"things that effect those performing PF Testing"

ERS-ATS INTERPRETATION TECHNICAL STANDARD 2021 UPDATE

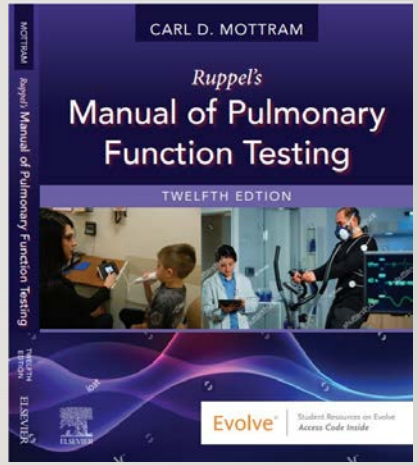
Carl D. Mottram, RRT RPFT FAARC

Associate Professor of Medicine

President - PFWConsulting LLC

DISCLOSURE OF INTERESTS

- Author of Ruppel's Manual of Pulmonary Function Testing 12th Edition 2022 Elsevier



- Member ATS-ERS Lung Volume Task Force
- Member ACCP ATS AARC CRS Task Force on Ethnicity's Effect on PF Interpretation
- Board Member – NBRC and Clinical Laboratory Standards Institute
- Consultant to the College of Physicians and Surgeons of British Columbia Diagnostic Accreditation Program

LEARNING OBJECTIVES

- Introduce the new ERS-ATS Interpretation Technical Standard
- Briefly review GLI and describe the new cut-points for quantifying the degree of abnormality
- Describe the new method of calculating a bronchodilator response and the change in the criteria for a positive response
- Focus on updates that effect testing

WHO COMES FIRST?

- ATS – ERS
- ERS - ATS
- ERS only or ATS only, but endorsed by the other

- Where it's published!

EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

ERS/ATS technical standard on interpretive strategies for routine lung function tests

Sanja Stanojevic, David A. Kaminsky, Martin R. Miller, Bruce Thompson, Andrea Aliverti, Igor Barjaktarevic, Brendan G. Cooper, Bruce Culver, Eric Derom, Graham L. Hall, Teal S. Hallstrand, Joerg D. Leuppi, Neil MacIntyre, Meredith McCormack, Margaret Rosenfeld, Erik R. Swenson

European Respiratory Journal 2022 60: 2101499; **DOI:** 10.1183/13993003.01499-2021

2021 vs 2022? I've heard both!

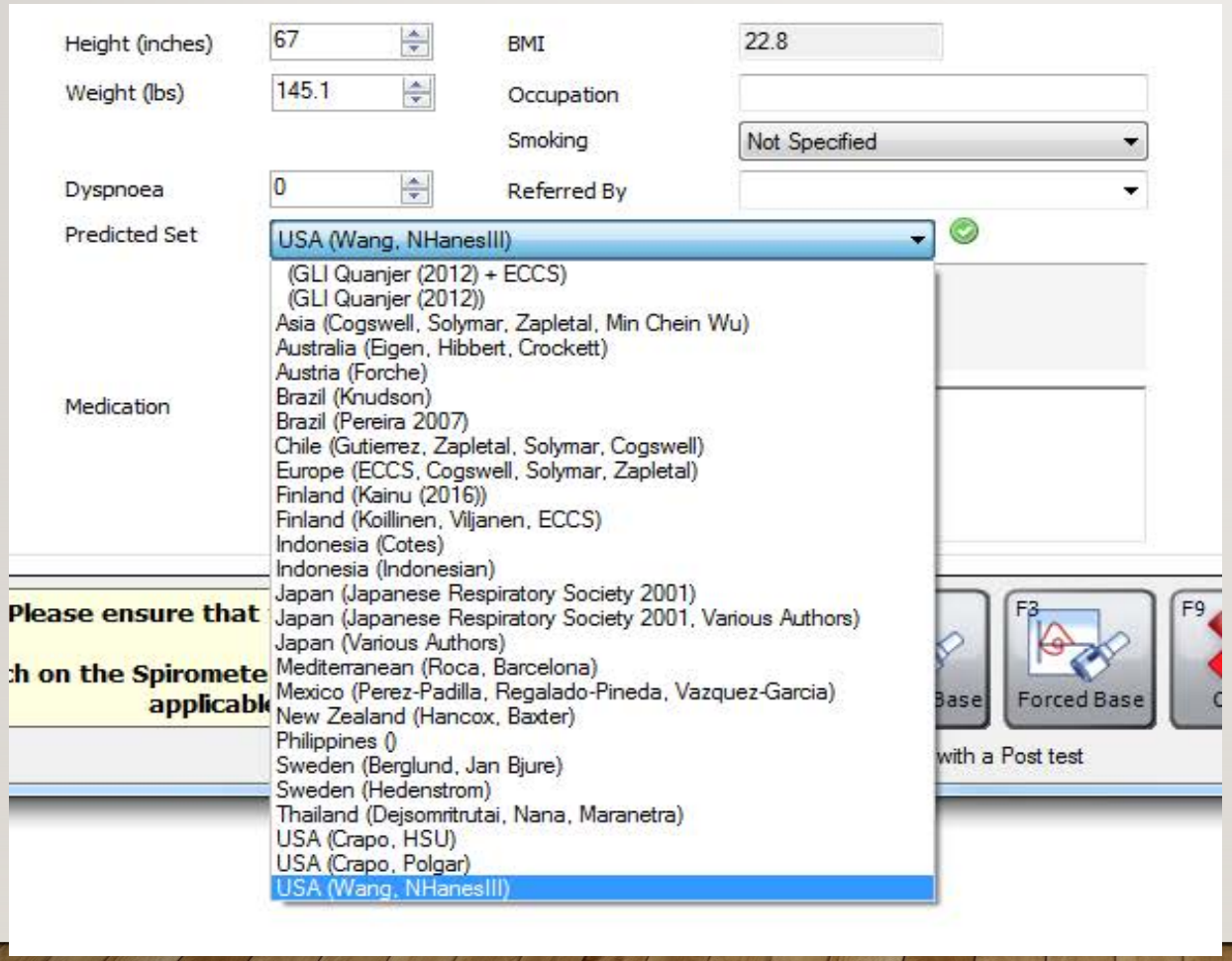
TABLE 1 COMPARISON SUMMARY 2005 VS 2021

TABLE 1 Summary of differences between the American Thoracic Society (ATS) and European Respiratory Society (ERS) 2005 [3] and 2021 interpretation standards

	2005 ATS/ERS statement	2021 ATS/ERS technical standard
General comments	• Using PFT interpretation to aid in clinical diagnosis and decision making	• More emphasis on using PFTs to classify physiology, not make a clinical diagnosis • Emphasis on uncertainty of interpretation, especially near LLN
Reference equations	• Use of race/ethnic-specific equations preferred over using adjustment factors • Spirometry: In USA: NHANES III recommended In Europe: no specific equations recommended • Lung volumes and D_{LCO}: In USA and Europe: no specific equations recommended	• Recommendation to use GLI reference equations for spirometry, lung volumes and D_{LCO} • More emphasis on incomplete understanding of role of race/ethnicity on lung function • Clarify that biological sex, not gender be used to interpret lung function
Defining normal range	• General use of LLN=5th percentile • Use of fixed ratio FEV_1/FVC <0.7 not recommended • Use of 80% predicted to define normal not recommended	• General use of LLN=5th percentile and ULN=95th percentile • Use of fixed ratio FEV_1/FVC <0.7 not recommended • Use of 80% predicted to define normal not recommended
Bronchodilator response	• ⩾12% and 200 mL in FEV_1 or FVC from baseline • 4 doses of 100 µg salbutamol; wait 15 min	• >10% of predicted value in FEV_1 or FVC • Choice of protocol for administering bronchodilator not specified
Interpretation of change over time	• Variable changes over time depending on normal *versus* COPD and time period (within a day, week to week, year to year)	• Conditional change score in children • FEV_1Q in adults
Severity of lung function impairment	• Using FEV_1 (includes obstruction or restriction): Mild: FEV_1 >70% predicted Moderate: 60–69% predicted Moderate-to-severe: 50–59% predicted Severe: 35–49% predicted Very severe: <35% predicted • D_{LCO}: Mild: >60% predicted and <LLN Moderate: 40–60% predicted Severe: <40% predicted	• For all measures use z-score: Mild: −1.65 to −2.5 Moderate: −2.51 to −4.0 Severe: <−4.1
Classification of physiological impairments	• Airflow obstruction: FEV_1/FVC <5th percentile, using largest VC; lung volumes to detect hyperinflation or air trapping; elevated airway resistance; central/upper airway obstruction • Restriction: TLC <5th percentile and normal FEV_1/VC Mixed: FEV_1/VC and TLC <5th percentile • Gas transfer impairment: D_{LCO}, K_{CO} <5th percentile Importance of adjustments for Hb, COHb	• Airflow obstruction: FEV_1/FVC <5th percentile, using FVC; lung volumes to detect hyperinflation or air trapping; dysanapsis; non-specific pattern and PRISm; central/upper airway obstruction • Restriction: TLC <5th percentile Simple *versus* complex restriction Hyperinflation Mixed • Gas transfer impairment: D_{LCO} <5th percentile Using V_A, K_{CO} to classify low D_{LCO}

REFERENCE SETS

Spirometry



DLCO

2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

Comparison of measured values to a healthy population

Global Lung Function Initiative (GLI) reference equations for spirometry [10], diffusing capacity [11] and lung volumes [12] should be used to define the expected range of values in healthy individuals.

Global Lung Function Initiative

GLI

Global Lung Function Initiative

About

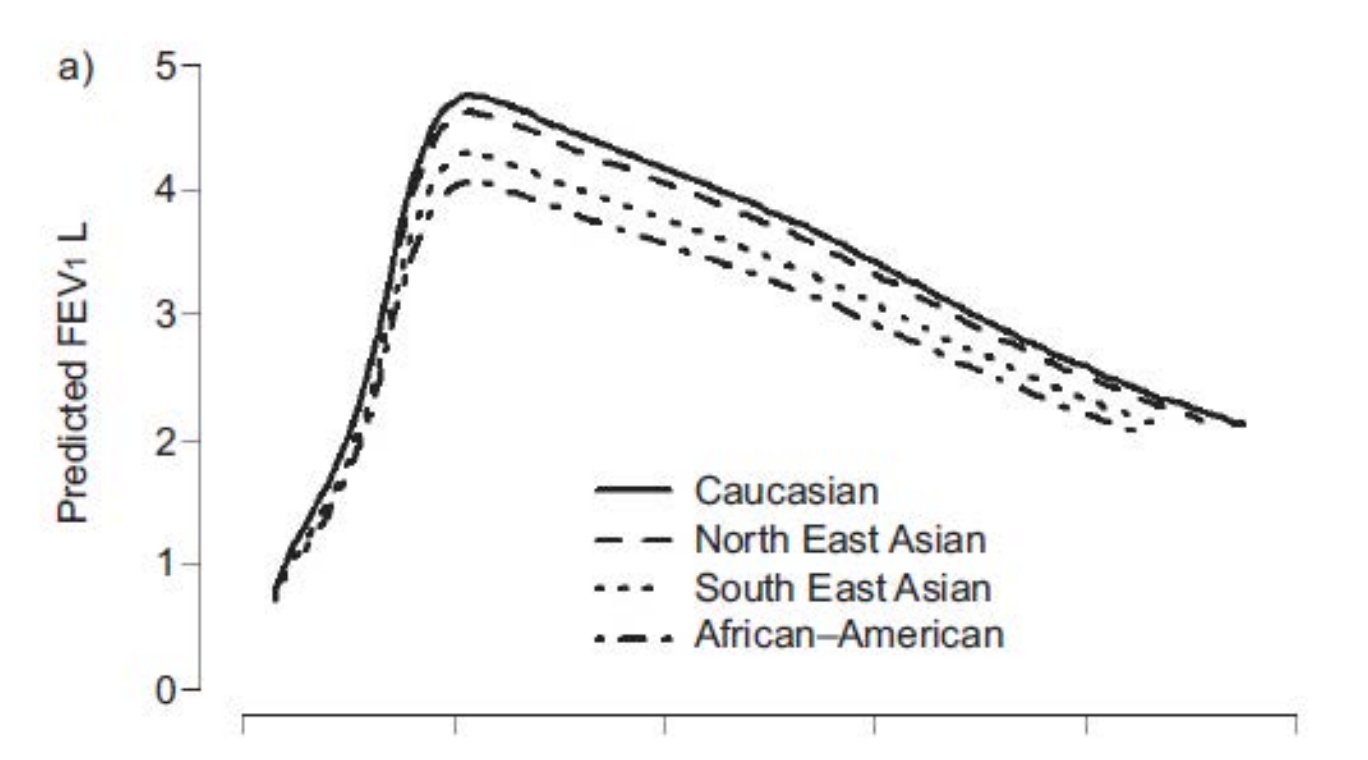
The Global Lung Function Initiative (GLI) has collected respiratory function outcomes from researchers and health care professionals from around the world. To date, the GLI Network has produced reference equations for Spirometry and

What reference values are you currently using?

GLI SPIROMETRY REFERENCE SET

Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations

Eur Respir J 2012; 40: 1324–1343



GLI SPIROMETRY REFERENCE SET

- 160,000 data pts from 72 centers in 33 countries
  - 97,759 records of healthy nonsmokers (55.3% females) aged 2.5–95 yrs.
  - Reference equations were derived for healthy individuals aged 3–95 yrs for Caucasians (n=57,395), African–Americans (n=3,545), and North (n=4,992) and South-East Asians (n=8,255).
    - Nine datasets with 13,247 records were included from Hong Kong, China, Taiwan, Thailand, and Korea
  - "Other" which is a 9% adjustment
    - Made up of 80% Caucasians

2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

AM J RESPIR CRIT CARE MED 1999;159:179–187–187.

- Standard states the change from the NHANES III (National Health and Nutrition Examination Survey) set recommended in 2005 was based on these factors:
  - NHANES III data are included in the GLI data set
  - Lacked representation from other cohorts.
  - Greater age range 3-95 vs 8-80 y.o.

- Pushback from the occupational community

Spirometric Reference Values from a Sample of the General U.S. Population

JOHN L. HANKINSON, JOHN R. ODENCRANTZ, and KATHLEEN B. FEDAN

Am J Respir Crit Care Med. 2020 Apr 15; 201(8): 1012.
Published online 2020 Apr 15. doi: 10.1164/rccm.201912-2530LE
PMCID: PMC7159417
PMID: 31930926

Reply to Townsend: The American Thoracic Society/European Respiratory Society 2019 Spirometry Statement and Occupational Spirometry Testing in the United States

Brian L. Graham[1,*] and Irene Steenbruggen[2]

"Therefore, for occupational spirometry testing in the United States, choosing to use the National Health and Nutrition Examination Survey III spirometry reference values is in full compliance with the 2019 Update of the American Thoracic Society/European Respiratory Society Spirometry Standards."

A Race-neutral Approach to the Interpretation of Lung Function Measurements

Cole Bowerman[1,2], Nirav R. Bhakta[3], Danny Brazzale[4], Brendan R. Cooper[5], Julie Cooper[5], Laura Gochicoa-Rangel[6], Jeffrey Haynes[7], David A. Kaminsky[8], Le Thi Tuyet Lan[9], Refiloe Masekela[10], Meredith C. McCormack[11], Irene Steenbruggen[12], and Sanja Stanojevic[2]; on behalf of the Global Lung Function Initiative

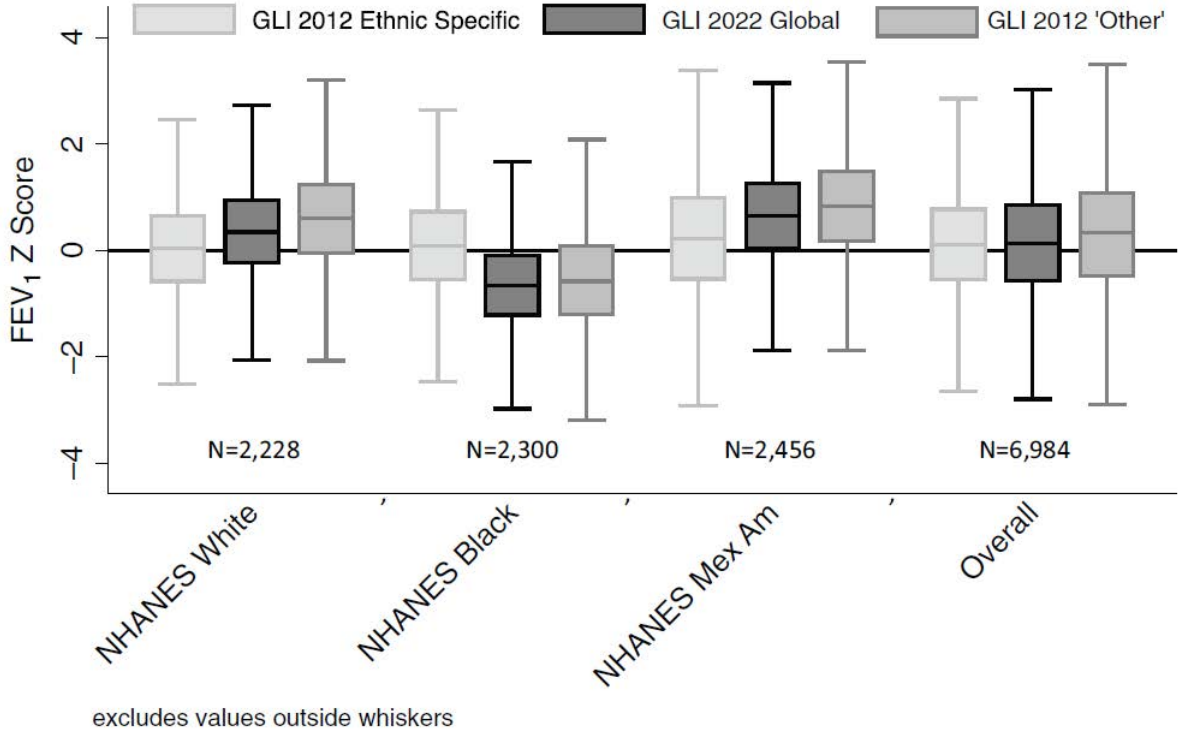


Figure 3. Calculated *z*-scores for FEV_1 values collected in healthy individuals in the National

Am J Respir Crit Care Med Vol 207, Iss 6, pp 768–774, Mar 15, 2023

25% rule

Application of GLI Global Spirometry Reference Equations Across a Large, Multicenter Pulmonary Function Lab Population

Amjad N. Kanj, MD, MPH[1]; Paul D. Scanlon, MD[1]; Hemang Yadav, MBBS[1]; William T. Smith, MD[1]; Tyler L. Herzog, MD[1]; Aaron Bungum[1]; Daniel Poliszuk[2]; Edward Fick RRT, CRT[1]; Augustine S. Lee, MD[3]; Alexander S. Niven, MD[1]

[1] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, MN

AJRCCM Articles in Press. Published July 31, 2023

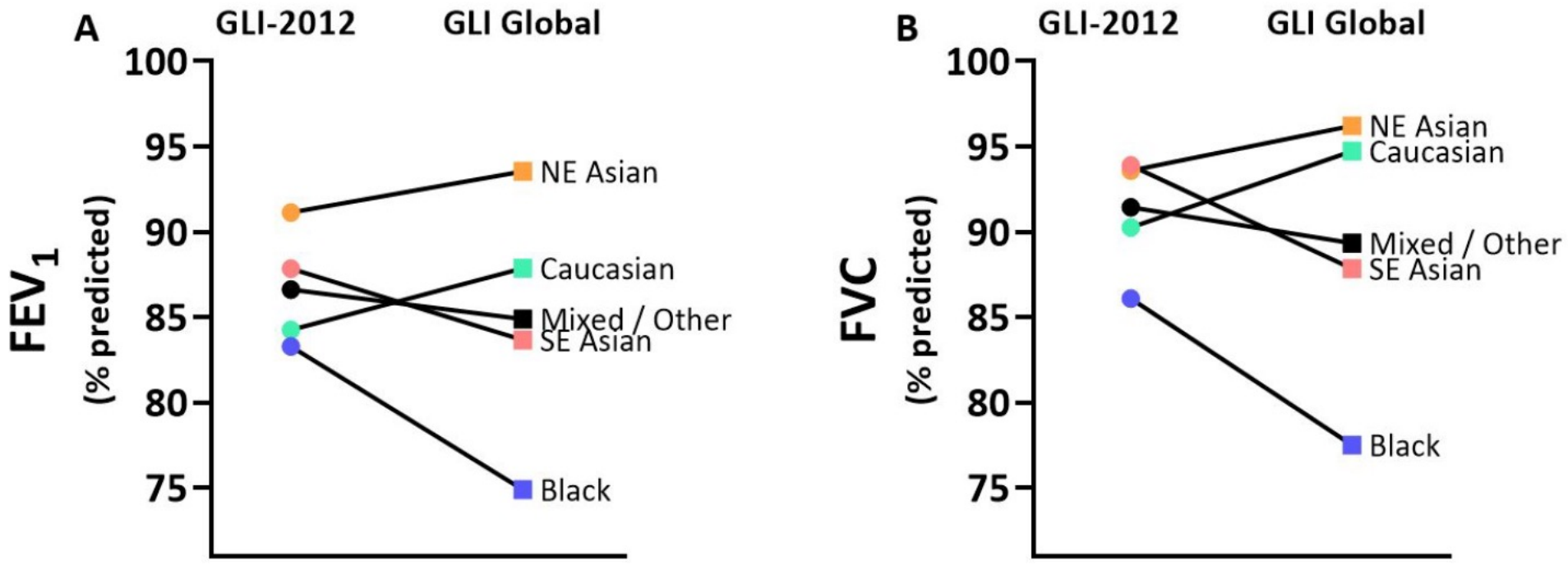


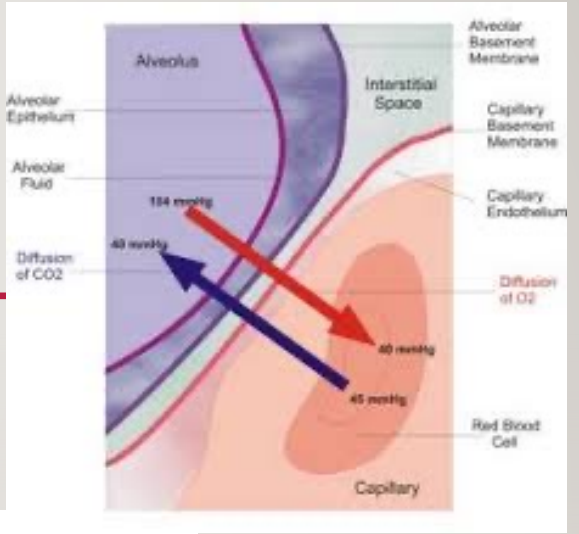
Figure 2: Absolute change in mean (A) FEV_1 and (B) FVC % predicted values using GLI-2012 and GLI-Global reference equations. In Caucasian and


BE
CAREFUL

GLI DLCO REFERENCE SET

Official ERS technical standards: Global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians

Eur Respir J 2017; 50



- N=9710
- Age range 4.5 to 91 years

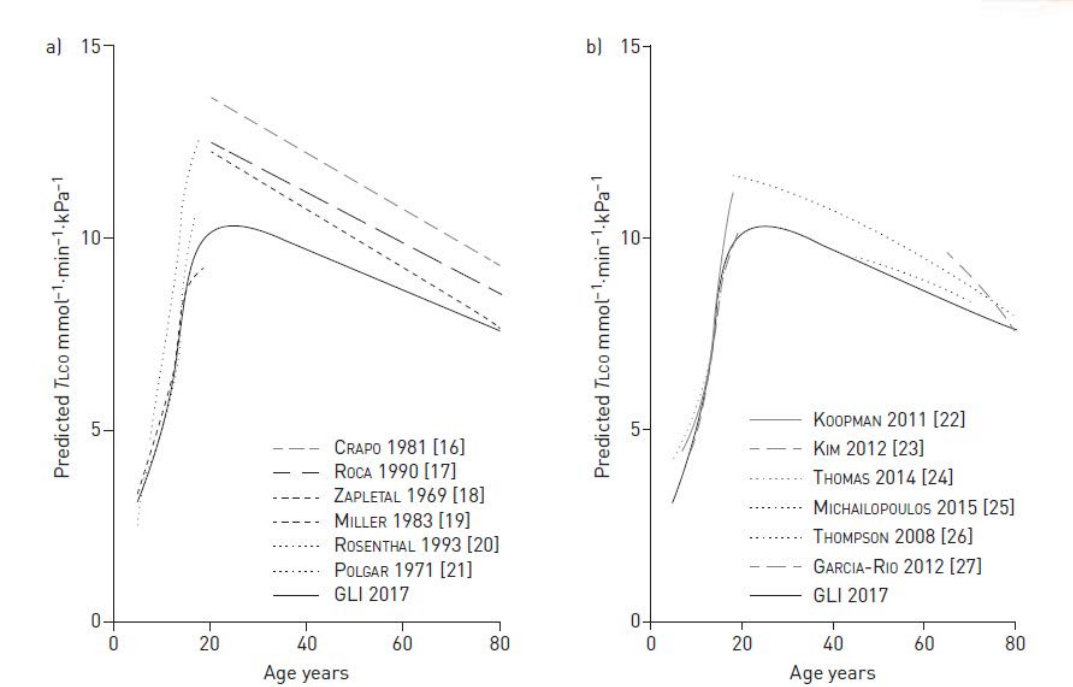
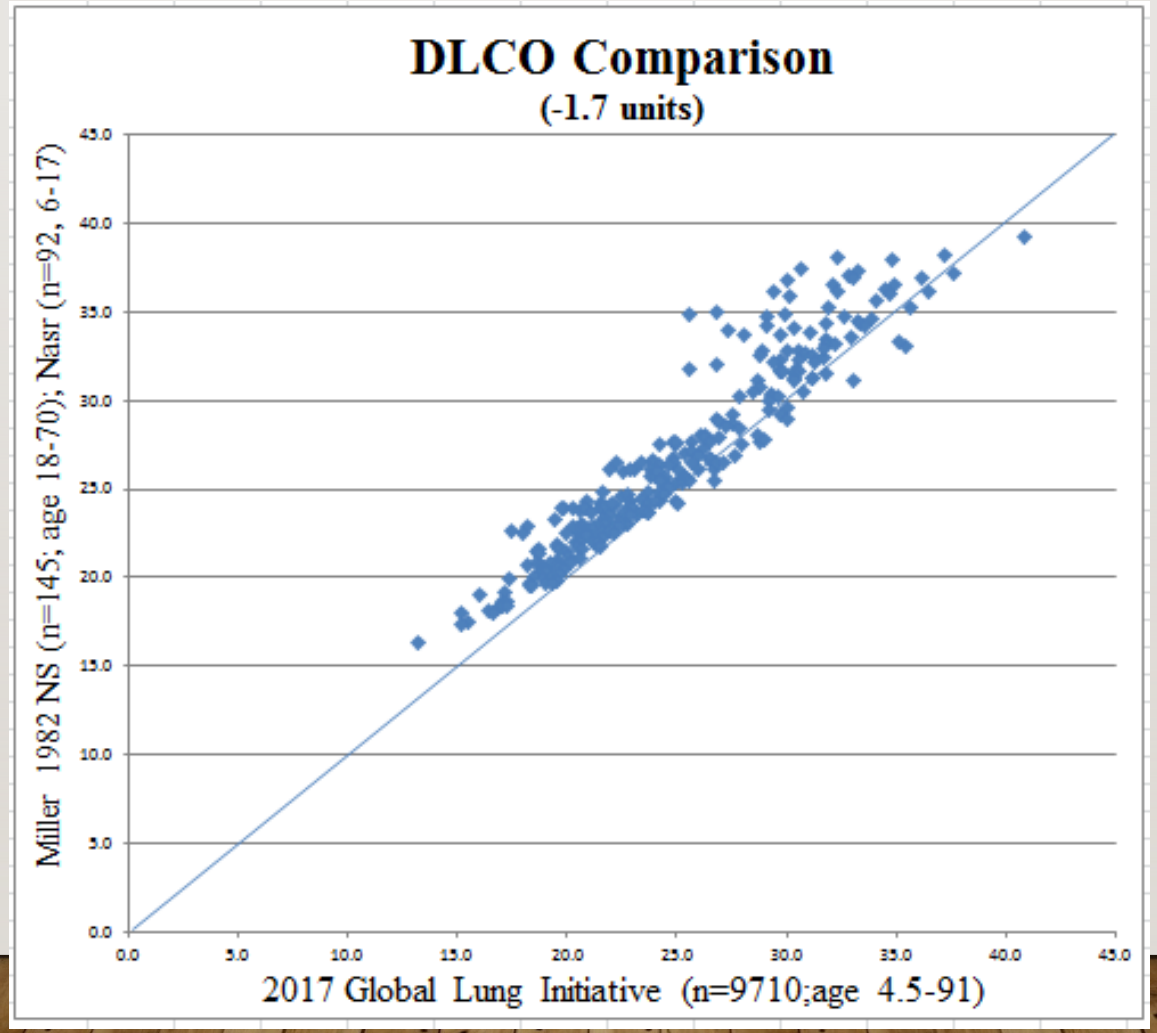


FIGURE 4 Comparison of transfer factor of the lung for carbon monoxide (T_{LCO}) reference equations to the current Global Lung Function Initiative (GLI) equations. Equations found in a) most commercially available equipment and b) more recently published studies.

IMPLEMENTING THE GLI DLCO REFERENCE SET AT MAYO CLINIC



GLI LUNG VOLUME REFERENCE SET

Official ERS technical standard: Global Lung Function Initiative reference values for static lung volumes in individuals of European ancestry

Graham L. Hall[1,2], Nicole Filipow[3], Gregg Ruppel [4], Tolu Okitika[1],

Eur Respir J 2021; 57

GLI LUNG VOLUME REFERENCE SET

- 7190 observations from participants of European ancestry between the ages of 5 and 80 years.

TABLE 2 Summary of the demographic characteristics of the available data for each lung volume index

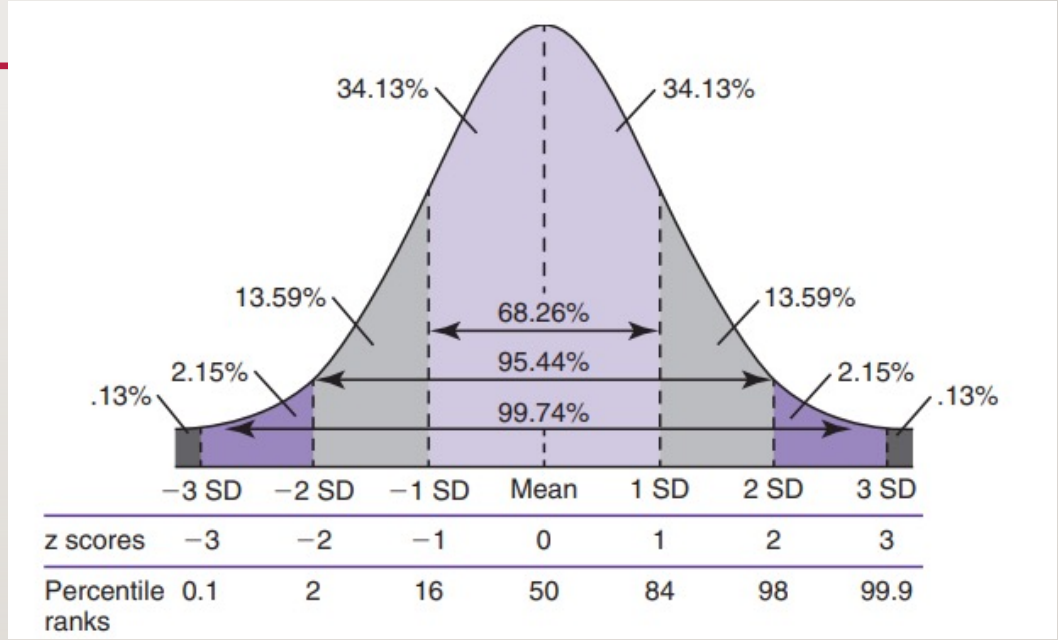
	Participants	Age years	Female
FRC			
He	683	22.3–87.0	399 (58.4)
N_2	489	3.2–50.0	263 (53.8)
Plethysmography	6018	6.0–91.0	3434 (57.1)
Combined techniques	7190	3.2–91.0	4096 (57.0)
TLC			
He	681	22.3–87.0	398 (58.4)
N_2	229	4.0–12.9	113 (49.3)
Plethysmography	5905	6.0–91.0	3367 (57.0)
Combined techniques	6815	4.0–91.0	3878 (56.9)
RV			
Combined techniques	5660	4.9–91.0	3296 (58.2)

2021 ERS-ATS TS on Interpretative Strategies

LLN (OR Z SCORES) VERSUS FIXED CUT-POINTS

GLI STATISTICAL MODEL

- Lambda, Mu and Sigma (LMS) statistical model considers expected mean, coefficient of variation (CV) and skewness.
- Population defined z-scores or percentile values describe the chance the observed result falls within the distribution of values in healthy individuals
  - Lower Limit of Normal = 5% (1-20)
  - Predicted value - 1.645 = LLN



Mottram CD, Manual of Pulm Func 12th 2022

GOLD CLASSIFICATION OF COPD SEVERITY BASED ON POST BRONCHODILATOR FEV1*

CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POST-BRONCHODILATOR FEV_1)

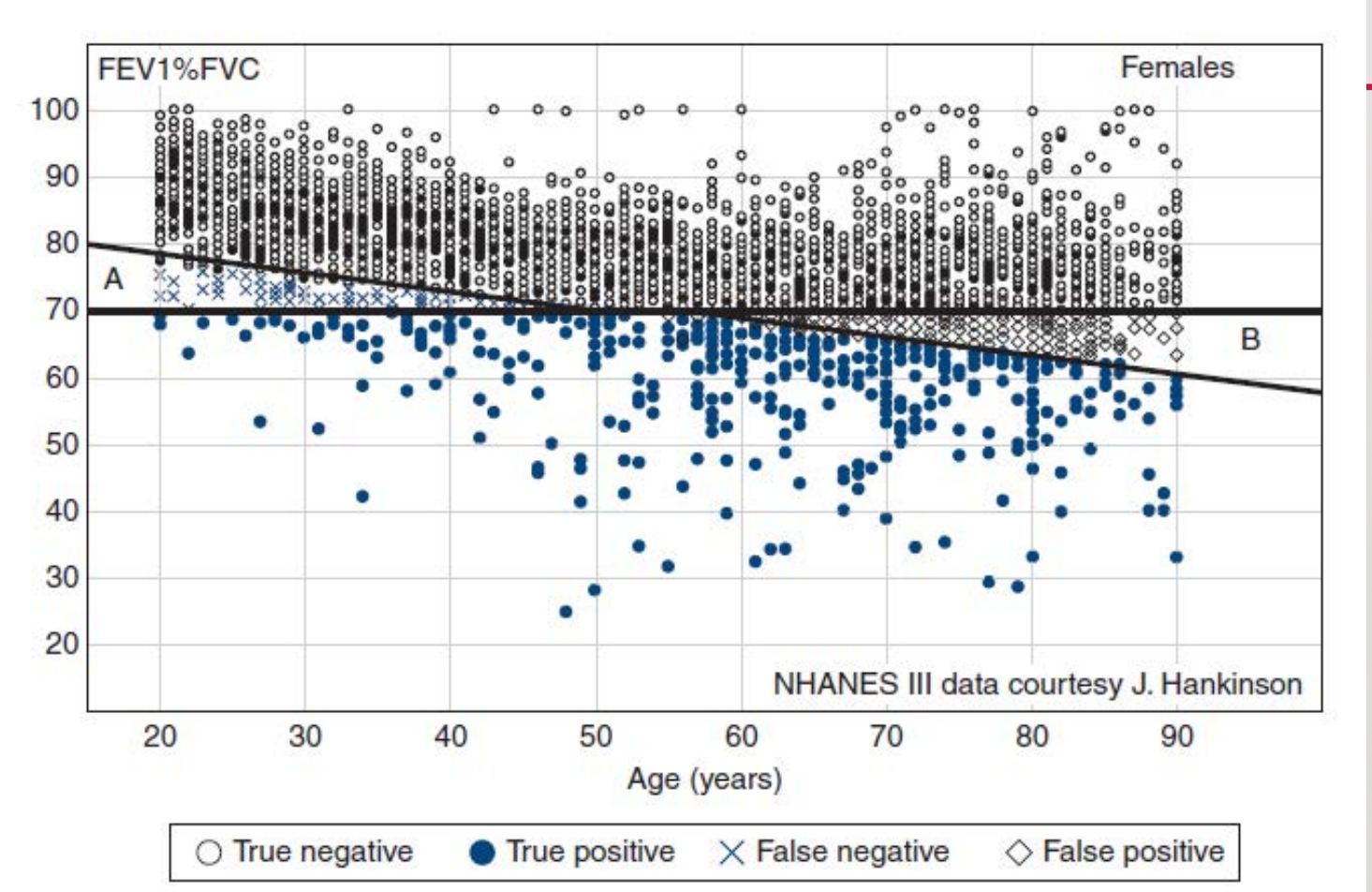
In patients with FEV1/FVC < 0.70:

GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

TABLE 2.4

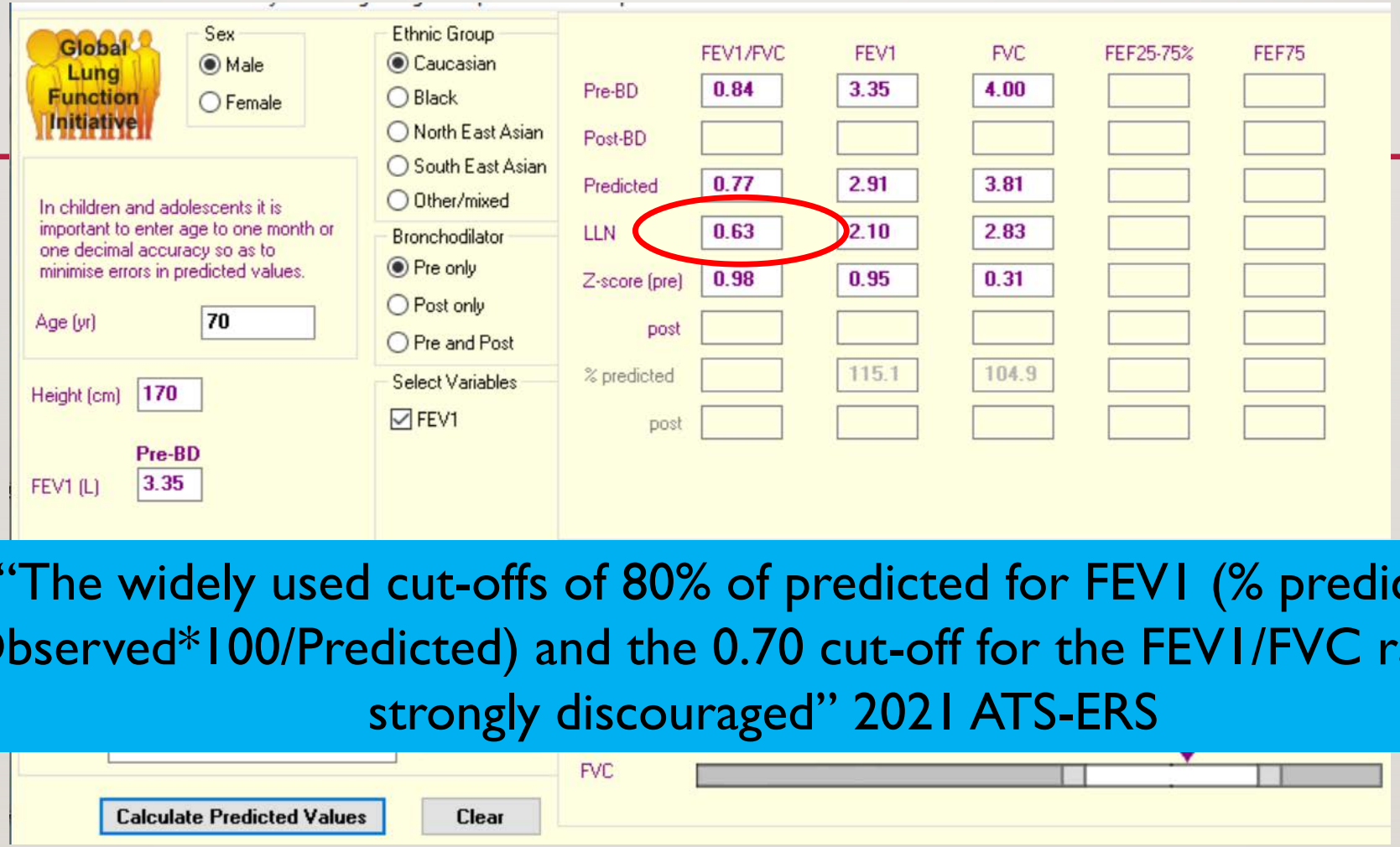
Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis management, and prevention of chronic obstructive pulmonary disease. (Updated 2020). http://www.goldcopd.org.

MISCLASSIFICATION USING A 70% FIXED CUT-POINT



Mottram CD Manual of Pulm Func 12th 2022

MISCLASSIFICATION USING A FIXED CUT-POINT



"The widely used cut-offs of 80% of predicted for FEV1 (% predicted = Observed*100/Predicted) and the 0.70 cut-off for the FEV1/FVC ratio are strongly discouraged" 2021 ATS-ERS

WHAT IS ABNORMAL?

<LLN

Or a z score of -1.645

2005 SEVERITY CLASSIFICATION - SPIROMETRY

Table 4. Severity of any spirometric abnormality based on the FEV_1 as % of predicted.

DEGREE OF SEVERITY	FEV_1, % predicted
MILD	>70%
MODERATE	60-69
MODERATELY SEVERE	50-59
SEVERE	35-49
VERY SEVERE	<35

"The number of categories and the exact cut-points are arbitrary."

Enright: Caution re shifting of disease severity, false positives, excess therapy, potential conflict of interest in clinical practice guidelines

Enright PL. Flawed interpretative strategies for lung function tests harm patients Eur. Respir. J., 2006; 27(6): 1322-1323

2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

- z-score cut levels between -1.65 and -2.5 have little difference in risk of death
- z-score between -2.5 and -4 exhibit a moderate risk of mortality.
- z scores >-4 had a high risk of mortality

TABLE 13.3

2021 ERS-ATS Interpretation 3-Tier system to assess the severity of lung function impairment using z-score values

Z score	
> −1.645	Normal
between −1.65 and −2.5	Mild
between −2.5 and −4	Moderate
< −4	Severe

Mottram CD Manual of Pulm Func 12th 2022

Table 7

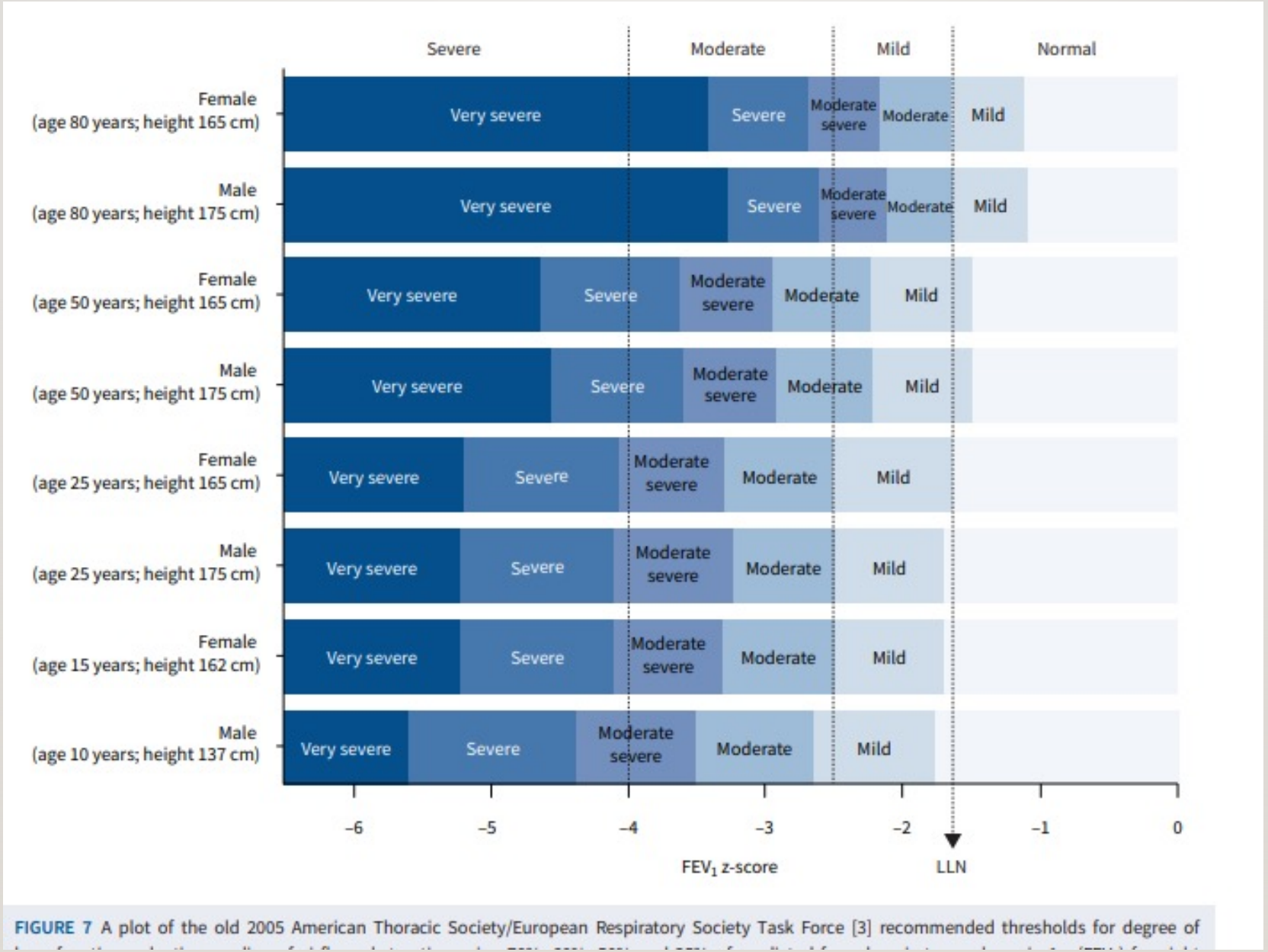
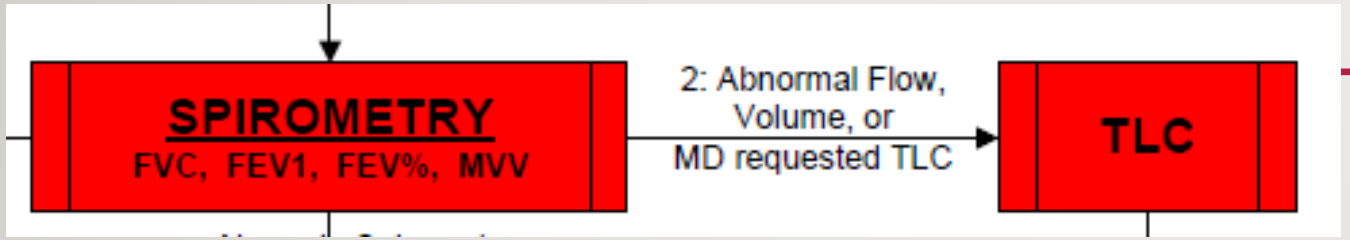
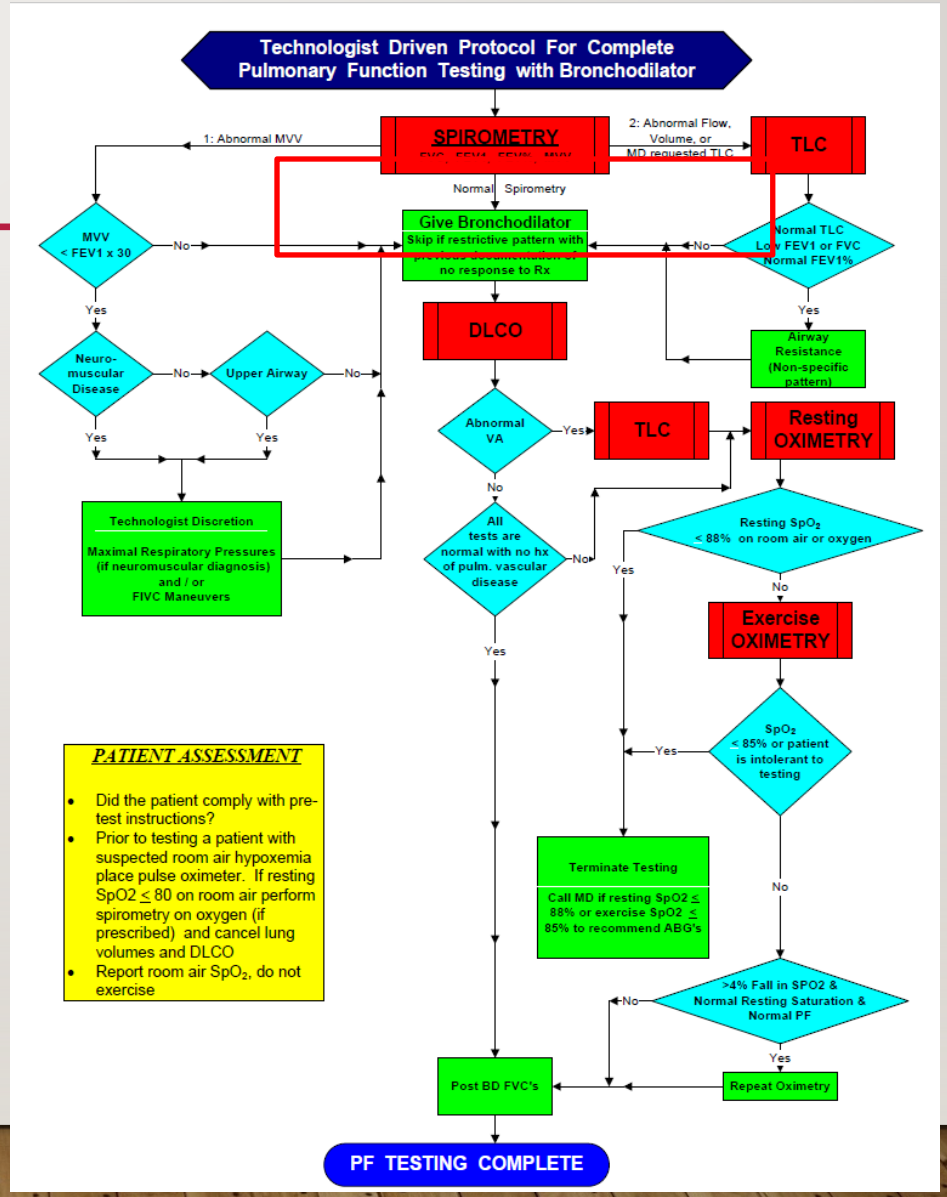


FIGURE 7 A plot of the old 2005 American Thoracic Society/European Respiratory Society Task Force [3] recommended thresholds for degree of

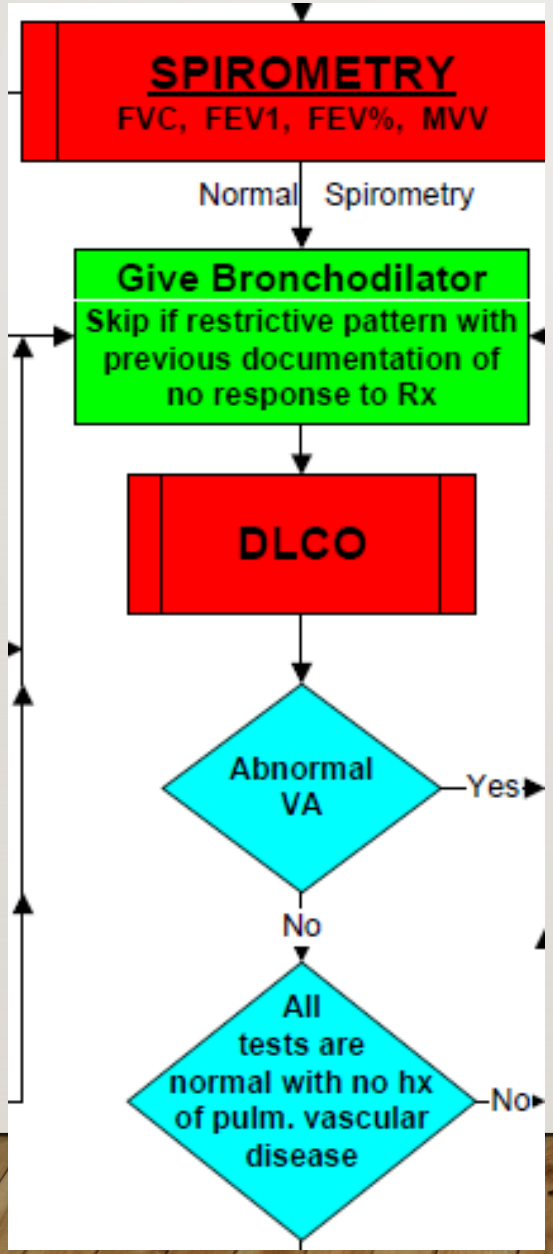
MAYO CLINIC'S PULMONARY FUNCTION TDPS

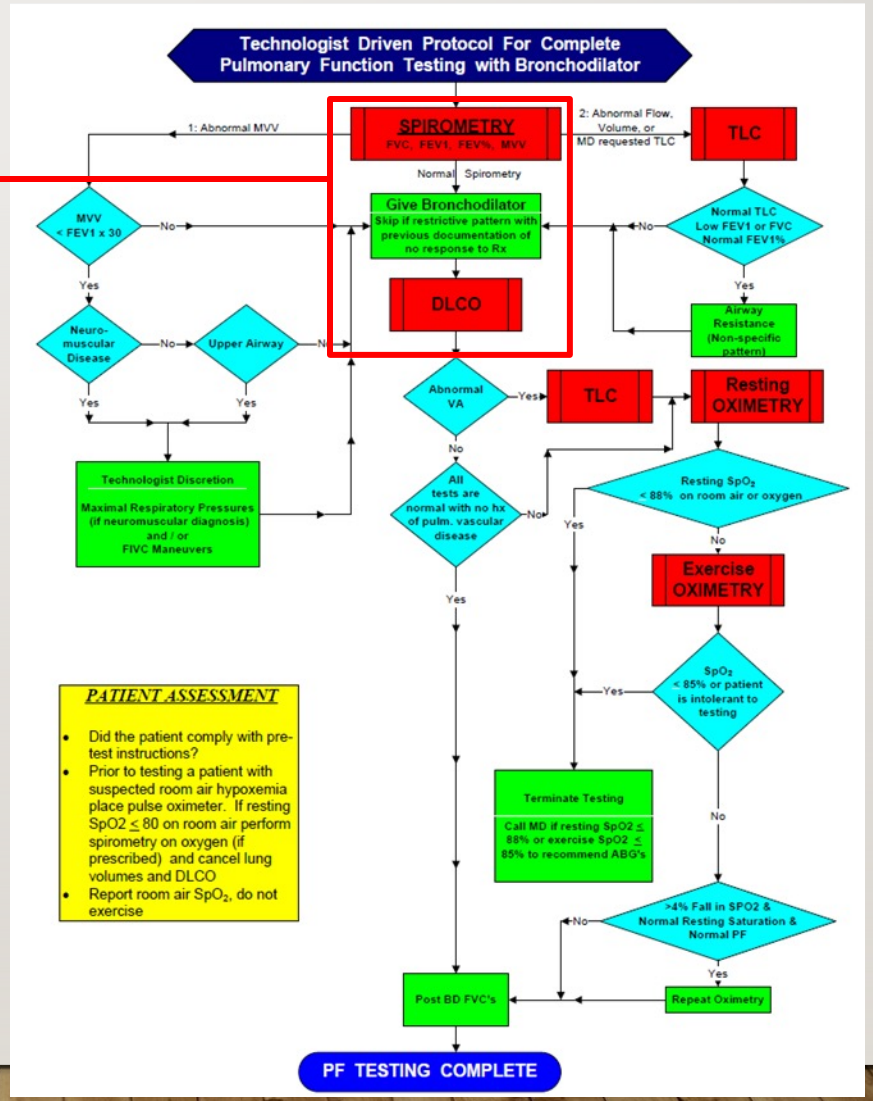


- System allows for MD override



NORMAL SPIROMETRY AND DLCO-VA – NO TLC





male 51 Years Wt: 101.5 kg BMI: 30 Ht: 184.9 cm Arm Span: Test: 3/30/2018

Medical Research Council (mMRC): 0 Cau

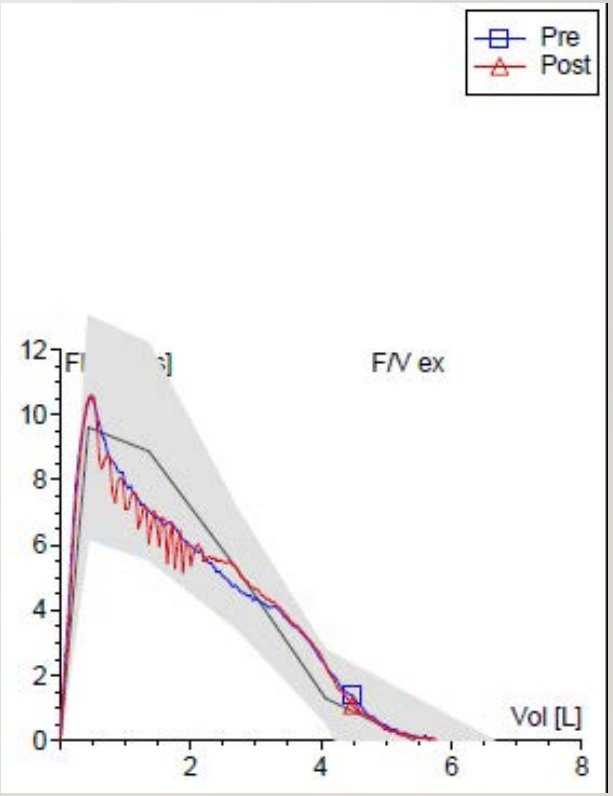
	PREDICTED	CONTROL	POST-DILATOR
Substance			Albuterol
Dose			2 Puff
Patient Position		Sitting	Sitting

SPIROMETRY

	NORMAL	LLN	FOUND	%PRED.	FOUND	%CHNG	%PRED.
VC MAX	5.43	4.23	5.68	105 %	5.81	2 %	107 %
FVC	5.43	4.23	5.68	105 %	5.73	1 %	106 %
FEV 1	4.23	3.29	4.47	106 %	4.46	-0 %	105 %
FEV1/FVC	78.3	67.4	78.7	100 %	77.8	-1 %	99 %
FEF25-75%	3.73	1.99	4.06	109 %	4.02	-1 %	108 %
PEF	9.6	6.2	10.5	110 %	10.6	1 %	110 %
FET			7.60		9.69	27 %	
MVV	162	129	144	89 %			

DIFFUSION CAPACITY

	NORMAL	LLN	FOUND	%PRED.	FOUND	%PRED
DLCO_SB	31.7	23.7	37.8	119 %		
DLCOcSB	31.7	23.7	36.0	114 %		
Hb			16.50			
VA_SB	7.14	5.99	7.46	104 %		



2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

Bronchodilator Responsiveness Testing (BDR)

2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

BDR = $\frac{\text{Post BD Value} - \text{Pre BD Value}}{\text{Predicted value (GLI)}} \times 100$

2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

- “Changes in FEV1 and FVC following bronchodilator responsiveness testing should be expressed as the percent change relative to the individual’s predicted value.” – “Using GLI”
- A change >10% of the predicted value indicates a positive response.
  - No more 12% and 200 ml

Case example

Name: **Anonymous Doe** MRN: ******* Sex: **F** DOB:**4/1/1962** Age: **60** Race: **C**

Height: **64 in** Weight: **92 lb** BMI: **15.8**

ICD-10 **Chronic obstructive pulmonary disease, unspecified**

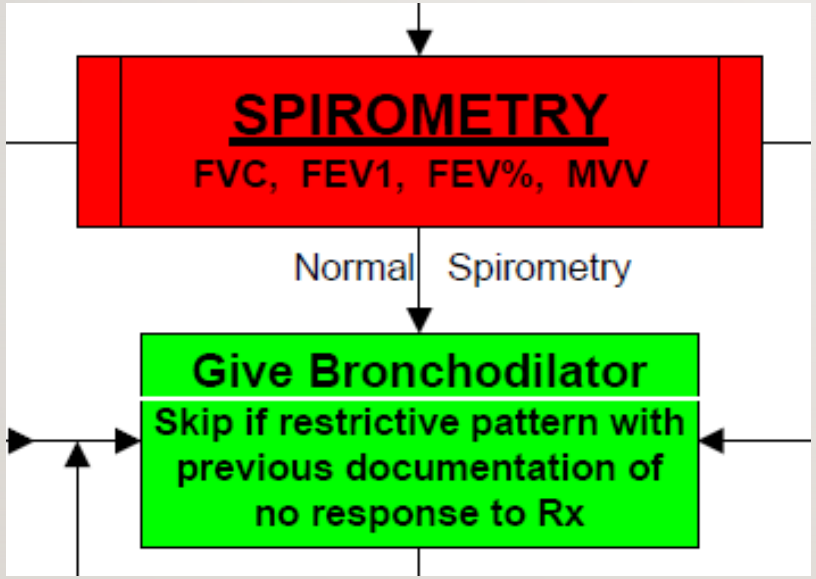
Tech: **Jeff Haynes RRT RPFT FAARC** Attending: **Haitham S. Al Ashry, M.D.** Referring: **Carole Bibeau, M.D.**

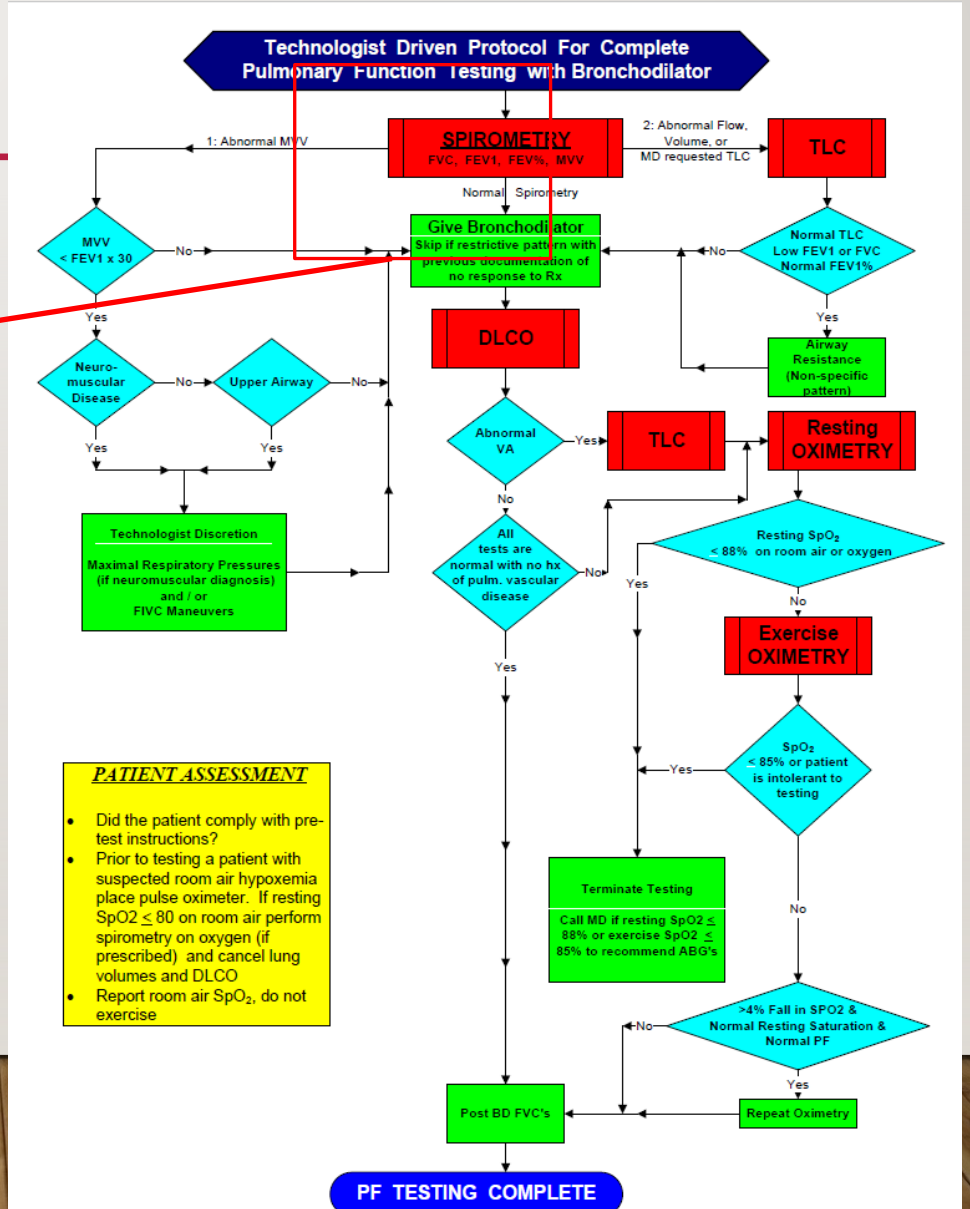
ATS/ERS compliant tests earn a ✔: Spiro ✔ DLCO ✔ VTG Predicteds: Spiro GLI 2012, DLCO GLI 2017, LV Quanjer

Spirometry (BTPS)		Pre Bronchodilator						Post Bronchodilator				
		Actual	LLN	ULN	Predicted	% Pred	Z-score	Actual	% Pred	Abs Chg	% Change	Z-score
StartTime		13:09	----	----	----	----	----	13:36	----	----	--	----
FVC	L	2.03	2.40	3.97	3.16	64	-2.46	2.38	75	350 mL	17	-1.68
FEV_1	L	0.67	1.88	3.08	2.49	27	-4.65	0.77	31	100 mL	15	-4.42
FEV_1 / FVC	%	33	67	90	79	42	-4.71	32	41	----	-3	-4.76
FEF_{25-75}	L/s	0.19	1.16	3.75	2.27	8	-4.14	0.21	9	0.02 L/s	11	-4.05
PEFR	L/s	2.89	4.60	8.04	6.32	46	----	3.02	48	0.13 L/s	4	----
MVV	L/m	----	40.8	142.8	91.8	----						
SVC	L	----	2.40	3.97	3.16	----						
ERV	L	----	0.44	1.16	0.80	----	----	----	----	----	--	----
IC	L	----	1.30	3.42	2.36	----	----	----	----	----	--	----
CPF	L/s	----	6.65	10.65	8.13	----	----	----	----	----	--	----

0.77 – 0.67 x100/2.49 = 4%

RESTRICTIVE PROTOCOL – NO BD FOLLOWING NON-RESPONSIVE PREVIOUS TEST





Case example

male 82 Years Wt: 90.0 kg BMI: 31 Ht: 170.6 cm Arm Span:

Medical Research Council (mMRC): 3 Cauc

	PREDICTED	CONTROL
Patient Position		Sitting

LUNG VOLUMES (Pleth)

	NORMAL	LLN	FOUND	%PRED
TLC	6.55	5.40	3.69	56 %
VC	3.44	2.46	1.60	47 %
FRCpleth	3.64	2.65	2.68	74 %

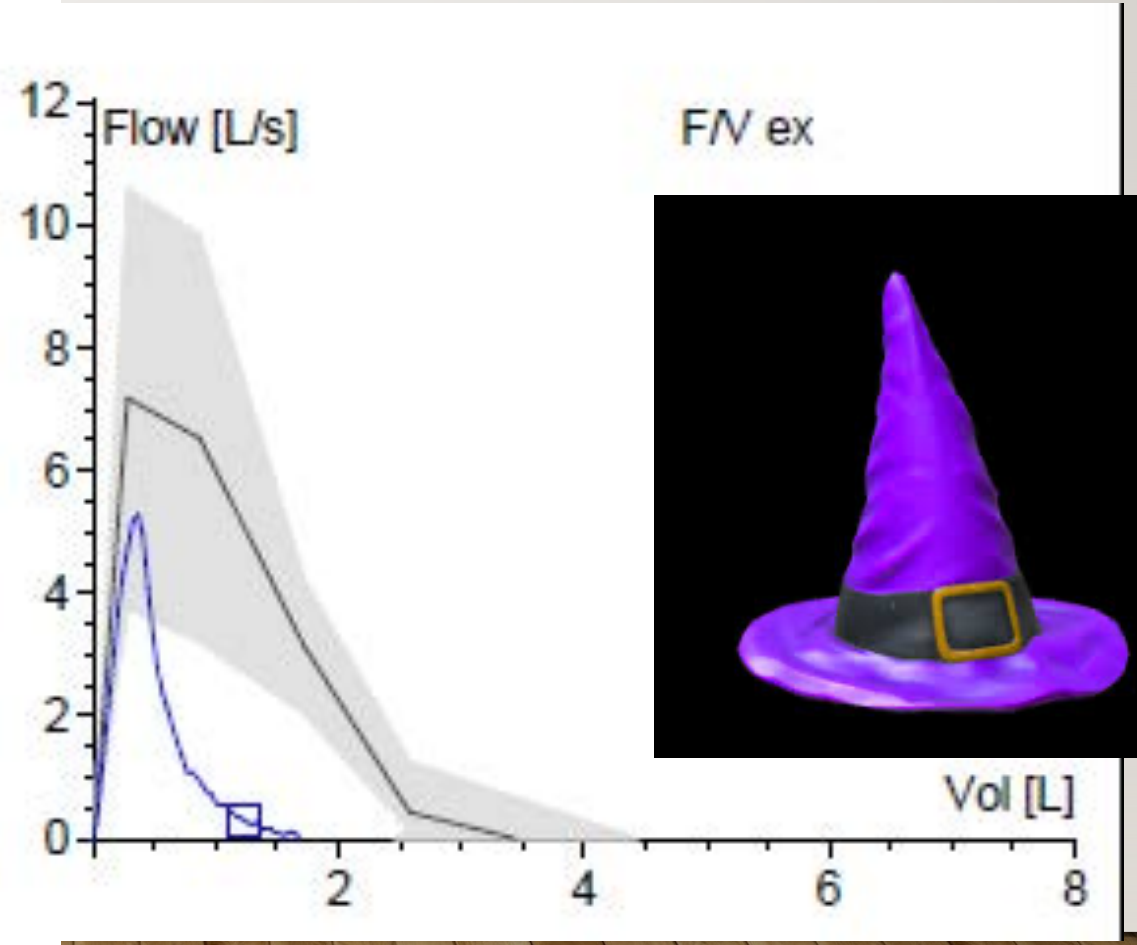
	NORMAL	ULN	FOUND	%PRED.
RV	2.81	3.48	2.08	74 %
RV % TLC	46	55	57	123 %

SPIROMETRY

	NORMAL	LLN	FOUND	%PRED.
VC MAX	3.44	2.46	1.68	49 %
FVC	3.44	2.46	1.67	49 %
FEV 1	2.55	1.74	1.21	48 %
FEV1/FVC	74.8	59.5	72.3	97 %
FEF25-75%	1.80	0.65	0.79	44 %
PEF	7.2	3.8	5.3	74 %
FET			6.19	
MVV	106	73	52	49 %

DIFFUSION CAPACITY

	NORMAL	LLN	FOUND	%PRED.
DLCO_SB	22.2	14.2	9.7	44 %
VA_SB	6.08	4.91	2.73	45 %



RESTRICTIVE PROTOCOL – NO BD FOLLOWING NON-RESPONSIVE PREVIOUS TEST

- 82-year-old male with known asbestosis
- Previous negative BD response
- No wheezing or hyperreactivity noted in medical record

2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES TS

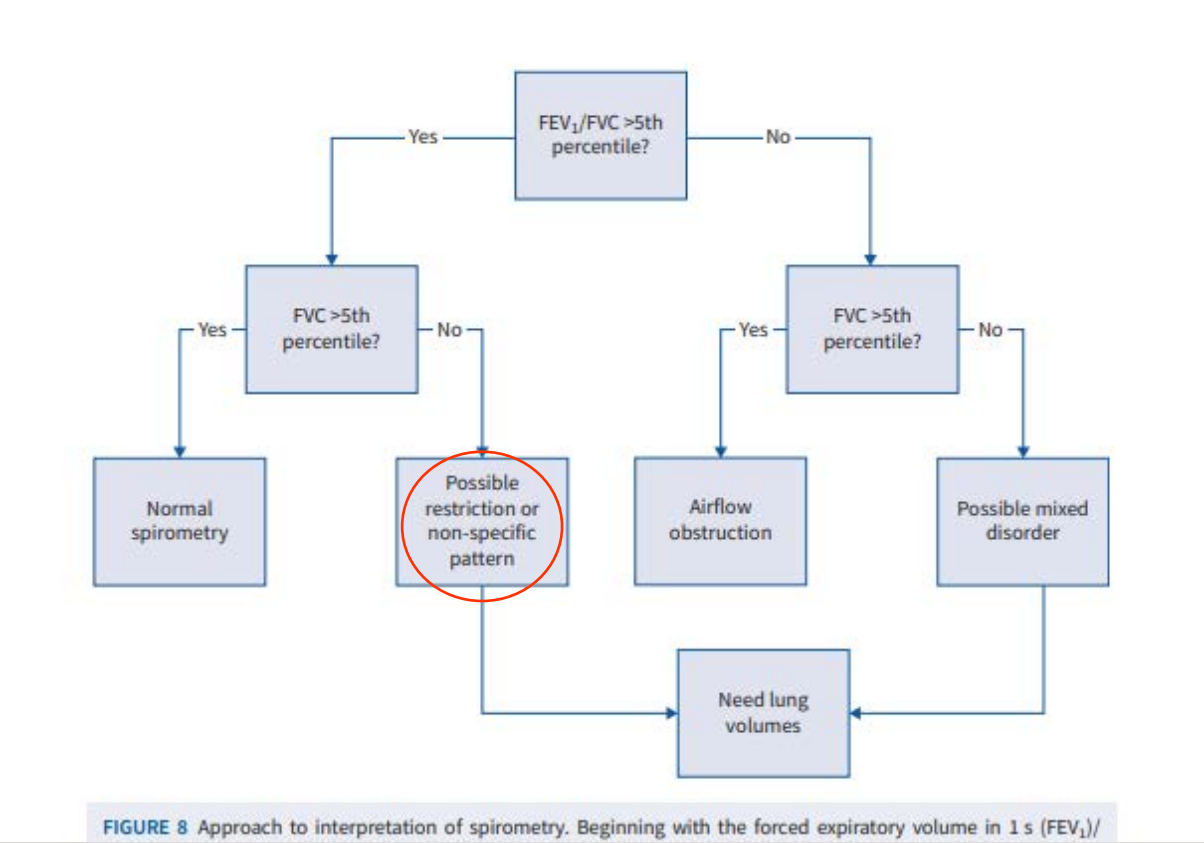


FIGURE 8 Approach to interpretation of spirometry. Beginning with the forced expiratory volume in 1 s (FEV_1)/

- What is "Obstruction" with normal FEV1/VC?
- "Nonspecific pattern"
- Most commonly seen in obesity and asthma*
- 9.5% of all PFT's at MC*
- 50% have increased Raw*

CHEST 2011; 139(4):878–886

Figure 13-7 Mottram CD. Manual of Pulmonary Function Testing 12th ed

male 59 Years Wt: 63.7 kg BMI: 20 Ht: 177.2 cm Arm Span: Test:

Medical Research Council (mMRC): Caucasia-

	PREDICTED		CONTROL
Patient Position			Sitting

LUNG VOLUMES (Pleth)

	NORMAL	LLN	FOUND	%PRED
TLC	7.08	5.93	7.59	107 %
VC	4.61	3.52	2.74	59 %
FRCpleth	3.59	2.60	5.46	152 %

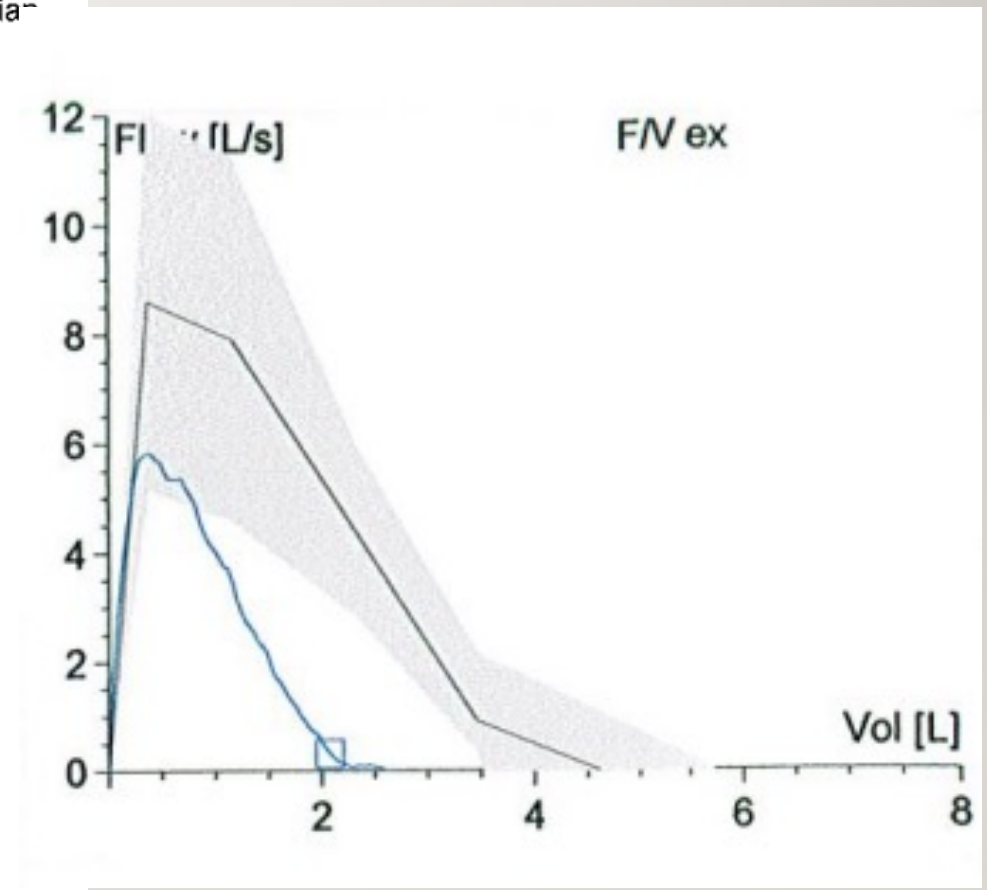
	NORMAL	ULN	FOUND	%PRED.
RV	2.39	3.06	4.85	203 %
RV % TLC	37	46	64	173 %

AIRWAYS RESISTANCE

	NORMAL	ULN	FOUND	%PRED
sR mid	4.65	7.87	9.51	205 %

SPIROMETRY

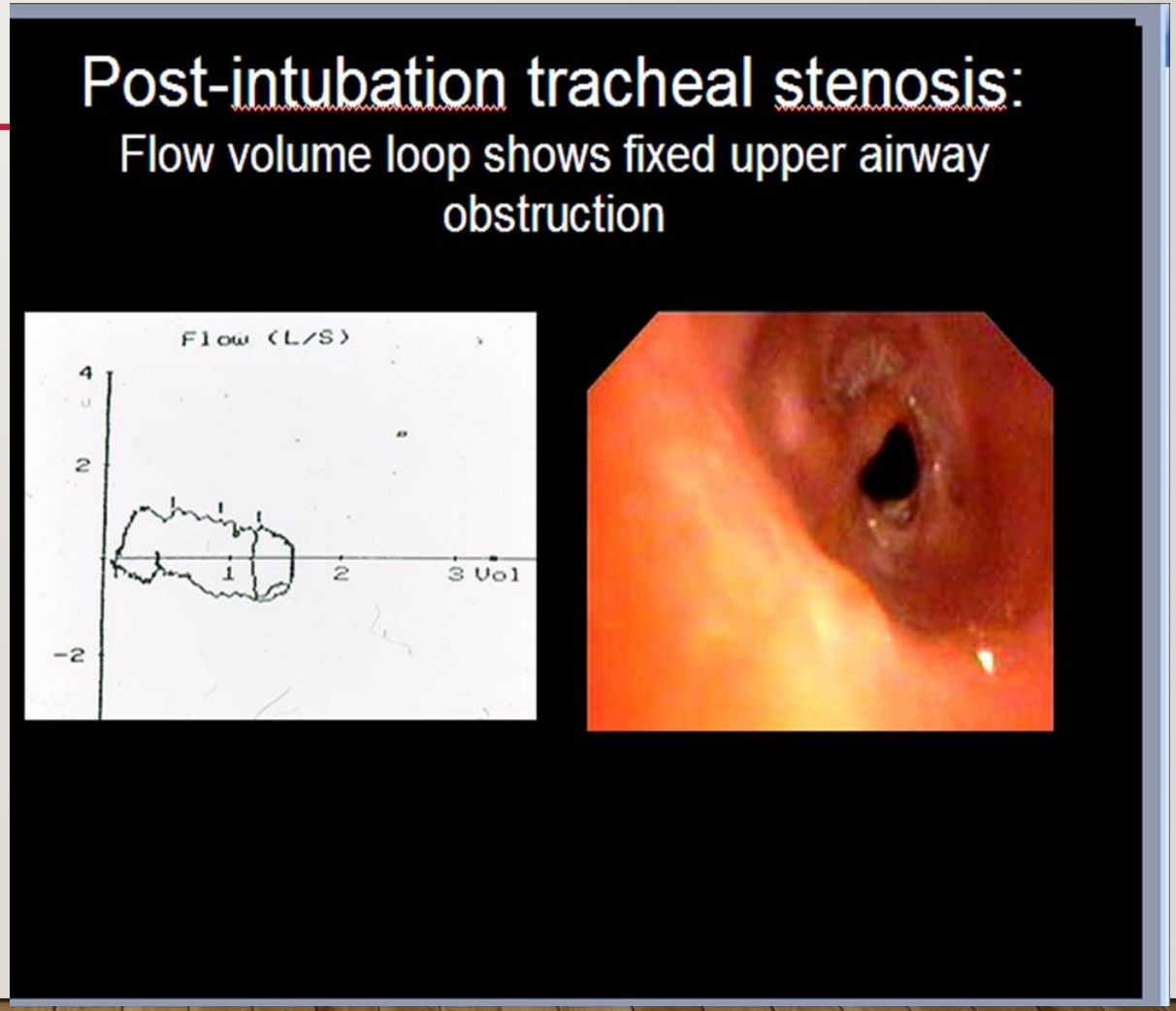
	NORMAL	LLN	FOUND	%PRED.
VC MAX	4.61	3.52	2.69	58 %
FVC	4.61	3.52	2.60	56 %
FEV 1	3.57	2.69	2.07	58 %
FEV1/FVC	77.6	65.6	79.5	103 %
FEF25-75%	2.98	1.47	2.02	68 %
PEF	8.6	5.2	5.9	68 %
FET			6.67	



2021 Interp. TS: *"Addition of BDR or SVC to characterize the abnormality"*

2022 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

- Central or upper airway obstruction
  - Fixed upper airway obstruction



2005 ATS-ERS TS ON INTERPRETATION

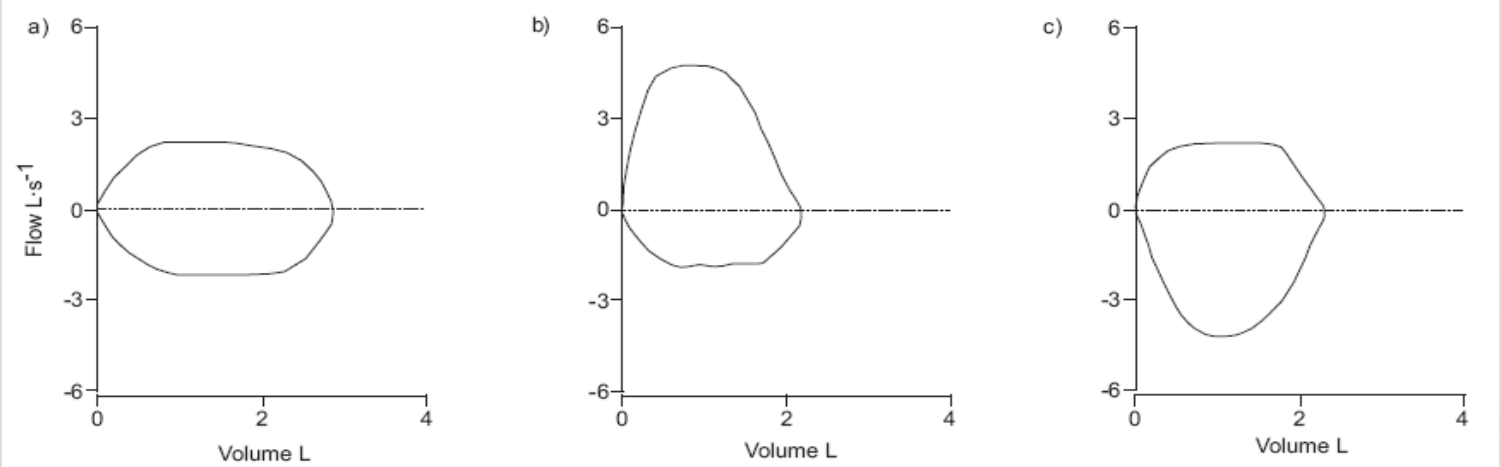


FIGURE 3. Idealised examples of a) fixed, b) variable extrathoracic, and c) variable intrathoracic airway obstruction.

"In is out, out is in"

Inspiratory loop – Extra-thoracic

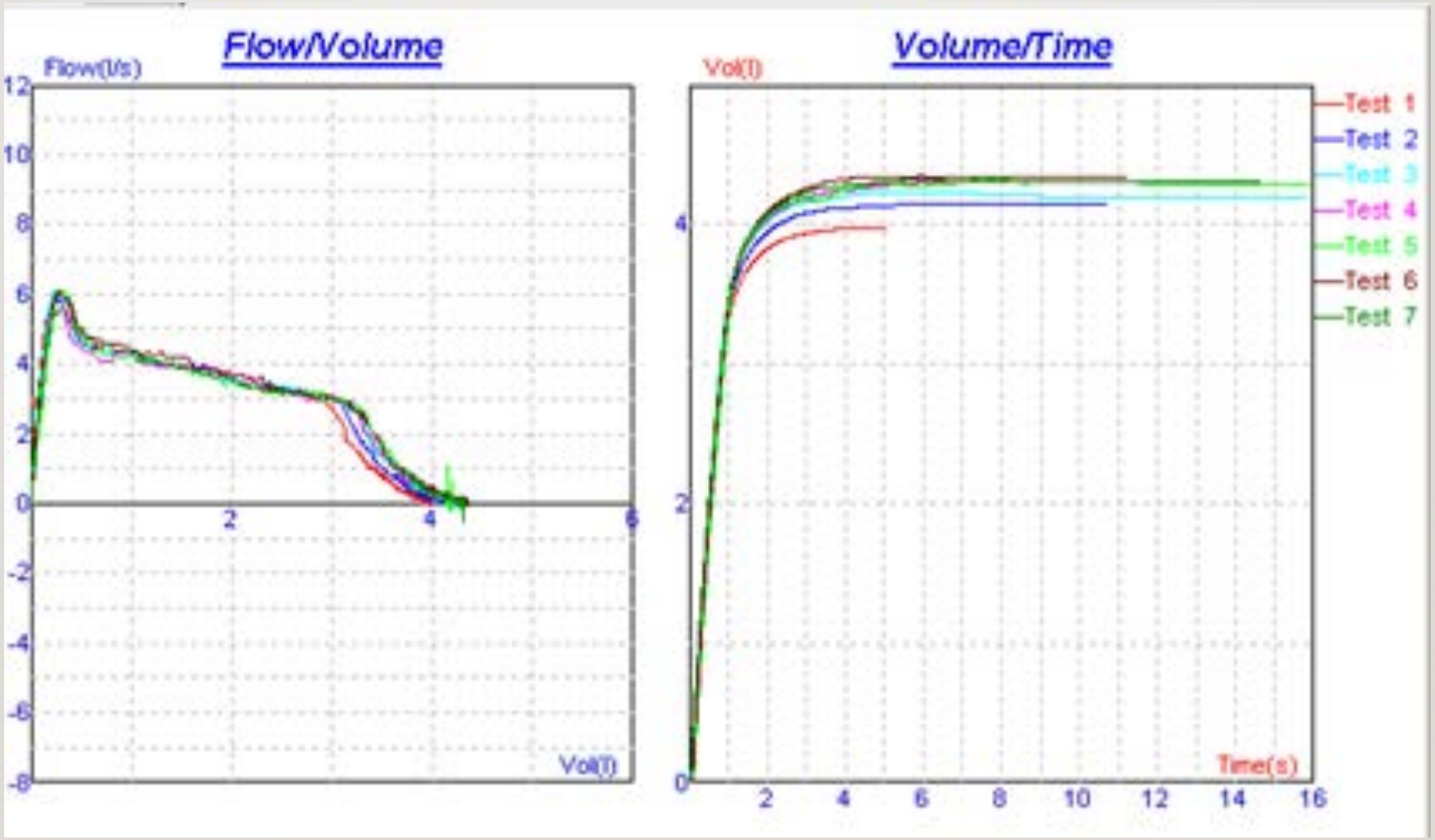
Expiratory loop – Intra-thoracic

TABLE 10 Lung function parameters capable of differentiating extrathoracic from intrathoracic obstruction

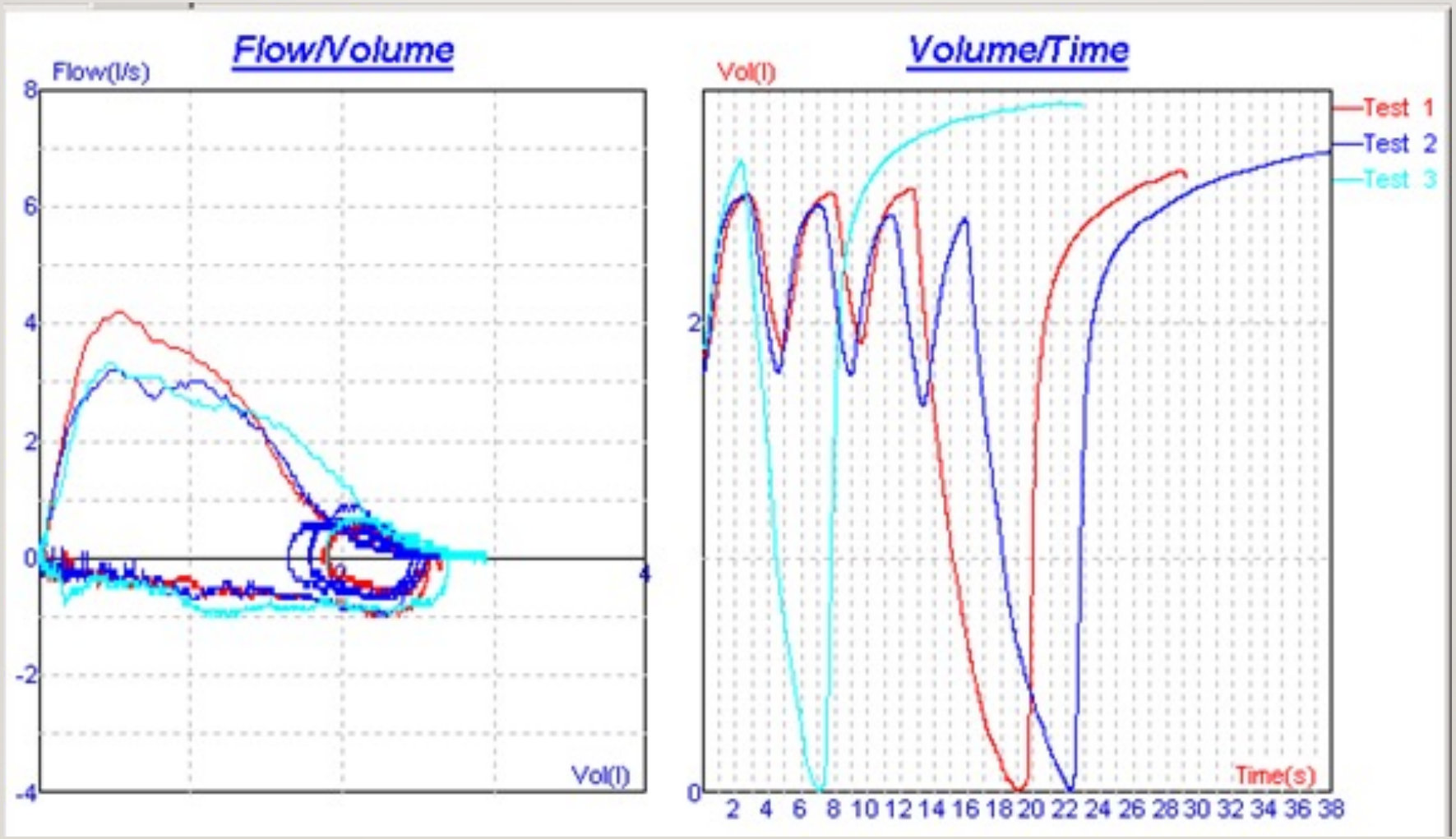
	Extrathoracic obstruction		Intrathoracic obstruction
	Fixed	Variable	
PEF	Decreased	Normal or decreased	Decreased
MIF_{50}	Decreased	Decreased	Normal or decreased
MIF_{50}/MEF_{50}	~1	<1	>1

PEF: peak expiratory flow; MIF_{50}: maximum inspiratory flow at 50% of forced vital capacity (FVC); MEF_{50}: maximum expiratory flow at 50% of FVC.

VARIABLE INTRA-THORACIC OBSTRUCTION



VARIABLE EXTRA-THORACIC OBSTRUCTION



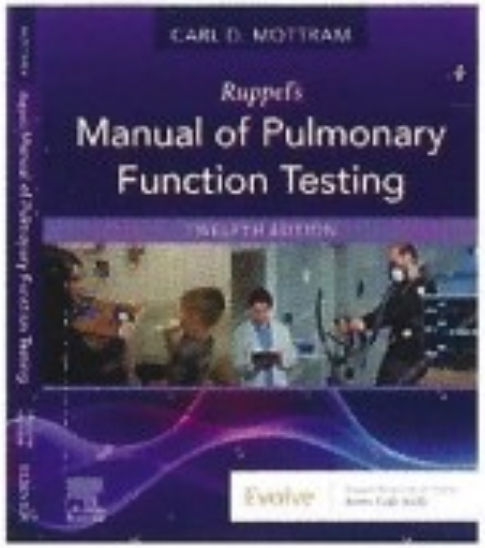
2021 ERS-ATS TS ON INTERPRETATIVE STRATEGIES

- FEV_1/PEF: Increased ratio of FEV_1 (in mL) to PEF (L/min) can alert the clinician to the need for an inspiratory and expiratory flow–volume loop
- An FEV_1/PEF ratio > 8 ml/L/min in adults suggests the presence of central or upper airway obstruction
  - Addition of a FV loop or FIVC to characterized the abnormality.

SUMMARY

- GLI recommended across spirometry, DLCO, and Lung volumes and the effect that may have on testing
  - Z – scores and the new cut-points for defining the degree of abnormality
- Bronchodilator responsiveness testing
  - 10% is now a positive response – predicted GLI
- Non-specific pattern – add BDR or SVCs (sRaw/sGaw)
- Central or upper airway obstruction – FEV_1/PEF ratio

QUESTIONS



Carl Mottram RRT RPFT FAARC
President - PFWConsulting LLC
PFWConsulting@gmail.com
507-261-4525

- Accreditation Readiness
- Clinical Trial Protocol Development
- Subject Matter Expert
- Lecturer and author