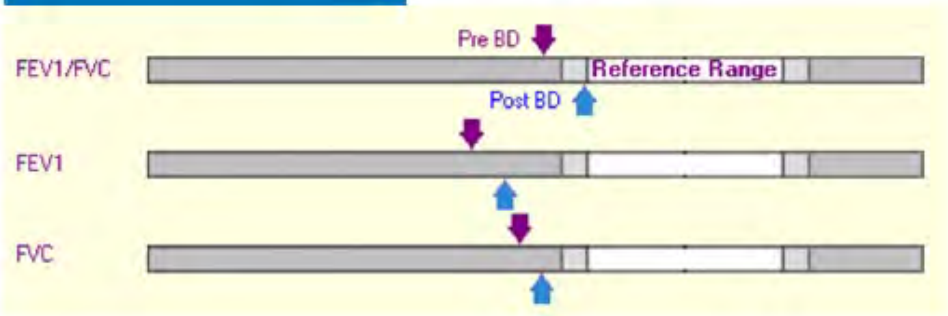



**Pre-Bronchodilator**



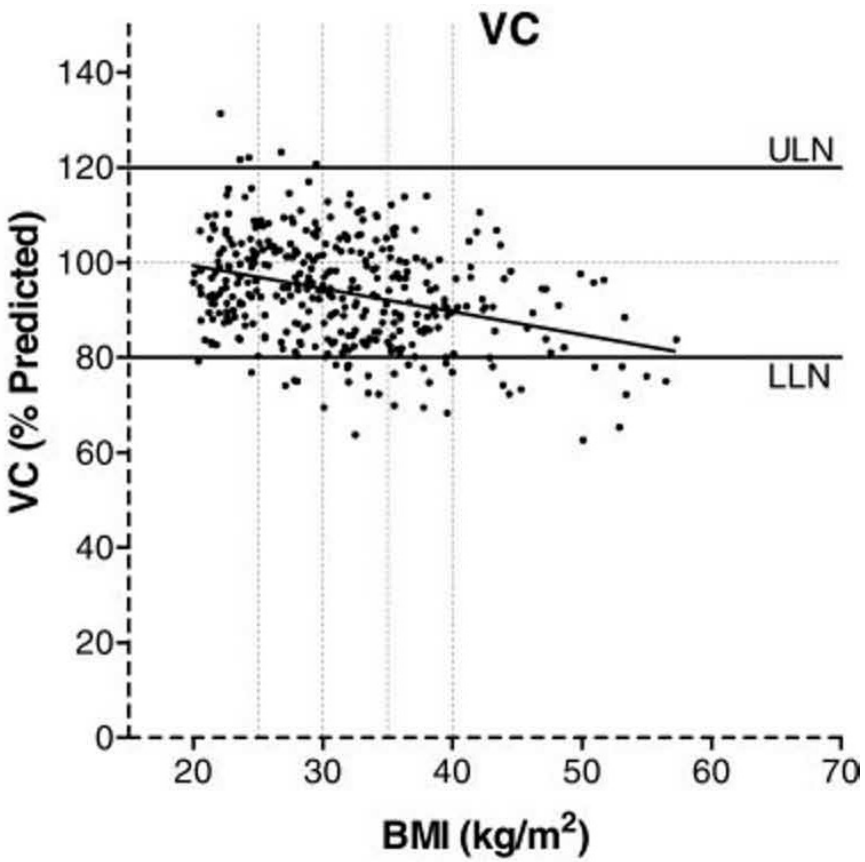
# Take Home Message Regarding The LLN

**LLN**
**z-score**
**-1.64**





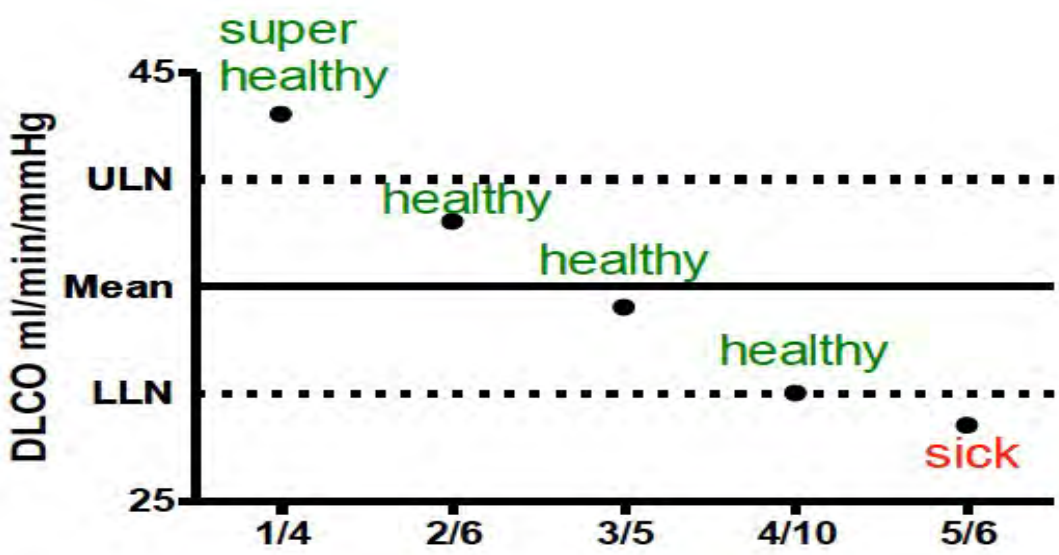
# Longitudinal Changes



# Interpretative strategies for lung function tests

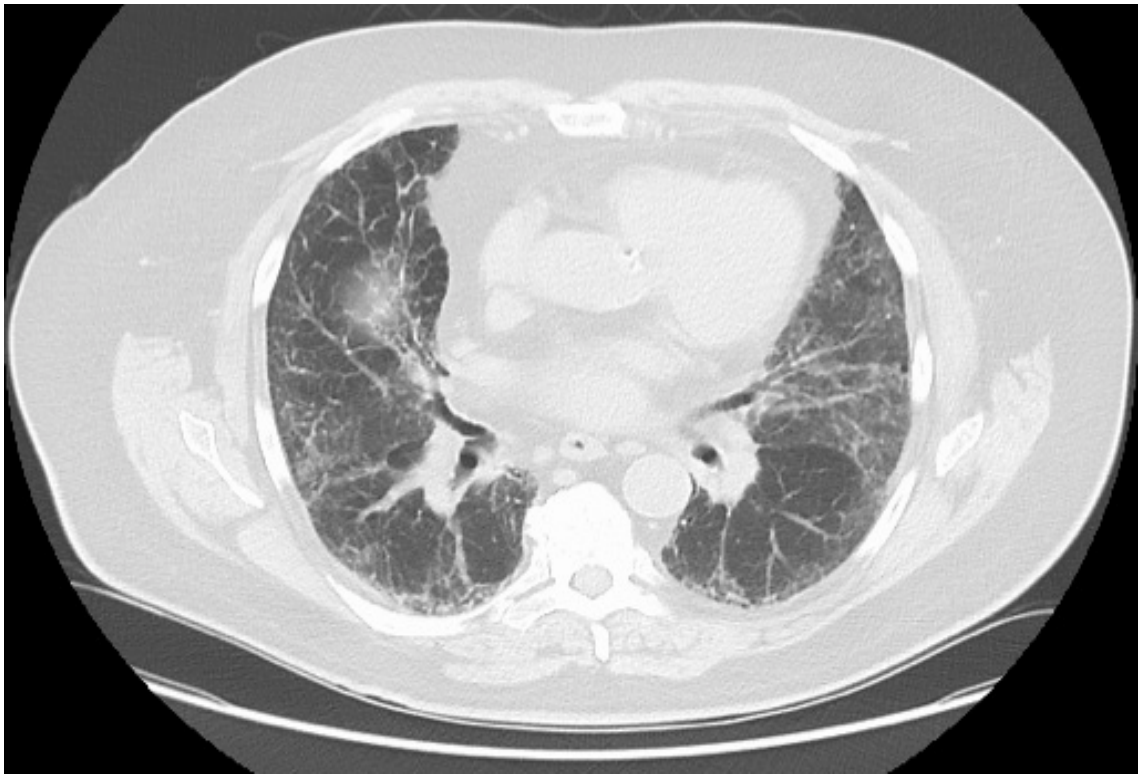
**R. Pellegrino, G. Viegi, V. Brusasco, R.O. Crapo, F. Burgos, R. Casaburi, A. Coates, C.P.M. van der Grinten, P. Gustafsson, J. Hankinson, R. Jensen, D.C. Johnson, N. MacIntyre, R. McKay, M.R. Miller, D. Navajas, O.F. Pedersen and J. Wanger**

| | FVC | $FEV_1$ | $MEF_{25-75\%}$ | $D_{L,CO}$ |
|---|---|---|---|---|
| **Within a day** | | | | |
| Normal subjects | ⩾5 | ⩾5 | ⩾13 | >7% |
| COPD patients | ⩾11 | ⩾13 | ⩾23 | |
| **Week to week** | | | | |
| Normal subjects | ⩾11 | ⩾12 | ⩾21 | >6 units |
| COPD patients | ⩾20 | ⩾20 | ⩾30 | >4 units |
| **Year to year** | ⩾15 | ⩾15 | | >10% |




super healthy = really disease-free lungs
healthy = disease-free lungs
sick = lung disease

# Can you have normal spirometry with ILD?



# Can you have normal spirometry with ILD?

| *Spirometry (BTPS)* | | Pre Bronchodilator | | | | | |
|---|---|---|---|---|---|---|---|
| | | Actual | Range | | Predicted | % Pred | Z-score |
| StartTime | | 09:00 | ---- | ---- | ---- | ---- | ---- |
| FVC | L | 2.42 | 1.78 | 3.56 | 2.65 | 91 | -0.42 |
| $FEV_1$ | L | 1.73 | 1.32 | 2.57 | 1.96 | 88 | -0.60 |
| $FEV_1$ / FVC | % | 71 | 60 | 89 | 76 | 93 | -0.51 |

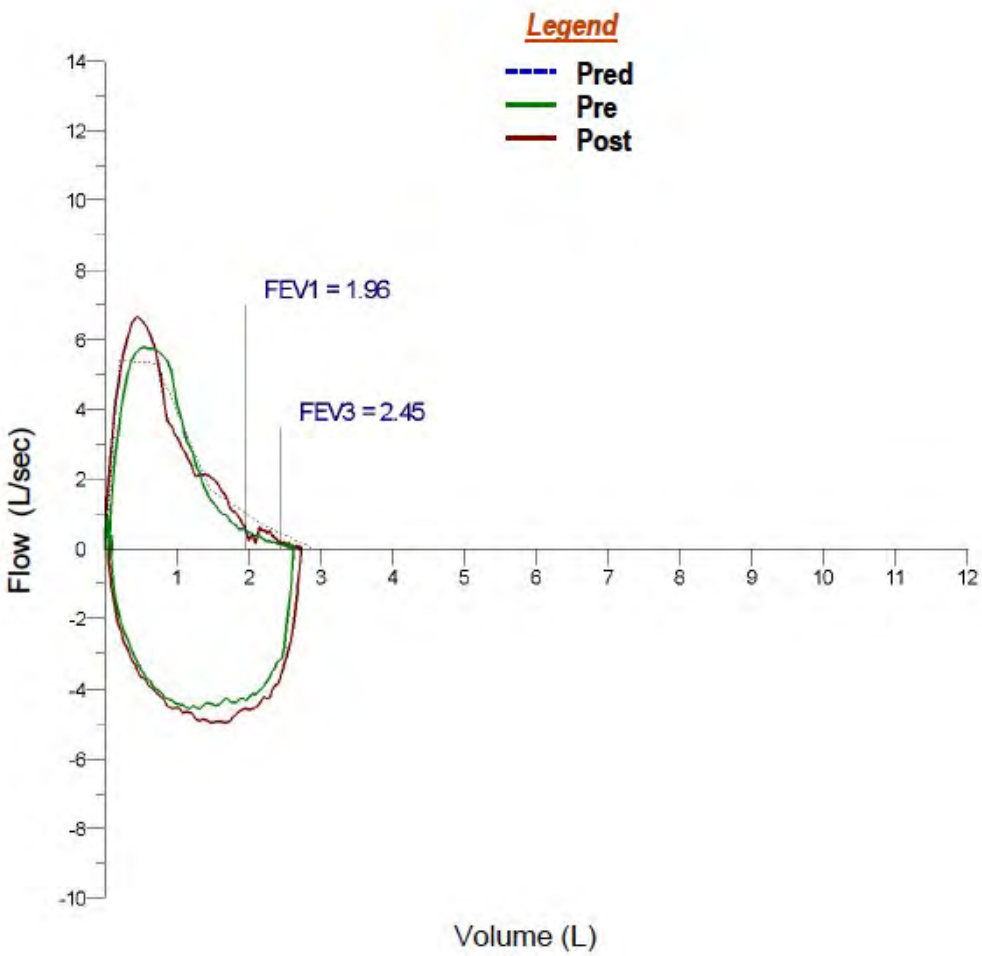
# Can you have normal spirometry with ILD?

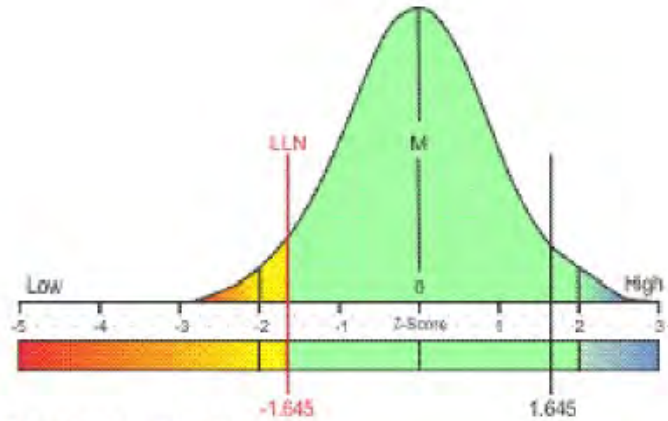
| ***Diffusion*** | | **Pre Bronchodilator** | | | | | |
|---|---|---|---|---|---|---|---|
| | | Actual | Range | | Predicted | % Pred | Z-score |
| DLCO | mL/min/mmHg | 8.72 | 15.35 | 29.06 | 20.84 | 42 | -5.08 |
| DLCO [Hb] | mL/min/mmHg | 8.72 | 15.35 | 29.06 | 20.84 | 42 | -5.08 |
| VA [BTPS] | L | 4.13 | 4.18 | 6.77 | 5.34 | 77 | -1.72 |
| KCO | mL/min/mmHg/L | 2.11 | 2.96 | 5.10 | 3.95 | 53 | -3.35 |

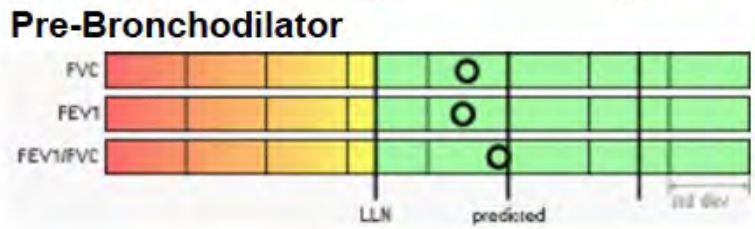
A PFT without DLCO is an *INCOMPLETE* PFT

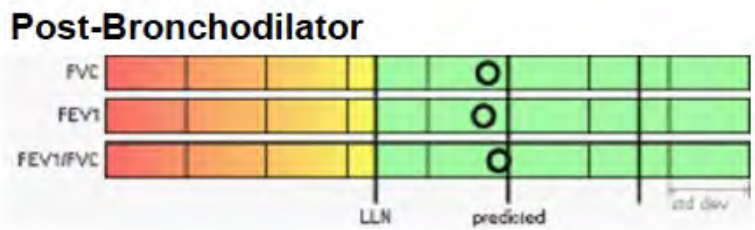
# Emphysema on CT

| *Spirometry (BTPS)* | | Pre Bronchodilator | | | | | |
|---|---|---|---|---|---|---|---|
| | | Actual | Range | | Predicted | % Pred | Z-score |
| StartTime | | 08:18 | ---- | ---- | ---- | ---- | ---- |
| FVC | L | 2.62 | 2.03 | 3.82 | 2.90 | 90 | -0.52 |
| $FEV_1$ | L | 1.96 | 1.53 | 2.81 | 2.18 | 90 | -0.57 |
| $FEV_1$ / FVC | % | 75 | 62 | 89 | 76 | 99 | -0.18 |


Legend
Pred
Pre
Post
FEV1 = 1.96
FEV3 = 2.45
Flow (L/sec)
Volume (L)


LLN
M
Low
High
Z-Score
-1.645
1.645


Pre-Bronchodilator
FVC
FEV1
FEV1/FVC
LLN
predicted


Post-Bronchodilator
FVC
FEV1
FEV1/FVC
LLN
predicted

# Emphysema on CT

| ***Diffusion*** | | Pre Bronchodilator | | | | | |
|---|---|---|---|---|---|---|---|
| | | Actual | Range | | Predicted | % Pred | Z-score |
| DLCO | mL/min/mmHg | 10.45 | 15.93 | 29.54 | 21.41 | 49 | -4.23 |
| DLCO [Hb] | mL/min/mmHg | 10.45 | 15.93 | 29.54 | 21.41 | 49 | -4.23 |
| VA [BTPS] | L | 4.52 | 4.27 | 6.82 | 5.42 | 83 | -1.26 |
| KCO | mL/min/mmHg/L | 2.31 | 3.03 | 5.14 | 4.00 | 58 | -3.06 |

A PFT without DLCO is an *INCOMPLETE* PFT

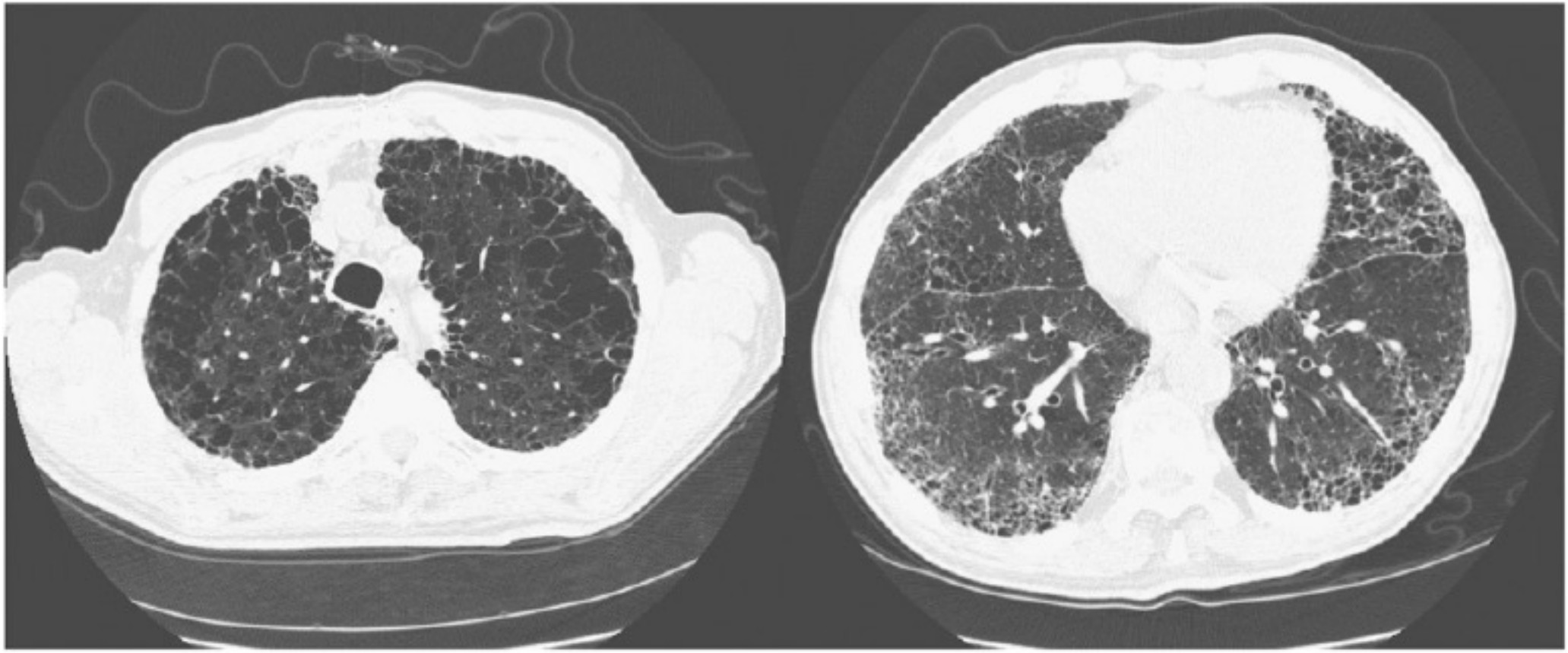
# Can you have normal spirometry with emphysema and pulmonary fibrosis?

CHEST Recent Advances in Chest Medicine

## Combined Pulmonary Fibrosis and Emphysema Syndrome

### A Review

*Matthew D. Jankowich, MD, FCCP; and Sharon I. S. Rounds, MD*



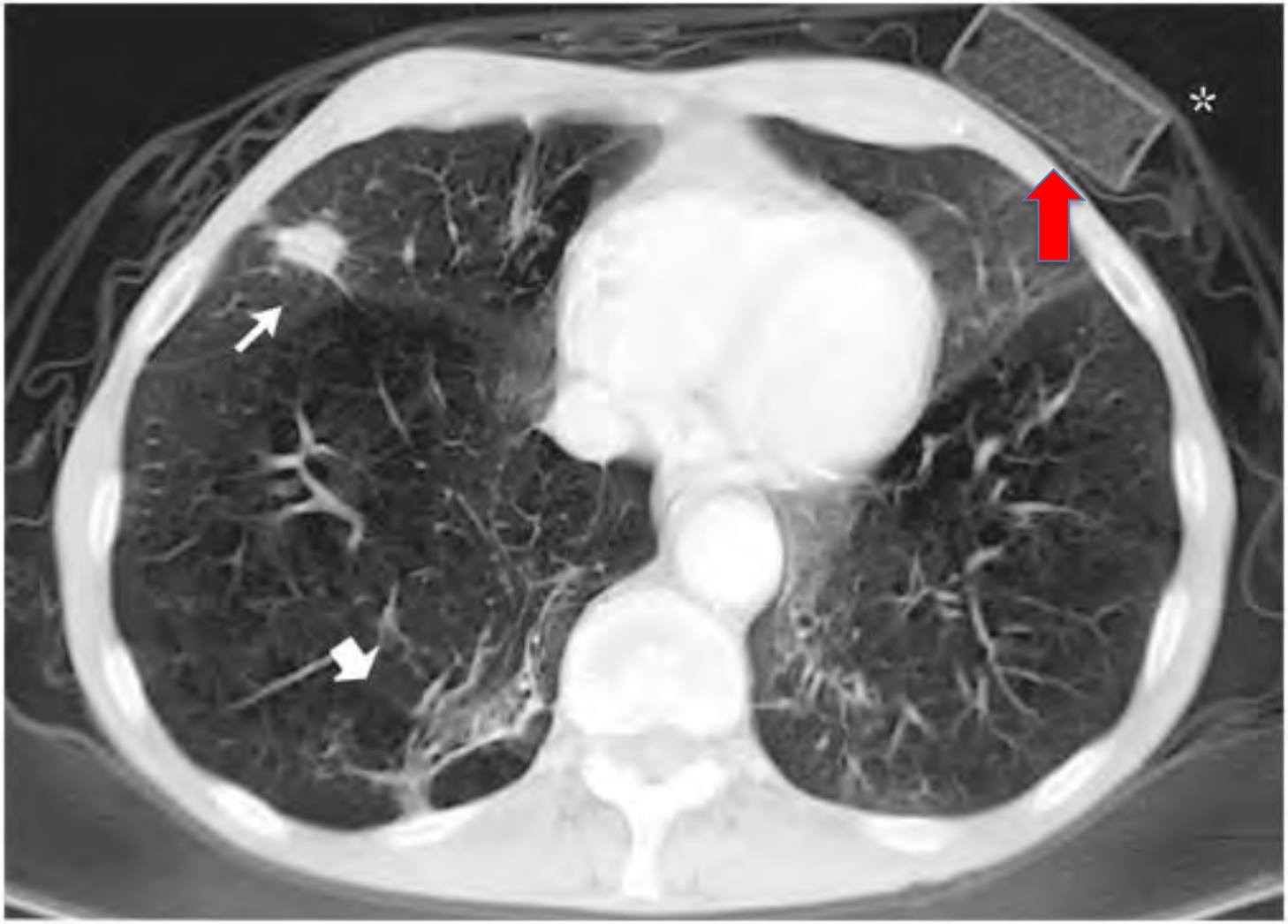
FVC 107%
FEV1 108%
DLCO 36%

A PFT without DLCO is an *INCOMPLETE* PFT

IMAGES IN CLINICAL MEDICINE

# Radiographic Evidence Linking Tobacco Use and Lung Cancer

David Michael McMullan, M.D., and Gordon Alan Cohen, M.D., Ph.D.

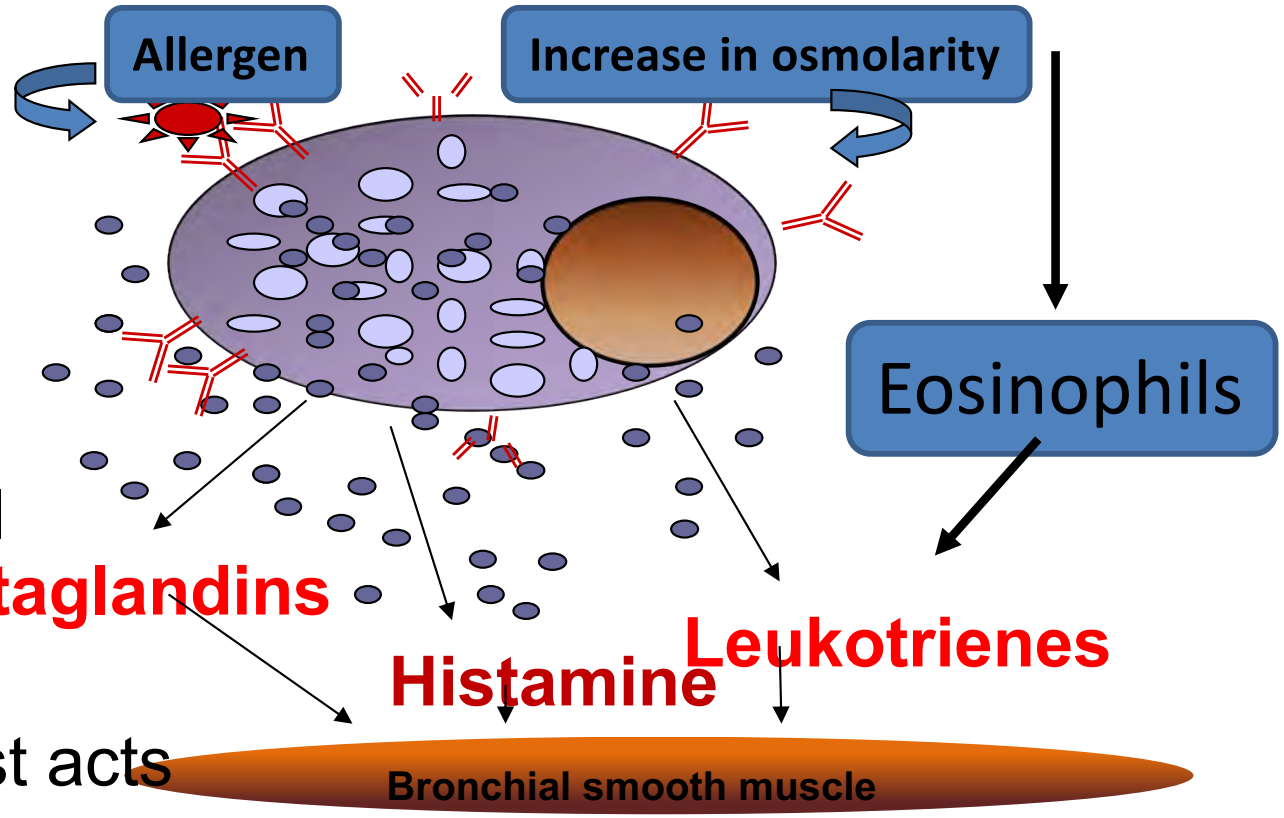


# “Bronchial challenge tests can determine whether or not a patient has asthma”

# Direct vs. Indirect Challenge Tests

***INDIRECT***
means the stimulus comes from cells
e.g. the mast cell

***DIRECT***
means the agonist acts on the smooth muscle

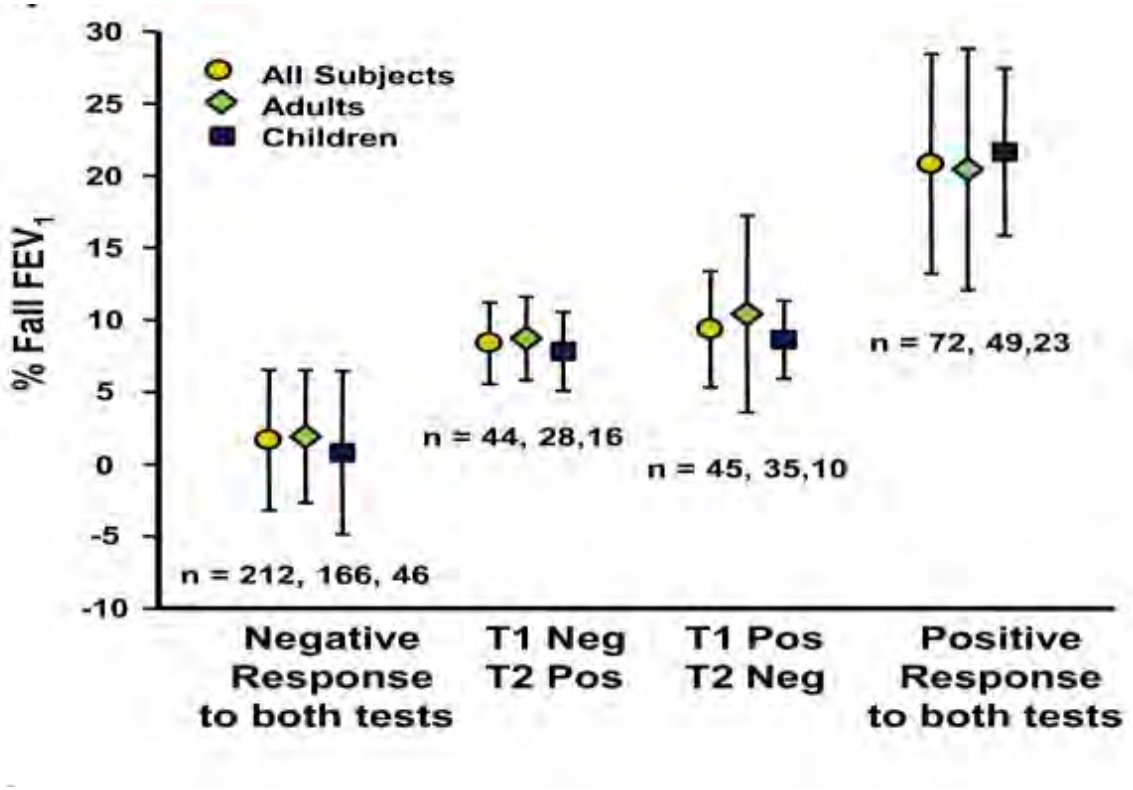



Courtesy of Ken Rundell PhD

# Exercise

# Is Exercise Reliable?

Anderson SD Respir Res. 2010;11:120.



# Field Testing vs. the PFT Lab

Rundell Med Sci Sport Exerc. 2000;32:309

Elite cold weather Olympic athletes with a + EIB test performed in the field

Exercise challenge test in a laboratory setting
( T 21° C, RH ~55%)

Treadmill at "race pace"

78% had a negative test

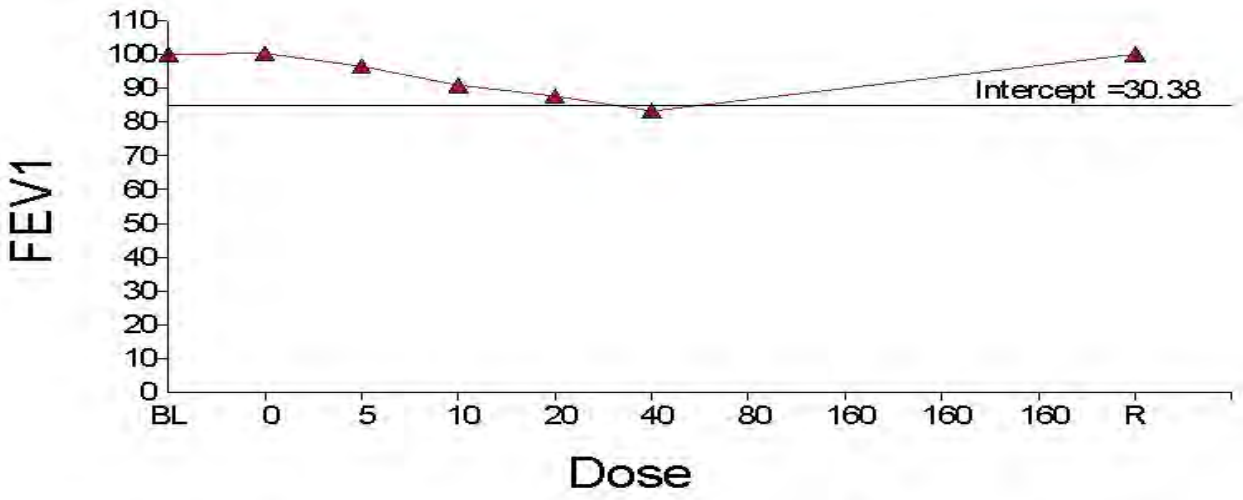
# Exercise Challenge

# Mannitol Challenge

# Mannitol Challenge

# Mannitol Challenge

20-year-old military recruit



Anderson SD. Respir Res 2009;10:4.

115 children with clinical asthma diagnosis

| | | |
|---|---|---|
| Mannitol | sensitivity | 63.2 |
| | specificity | 81.4 |


## Pre-Test Screening

SABA (6 hrs): _____

BID LABA (36 hrs): _____

QDay LABA (48 hrs): _____

Ipratropium (12 hrs): _____

LAMA (1 week): _____

Long-term ICS (4 weeks*): _____

Long-term Montelukast (4 weeks*): _____

*When the goal is to test the patient without the influence of anti-inflammatories

Recent Chest Infection? (4 weeks): _____

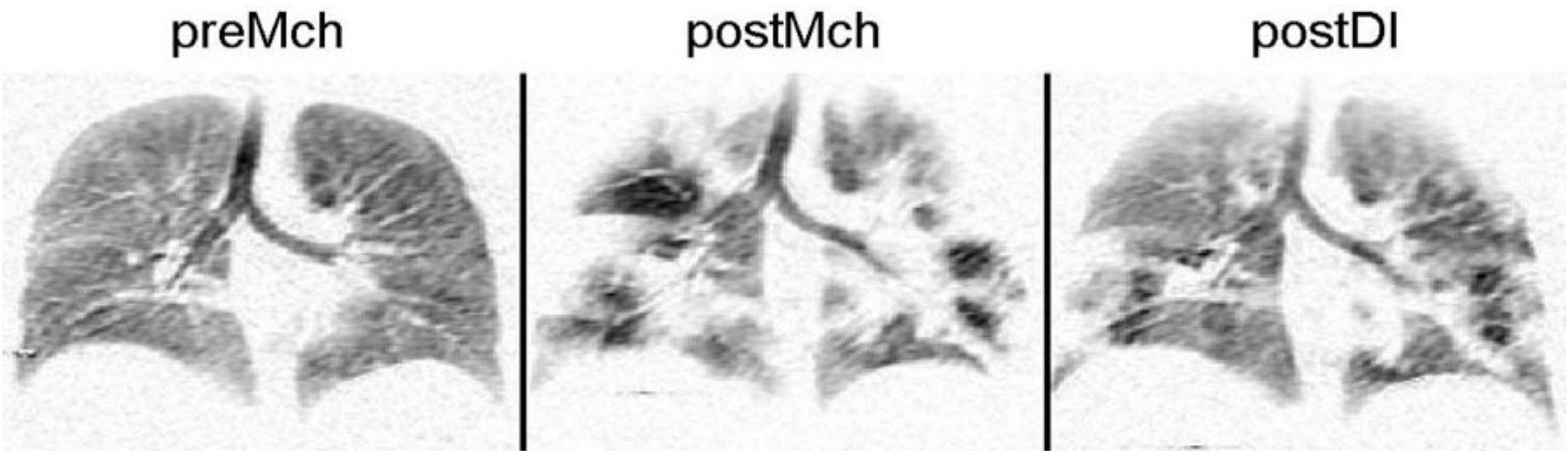
| Protocol Step | Breaths (Dose) | $FEV_1$ | % Change |
|---|---|---|---|
| Baseline | n/a | | (% predicted in this row) |
| 0.0625 mg/ml | 6 (2.6 ug) | | |
| .25 mg/ml | 6 (10.6 ug) | | |
| 1 mg/ml | 6 (42.5 ug) | | |
| 4 mg/ml | 6 (170 ug) | | |
| 16 mg/ml | 6 (680 ug) | | |
| Bronchodilator | n/a | | |

Anderson SD. Respir Res 2009;10:4.

115 children with clinical asthma diagnosis

| | | |
|---|---|---|
| MCT $PC_{20}$ 16 mg/ml | sensitivity | 66.2 |
| | specificity | 62.9 |

# Methacholine and DI



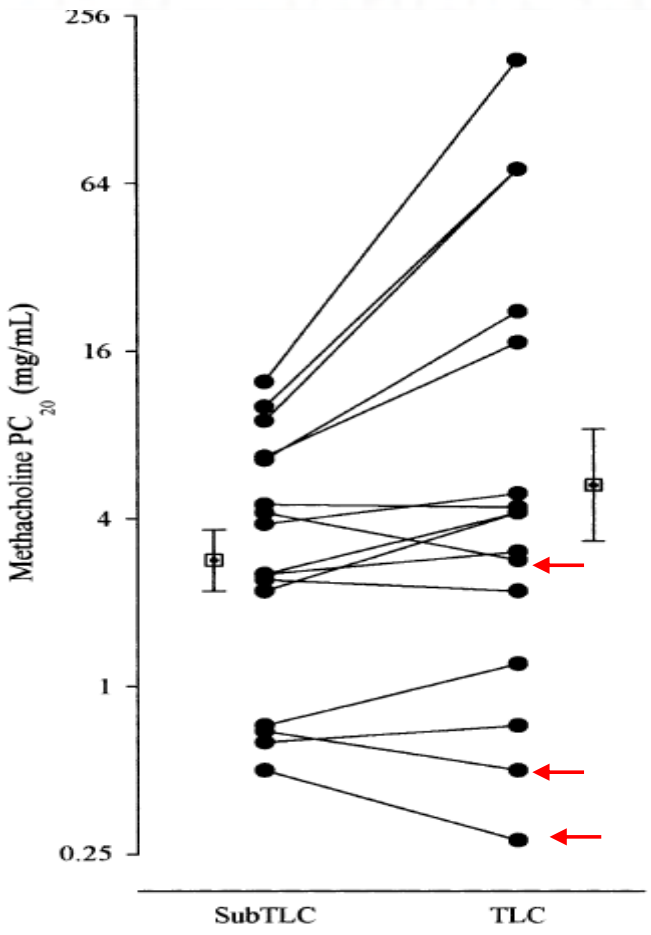
# Dosimeter methacholine challenge: Comparison of maximal versus submaximal inhalations

(J Allergy Clin Immunol 2004;114:517–9.)

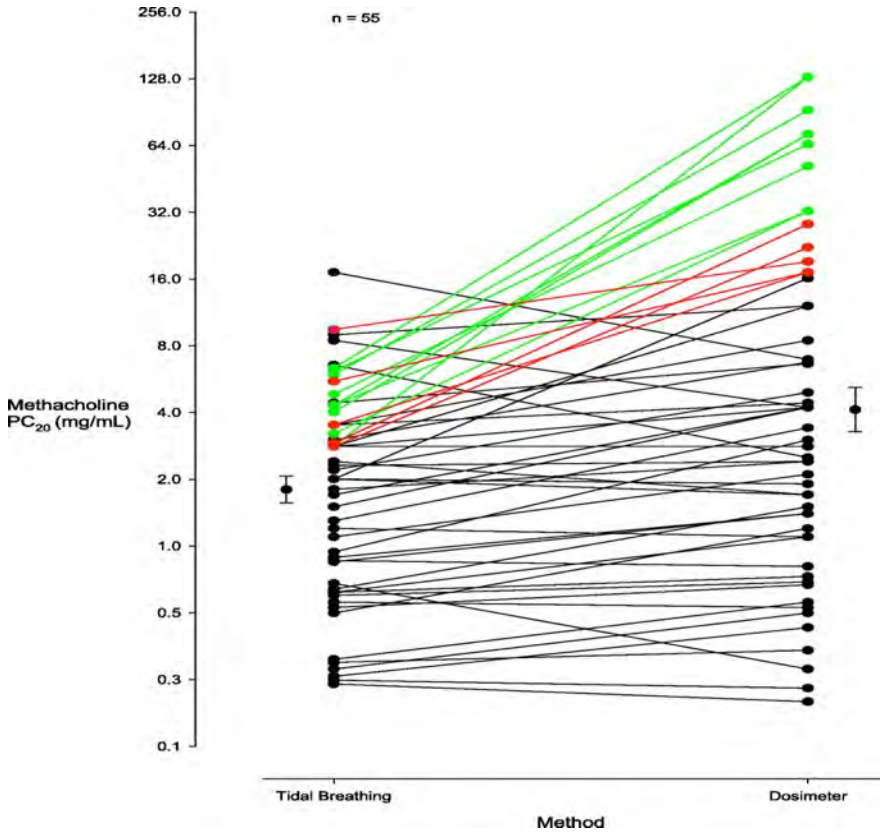
| | subTLC | Full TLC | p |
|---|---|---|---|
| PC20 | 2.8 | 5.2 | 0.02 |

5 of 16 had a negative test with full TLC

3 had a paradoxical response



Cockcroft, Davis. J Clin Allergy Immunol 2006;117:1244




- 50% with PC20 > 2 had negative test with dosimeter
- 25% of all subjects had a negative test with dosimeter
- 2 had a >120 mg increase in PC20

# A positive methacholine challenge based on specific airway conductance: A case report

Jeffrey Haynes RRT RPFT

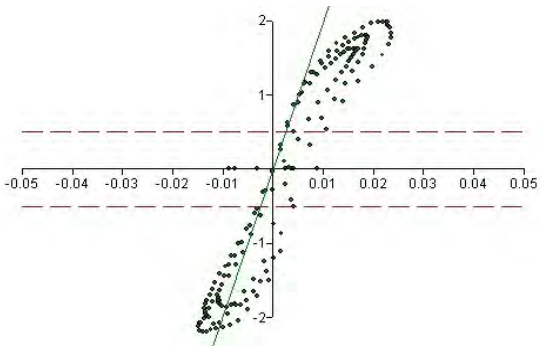
## Spirometry (BTPS)

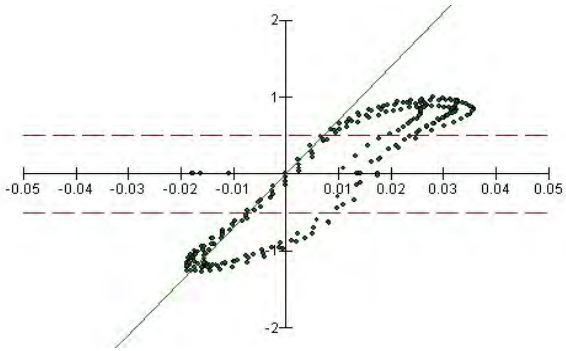
### Pre Bronchodilator

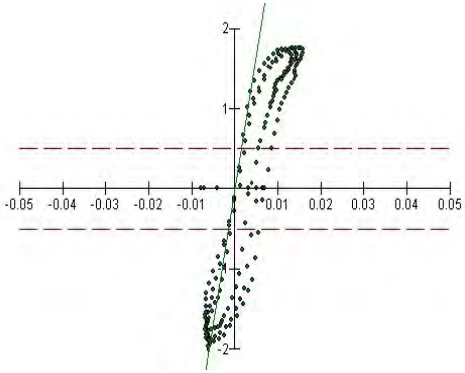
| | | Actual | CI Range | | Predicted | % Pred | Z-score |
|---|---|---|---|---|---|---|---|
| StartTime | | 08:26 | ---- | ---- | ---- | ---- | ---- |
| FVC | L | 3.87 | 4.10 | 6.08 | 5.09 | 76 | -2.01 |
| $FEV_1$ | L | 2.93 | 3.36 | 5.06 | 4.21 | 70 | -2.52 |
| $FEV_1$ / FVC | % | 76 | 72 | 94 | 83 | 92 | -1.17 |
| $FEF_{25-75}$ | L/s | 2.10 | 2.69 | 5.99 | 4.34 | 48 | -2.00 |
| PEFR | L/s | 10.39 | 7.64 | ---- | 9.83 | 106 | ---- |
| PIFR | L/s | 6.13 | ---- | ---- | 6.55 | 94 | ---- |

### Challenge Summary

| | | Predicted | Baseline | | Maximum Response | | Post Bronchodilator | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Units | Mean | Actual | % Pred | Actual | % BL | Actual | % BL |
| $FEV_1$ | L | 4.21 | 2.93 | 70 | 2.70 | 92 | 3.14 | 107 |







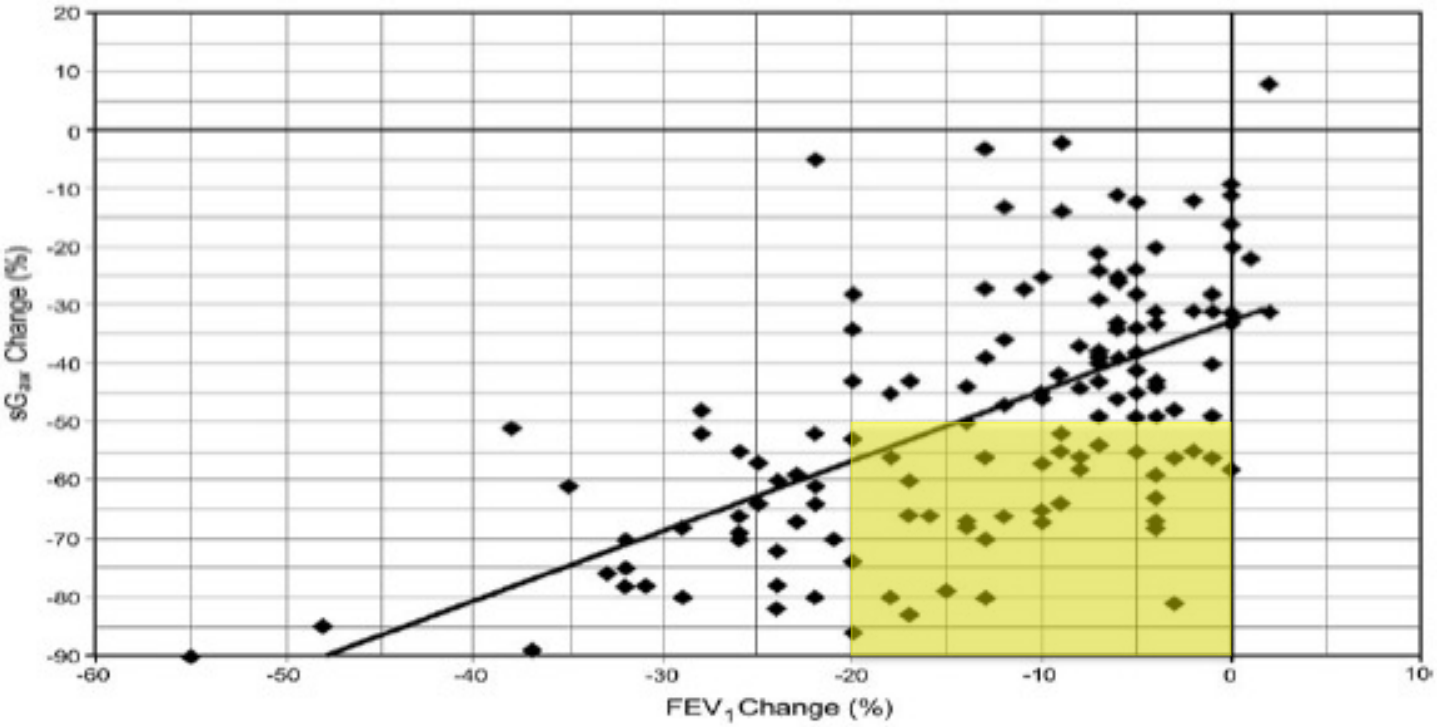
# A positive methacholine challenge based on specific airway conductance: A case report

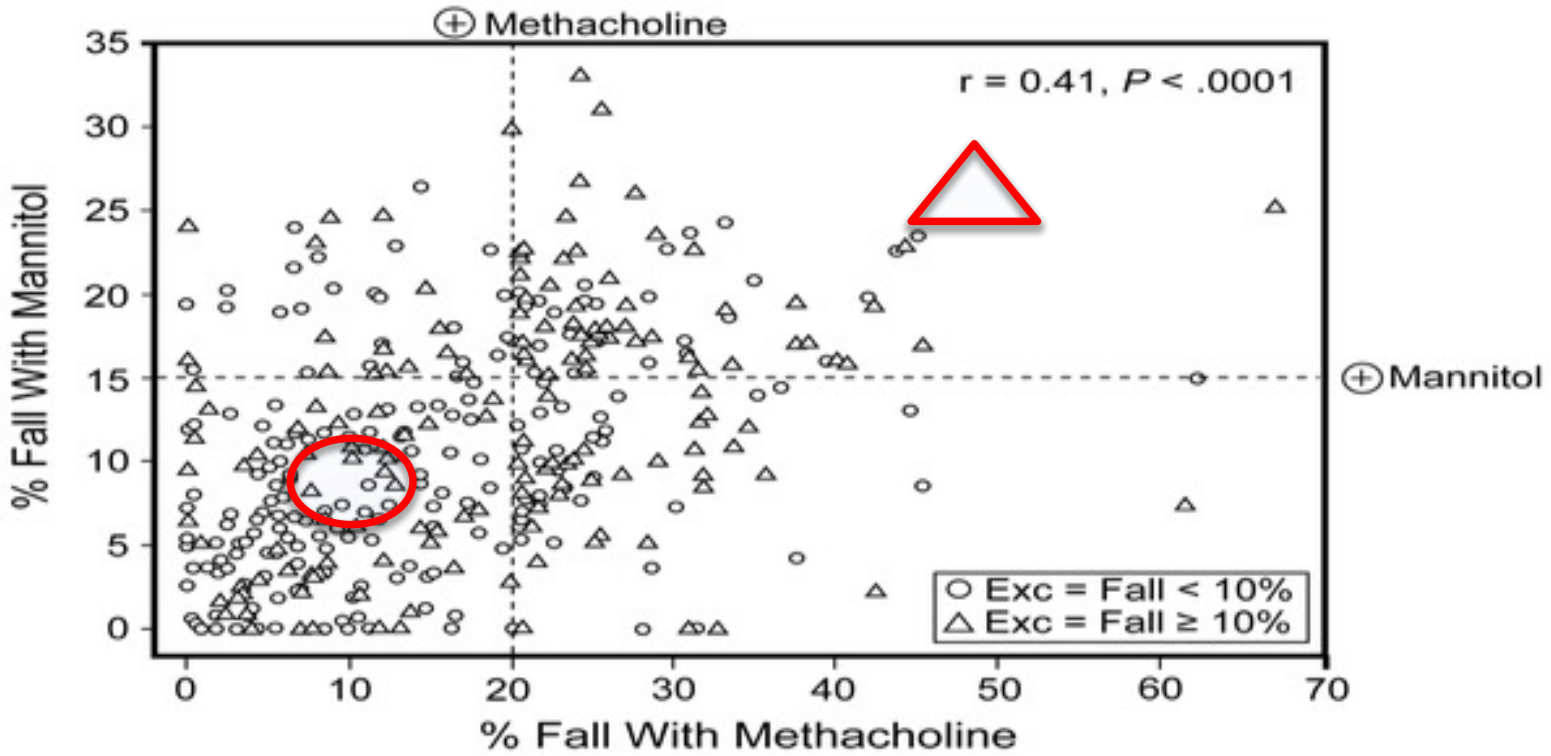
Jeffrey Haynes RRT RPFT

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Raw | 1.63 | Raw | 4.35 | +167% | Raw | 1.22 | -25% |
| sGaw | .26 | sGaw | 0.07 | -73% | sGaw | .33 | +27% |
| $FEV_1$ | 2.93 | $FEV_1$ | 2.70 | -8% | $FEV_1$ | 3.14 | +7% |

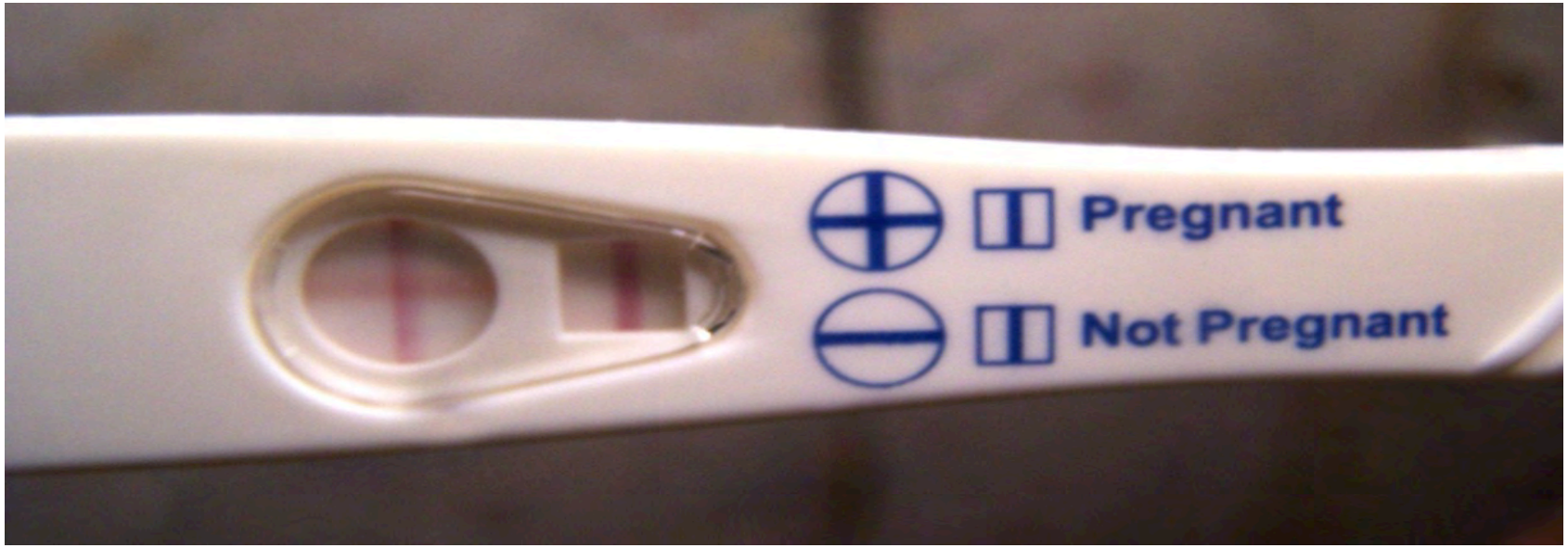
# Limitations: $FEV_1$ for all?

Khalid Respir Care 2009;54(9):1168




Methacholine
Mannitol
r = 0.41, P < .0001
% Fall With Mannitol
% Fall With Methacholine
0
5
10
15
20
25
30
35
0
10
20
30
40
50
60
70
Exc = Fall < 10%
Exc = Fall ≥ 10%

# There's no pregnancy test for asthma



# Key Points

- There's no substitute for PFTs
- It really makes no sense to withhold maintenance medications in patient with established lung disease
- Caffeine does not need to be withheld prior to PFTs
- 80% of predicted is not the LLN
- Patients may benefit from BD even if $FEV_1$ doesn't change
- MCT is not a "pregnancy test" for asthma