



PULMONARY FUNCTION TESTING

2023 UPDATE

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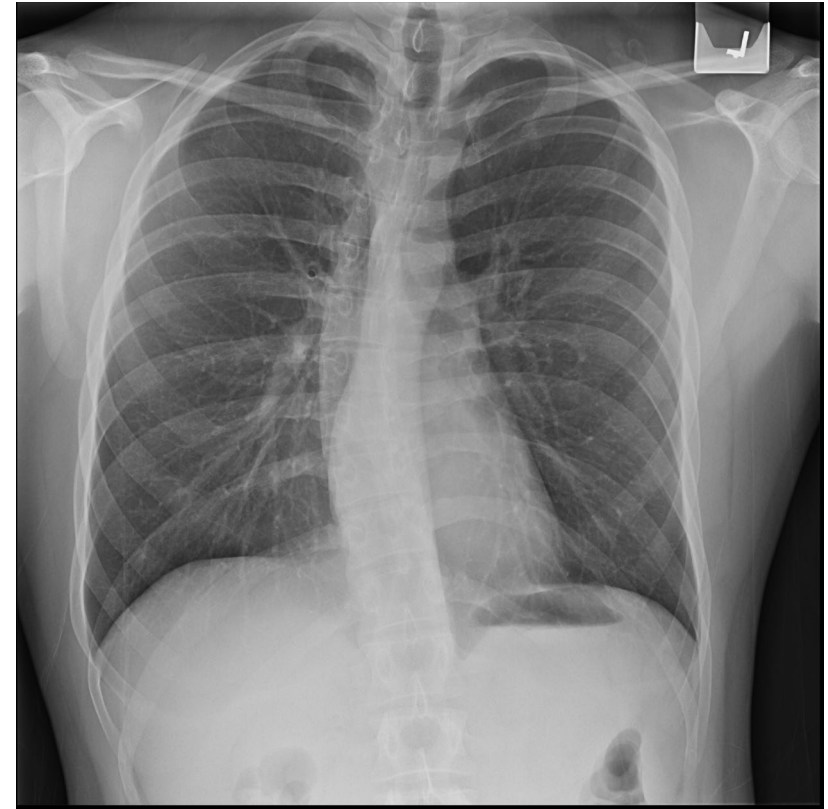
@niven_alex

OBJECTIVES

- Apply “new” ATS/ERS pulmonary function (PF) interpretation standards to case examples
- Describe anticipated differences in PF interpretation using “race neutral” reference equations
- Explain evolving PF lab infection control standards following the COVID-19 pandemic

CASE

- 21 year old patient with unexplained dyspnea
- Childhood asthma, competitive high school sports
- “Noisy breathing” with ROTC activities
- Multiple food, environmental allergies
- Positive MCT, “possible PVFM”
- Dulera, Symbicort, Advair, Singulair, Albuterol, Xolair
- Normal physical exam, CBC, BMP, TSH, CXR



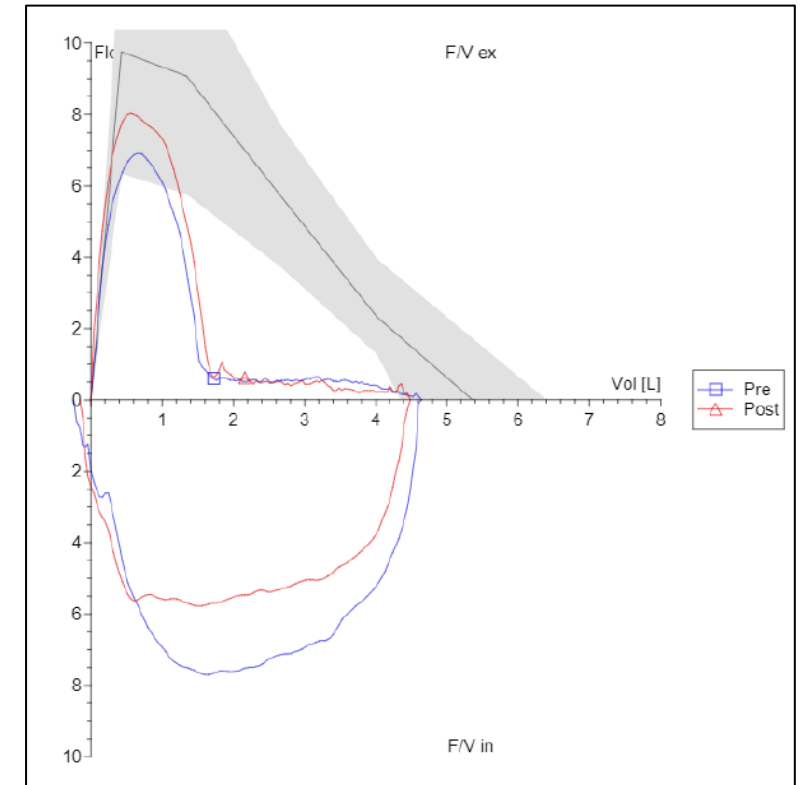
21 year old male

Ht 175.3 cm

Wt 72.6 kg

BMI 24 kg/m²

	Measured	% Predicted	Post-BD
TLC (L)	6.62	100%	
RV (L)	1.75	125%	
RV/TLC	26	125%	
FVC (L)	4.51	84%	4.56 (1%)
FEV ₁ (L)	1.68	37%	2.13 (10%)
FEV ₁ /FVC	37.3		
DLCO (adj)	37.5	115%	

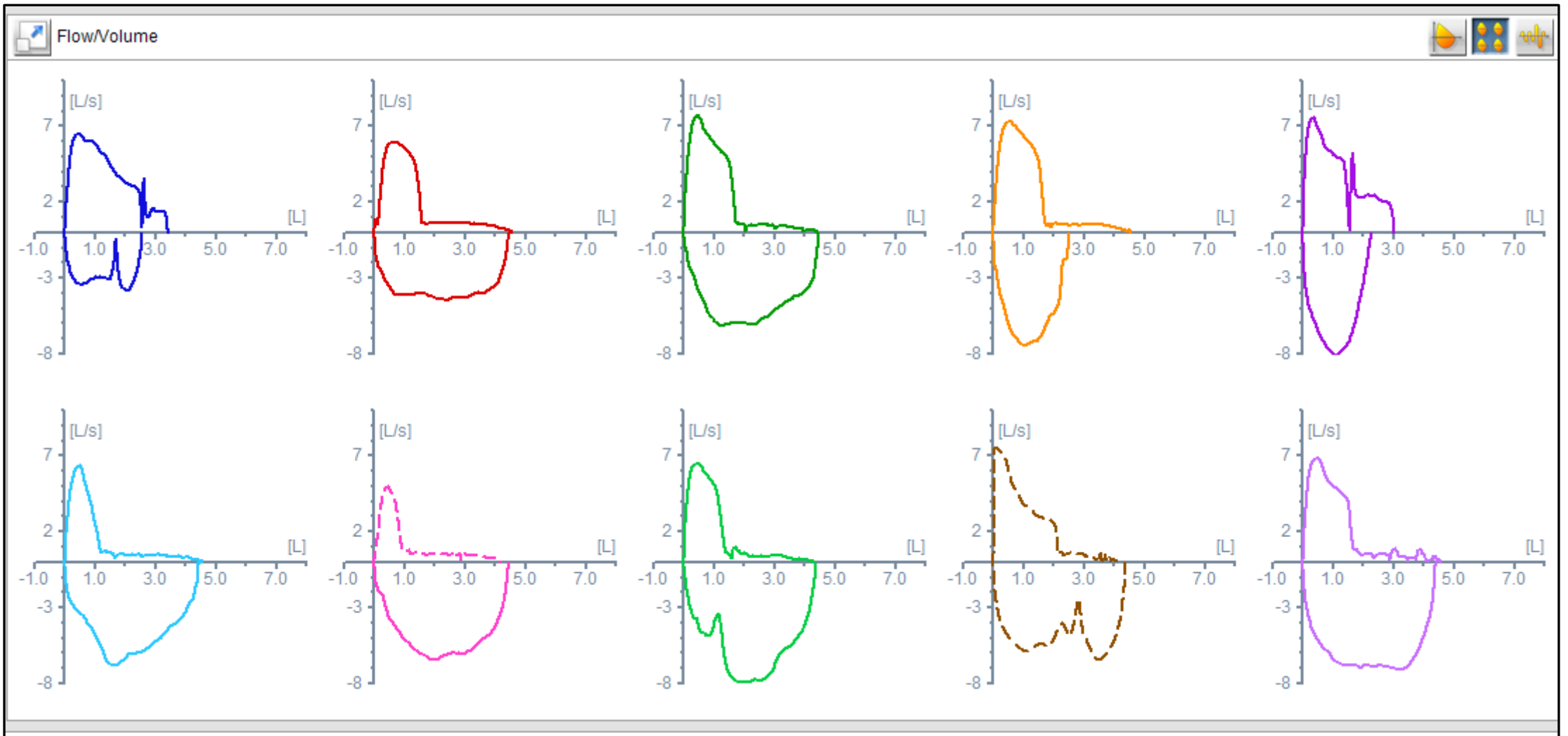


What is the most appropriate next step?

- A. Review individual FVL efforts
- B. Inspiratory / expiratory CT chest
- C. Perform bronchoscopy
- D. Initiate mepolizumab

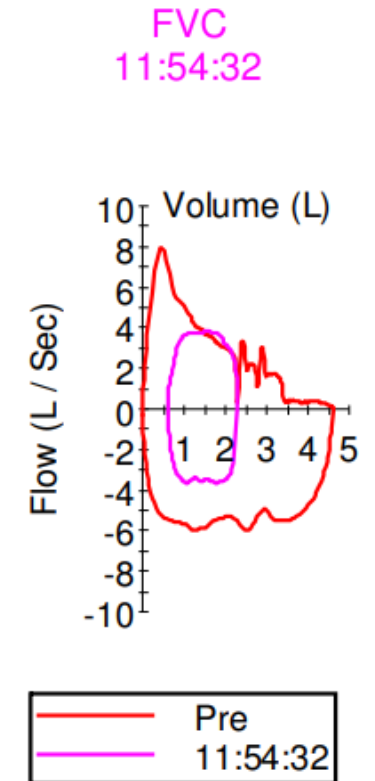
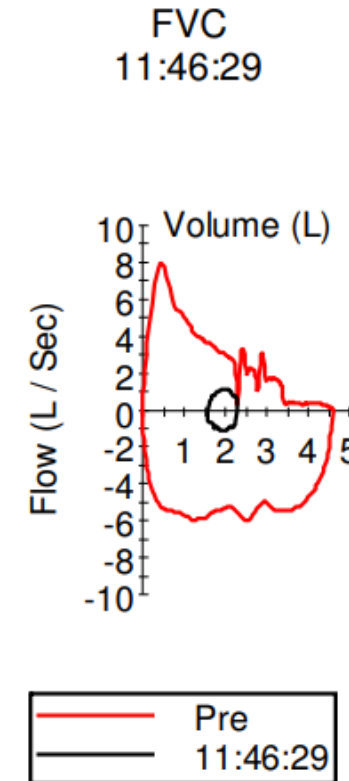
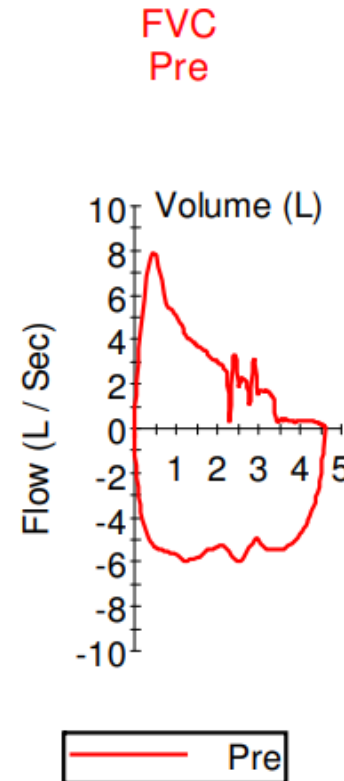
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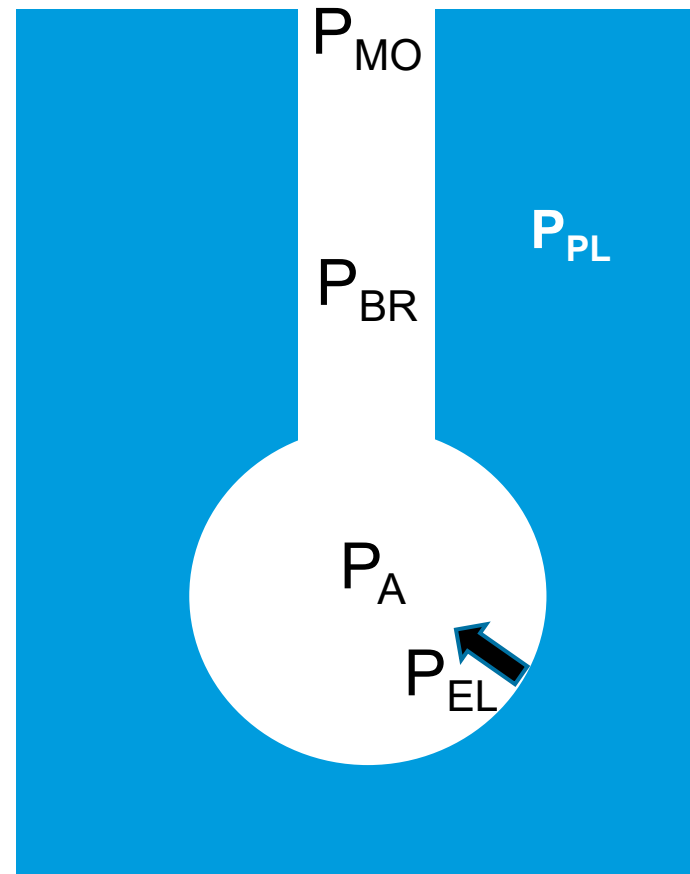
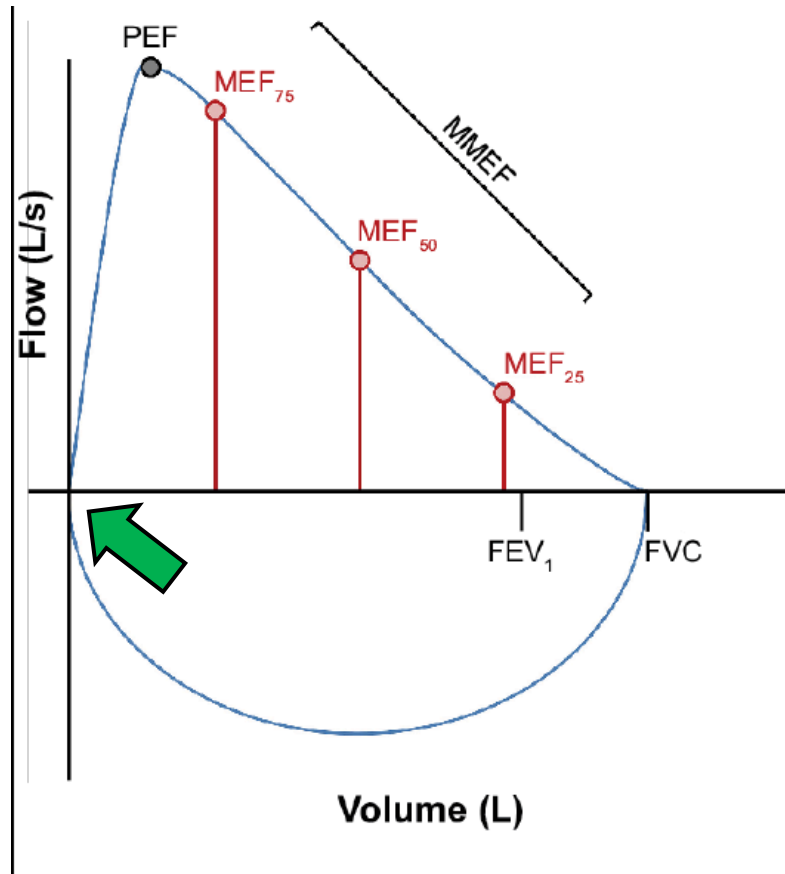


Evaluation

- Normal
 - Inspiratory / expiratory CT
 - Bronchoscopy
 - CPET
 - Impulse oscillometry
- Possible PVFM at end exercise



ANATOMY OF FLOW VOLUME CURVE

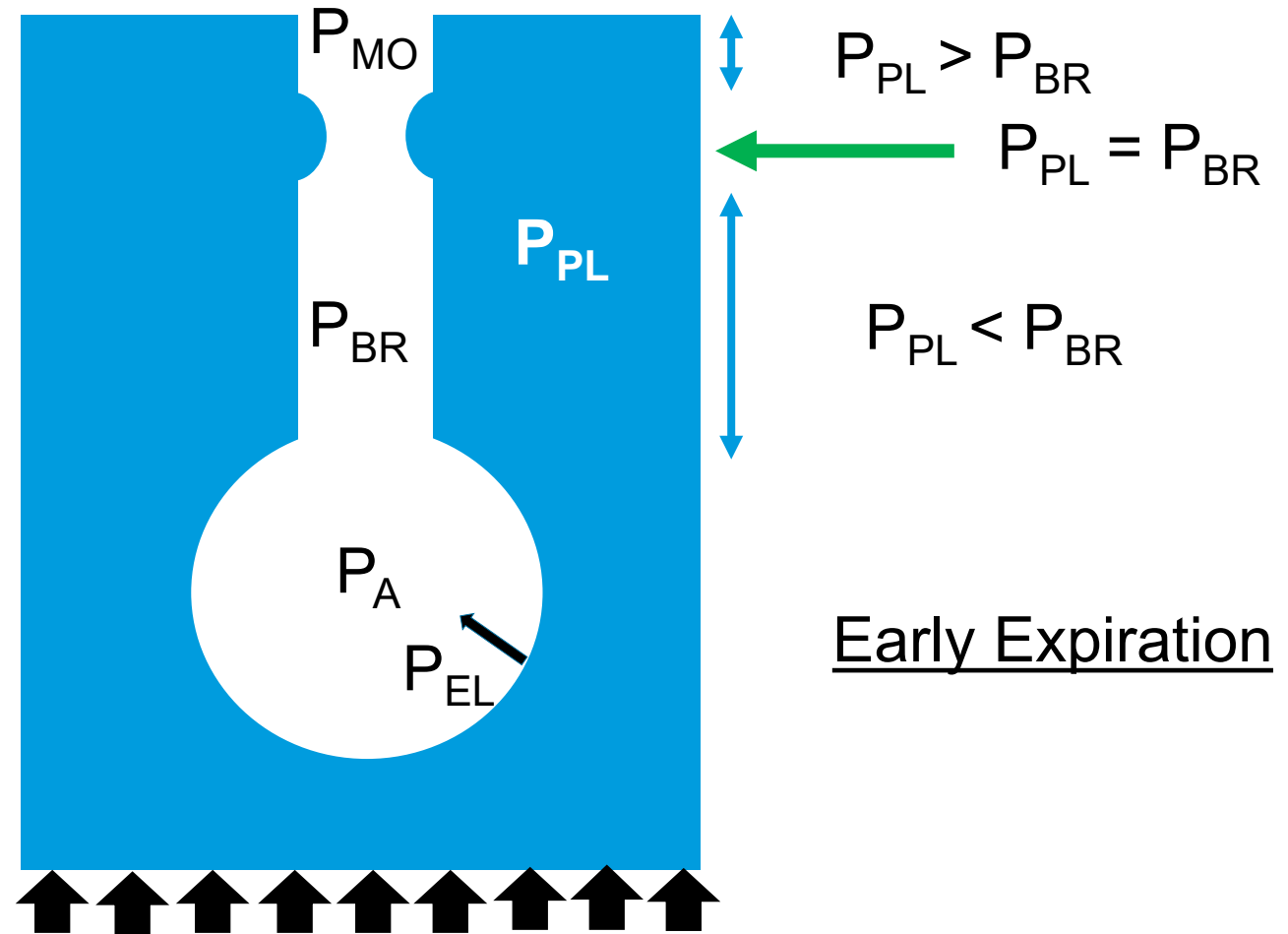
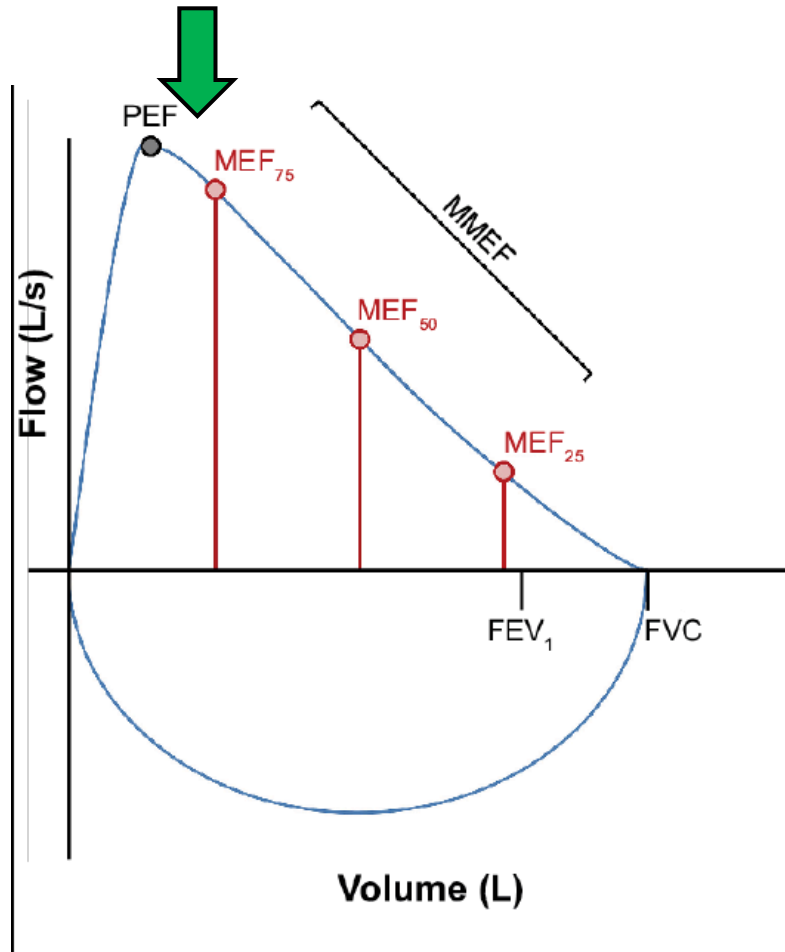


Full Inspiration

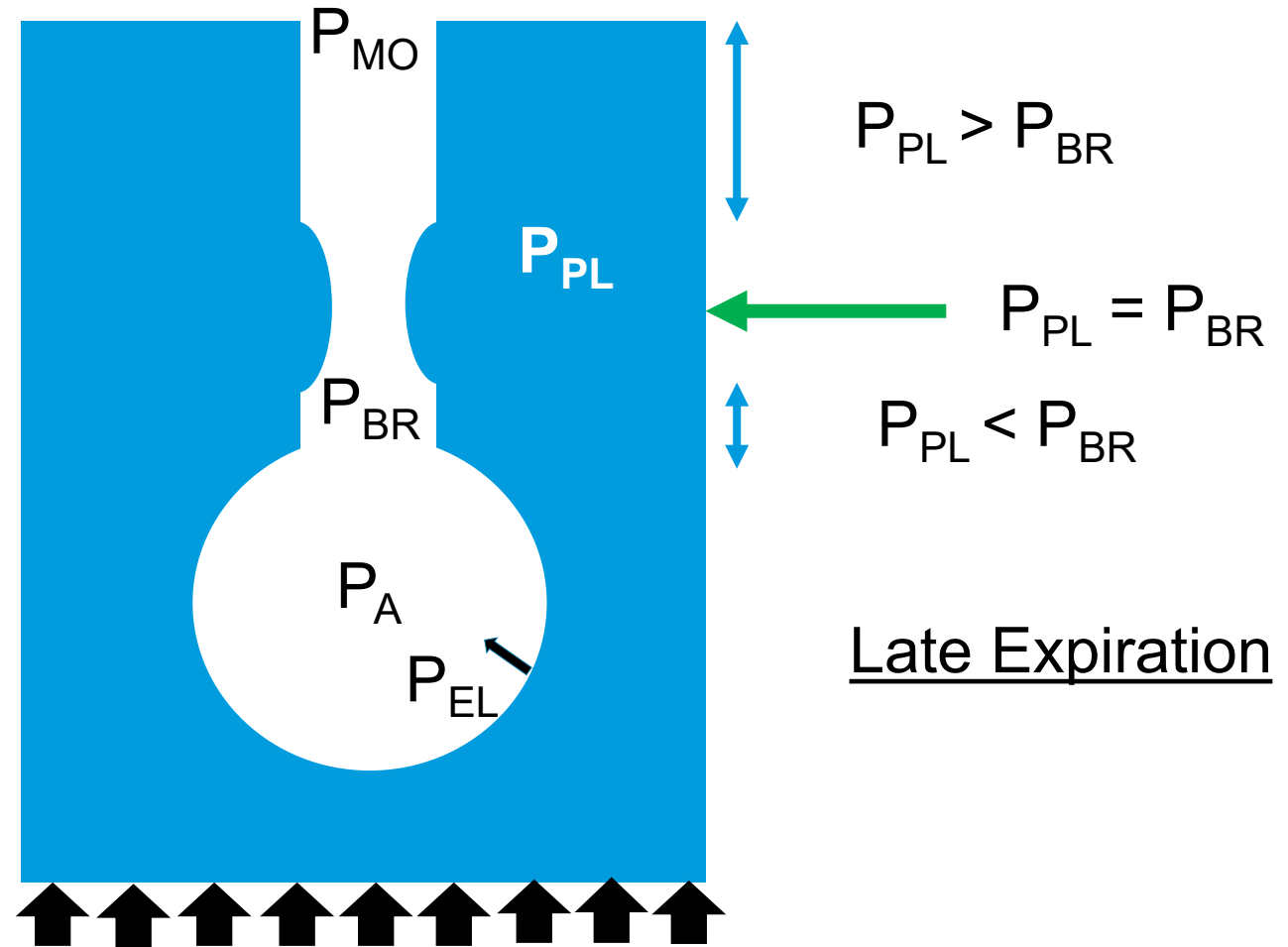
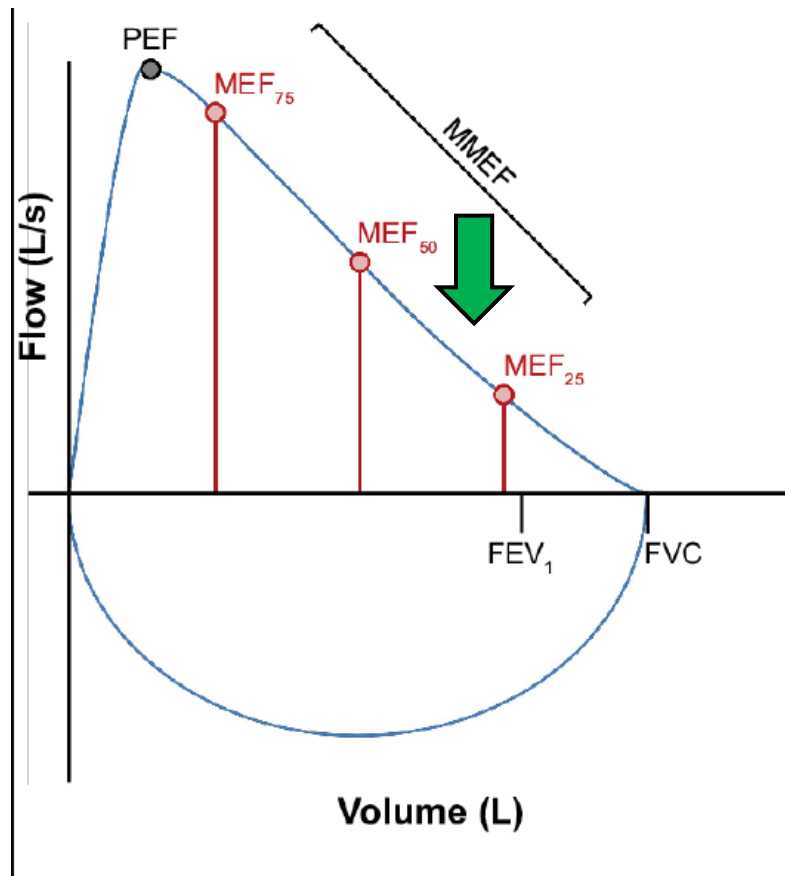
$$P_A = P_{BR} = P_{MO} = P_B$$

$$P_{PL} = P_B - P_{EL}$$

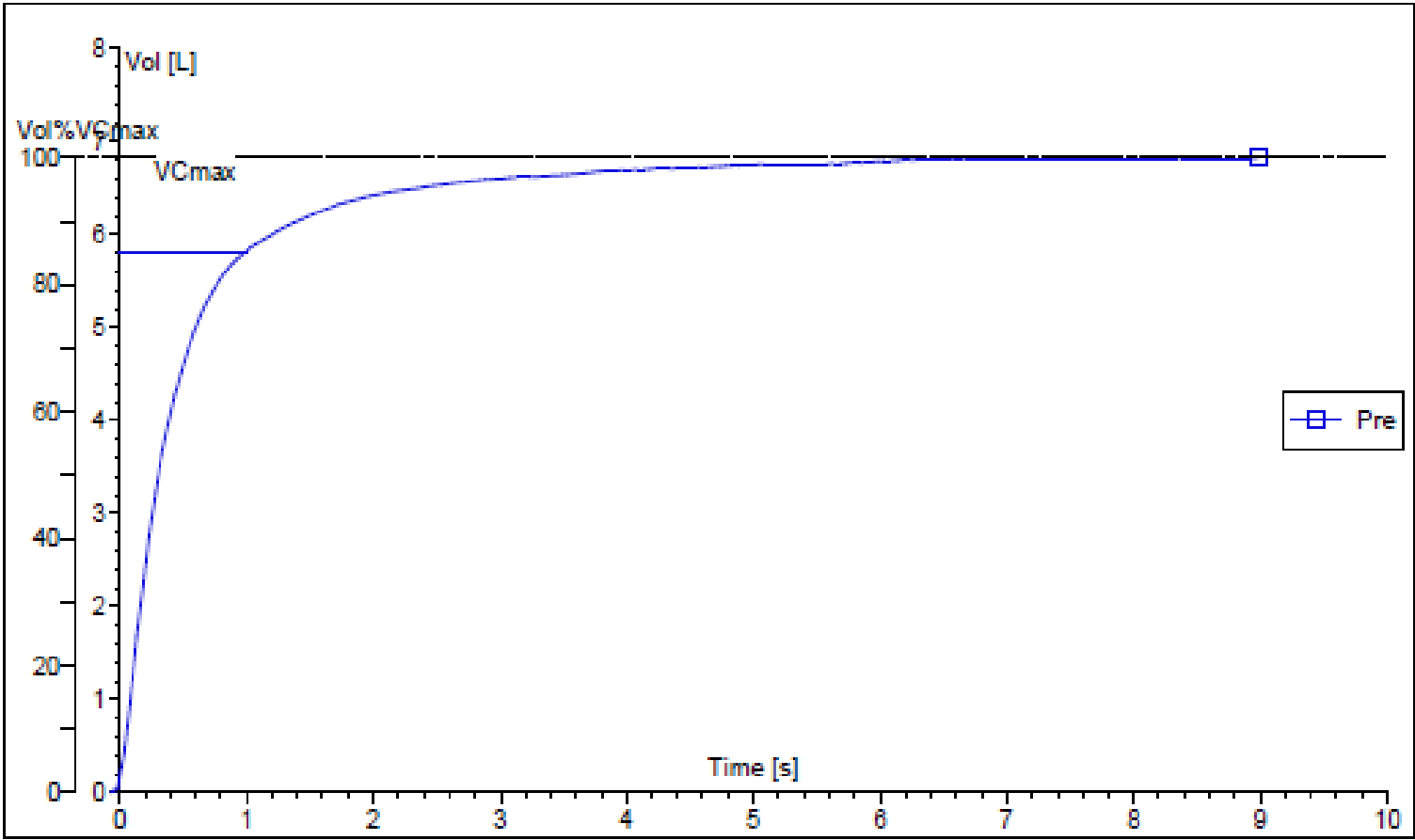
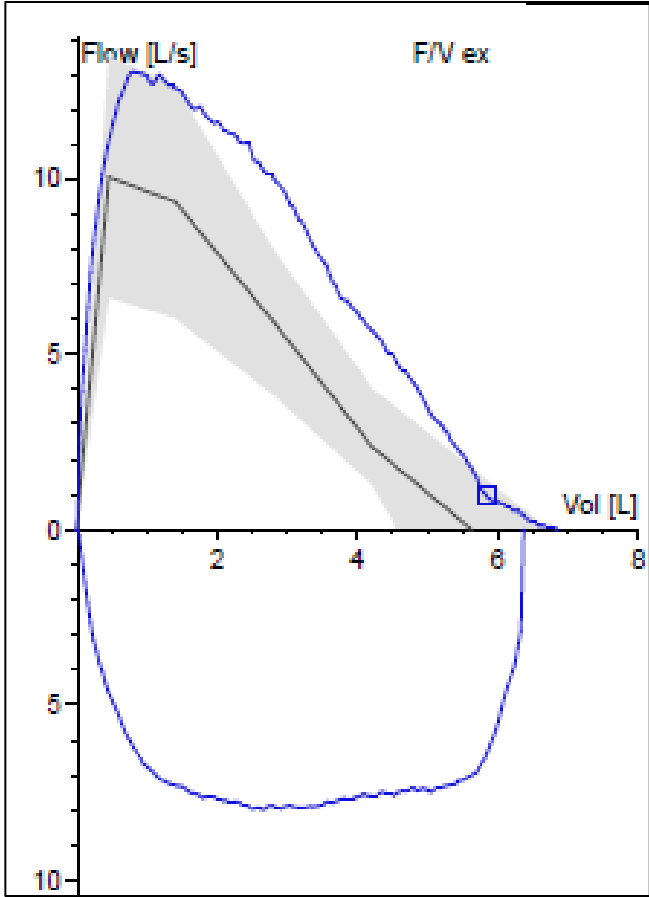
ANATOMY OF THE FLOW VOLUME CURVE



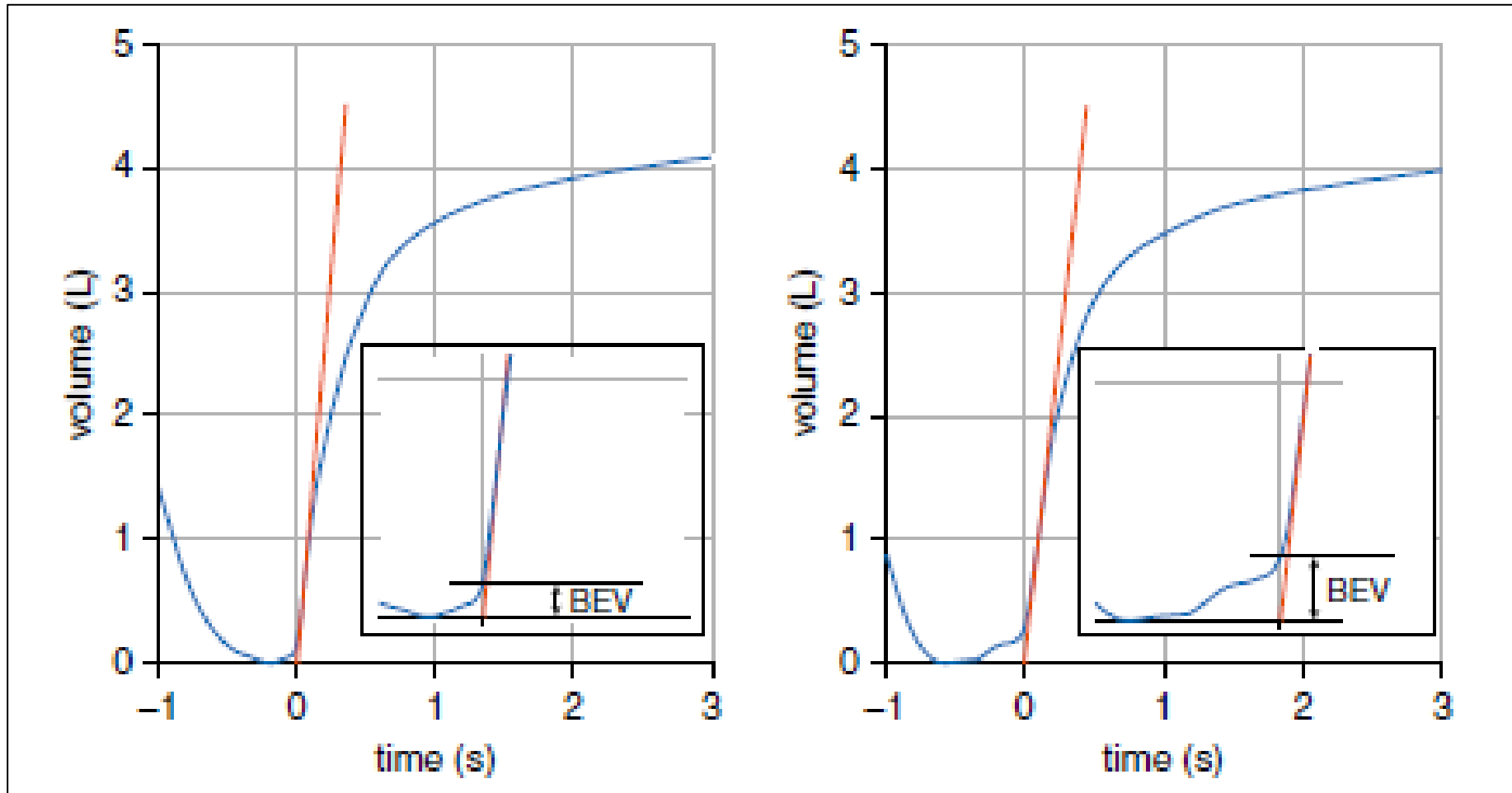
ANATOMY OF THE FLOW VOLUME CURVE



ACCEPTABILITY CRITERIA



BACK EXTRAPOLATED VOLUME



ACCEPTABILITY CRITERIA

- Back extrapolated volume \leq 5% FVC or 0.100 L (greater value)
- No evidence of faulty zero flow setting
- No cough, glottic closure in first second of expiration
- Achieve one of three end of forced expiration criteria:
 - Expiratory plateau (\leq 0.025 L in last second of expiration)
 - Expiratory time \geq 15 s
 - FVC repeatable or is $>$ than largest prior FVC
- No evidence of obstructed mouthpiece, leak
- If FIVC $>$ FVC, difference is \leq 0.100 L or 5% FVC (greater value)

REPEATABILITY VS REPRODUCIBILITY

Repeatability Criteria

- Difference between two largest FVC, $FEV_1 < 0.150$ L
- “Three acceptable, two repeatable maneuvers”
- Largest FVC, FEV_1 reported
 - May be from different maneuver

Reproducibility Criteria

- Reproducible results over time
 - FEV_1 most reproducible
- Mayo Lab Standards
 - FVC 0.250 L
 - FEV_1 0.220 L
 - TLC 0.320 L
 - DLCO 3.2 ml/(min*mmHg)

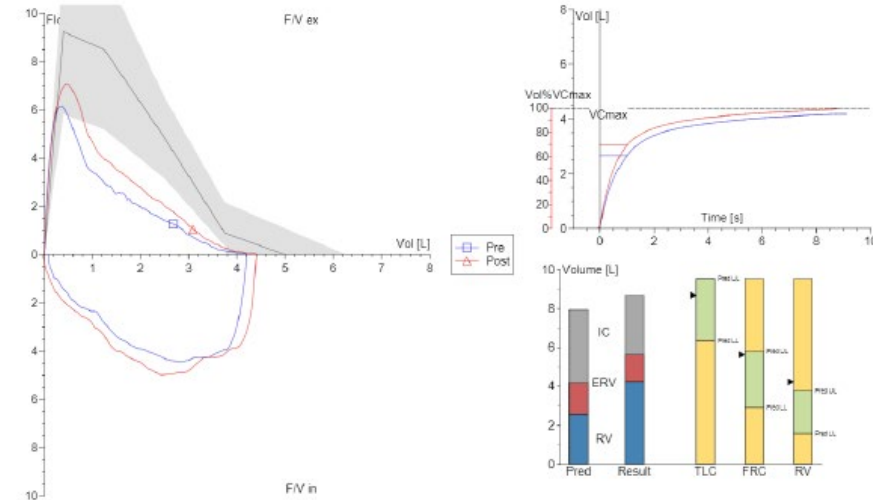
63 year old male

Ht 185.5 cm

Wt 97.9 kg

BMI 28 kg/m²

	Measured	% Predicted	Z score	Post-BD
TLC (L)	8.69	109%	0.77	
RV (L)	4.24	165%	2.25	
RV/TLC	49	154%		
FVC (L)	4.17	84%	-1.10	4.36 (4%)
FEV ₁ (L)	2.65	70%	-1.92	3.06 (11%)
FEV ₁ /FVC	63.5		-1.70	
DLCO (unadj)	26.5	90%	-0.63	



How do you grade airflow obstruction severity?

A. ATS 1994

B. ATS 2005

C. Z score

D. GOLD

E. FEV₁Q

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A. ATS 1994

B. ATS 2005

C. Z score

D. GOLD

E. FEV₁Q

AIRFLOW OBSTRUCTION SEVERITY

FEV1 (% pred)	ATS 1994	ATS 2005	Z score	GOLD	FEV1Q
2.65 (70%)	Mild	Moderate	Mild	Moderate (GOLD 2)	5.3

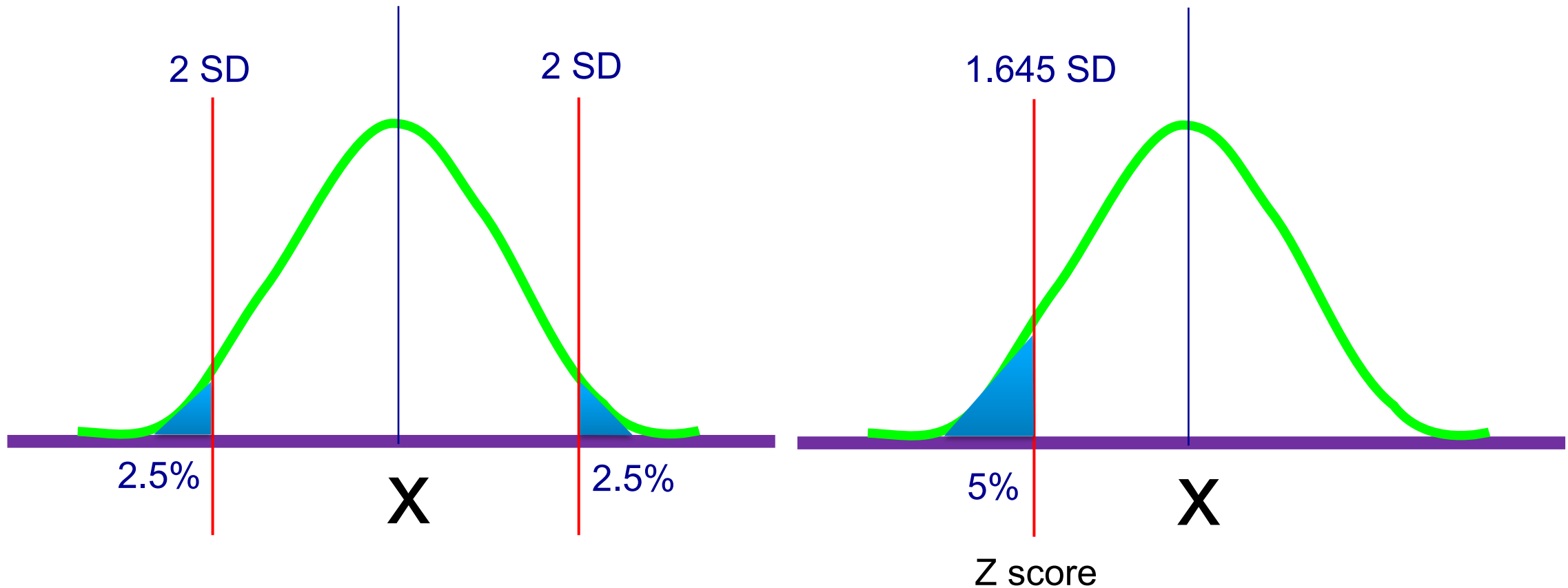
ATS. Am J Respir Crit Care Med 1995; 152: 1107-36

Miller MR et al. Eur Respir J 2005; 26: 319-338

GOLD 2023 Report <https://goldcopd.org/2023-gold-report-2/> accessed September 1, 2023

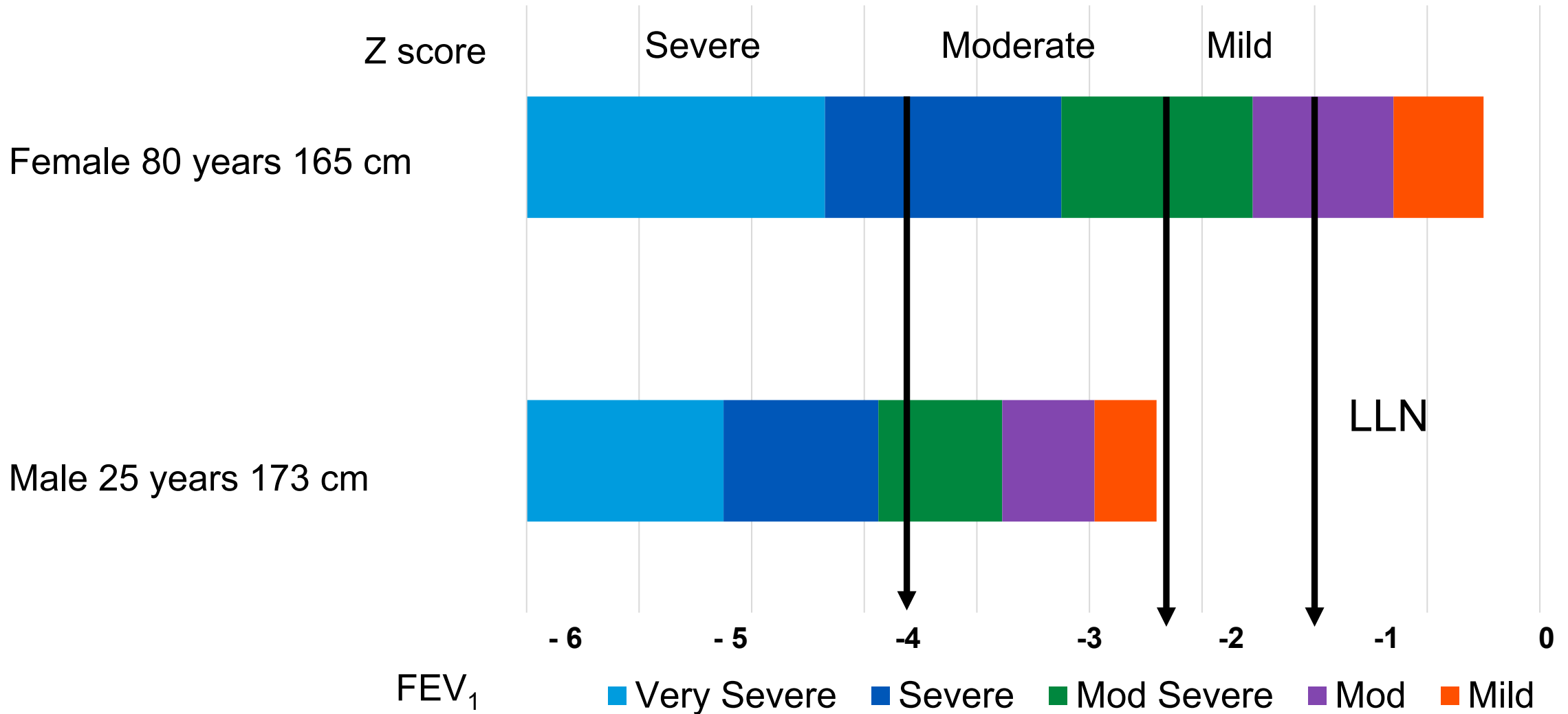
Stanojevic S et al. Eur Respir J 2022; 60(1): 2101499

REFERENCE VALUES IN PULMONARY TESTING



ATS. Am Rev Respir Dis 1991;144: 1202-1218
Pellegrino R et al. Eur Respir J 2005; 26: 948-968

SEVERITY SCORING USING Z SCORES



PFT INTERPRETIVE STRATEGIES

- Use z scores (+/- 1.645 SD; 5th, 95th percentile) for LLN
- Bronchodilator response defined as $\Delta \geq 10\%$ predictive value

$$(\text{FEV}_{1\text{post}} - \text{FEV}_{1\text{pre}}) / \text{FEV}_{1\text{pred}} \times 100$$

- Limited data to guide lung function changes over time
- $\text{FEV}_1\text{Q} = \text{Observed FEV}_1 \text{ (L)} / \text{sex-specific first percentile of FEV}_1 \text{ distribution}$
- 0.5 L (men), 0.4 L (women)
- Index approximates “turnovers” remaining of a lower survivable FEV_1 limit

Stanojevic S et al. Eur Respir J 2022; 60(1): 2101499

Hall GL et al. Eur Respir J 2021; 57: 2000289

Elmaleh-Sachs A et al. Am J Respir Crit Care Med 2021; 205(6): 700-710

McCormack MC et al. Am J Respir Crit Care Med 2021; 206(6):723-6



What spirometry reference equations do you use?

A. NHANES

B. ECCS/ERS

C. GLI-2012

D. GLI Global



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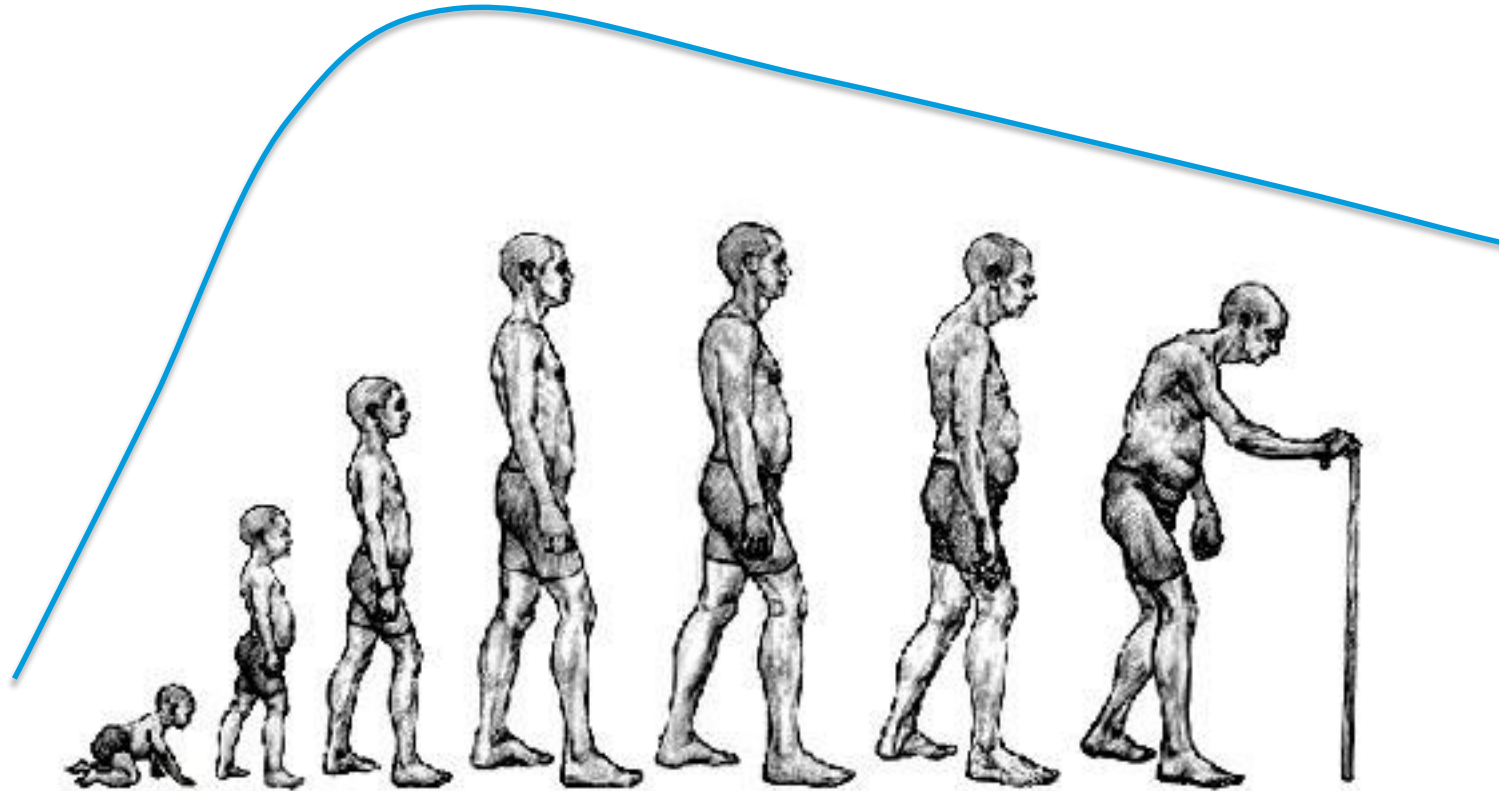
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LUNG FUNCTION AND AGING

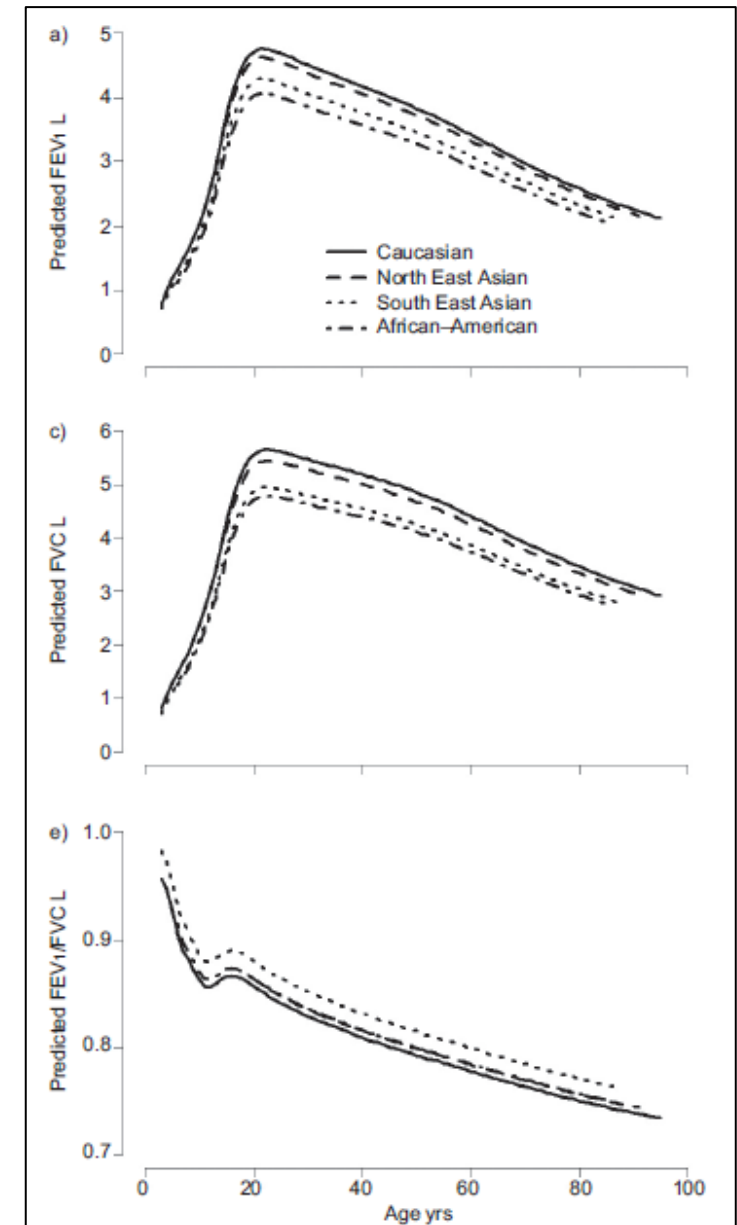


Sharma G et al. Clin Interv Aging 2006; 1(3): 253-260

SOURCES OF VARIABILITY

FVC, FEV₁ {

Age	8%	— FEV ₁ /FVC
Standing height	20%	
Gender	30%	
Ethnic group	10%	
Body weight	2%	
Technical factors	3%	
Unexplained	30%	



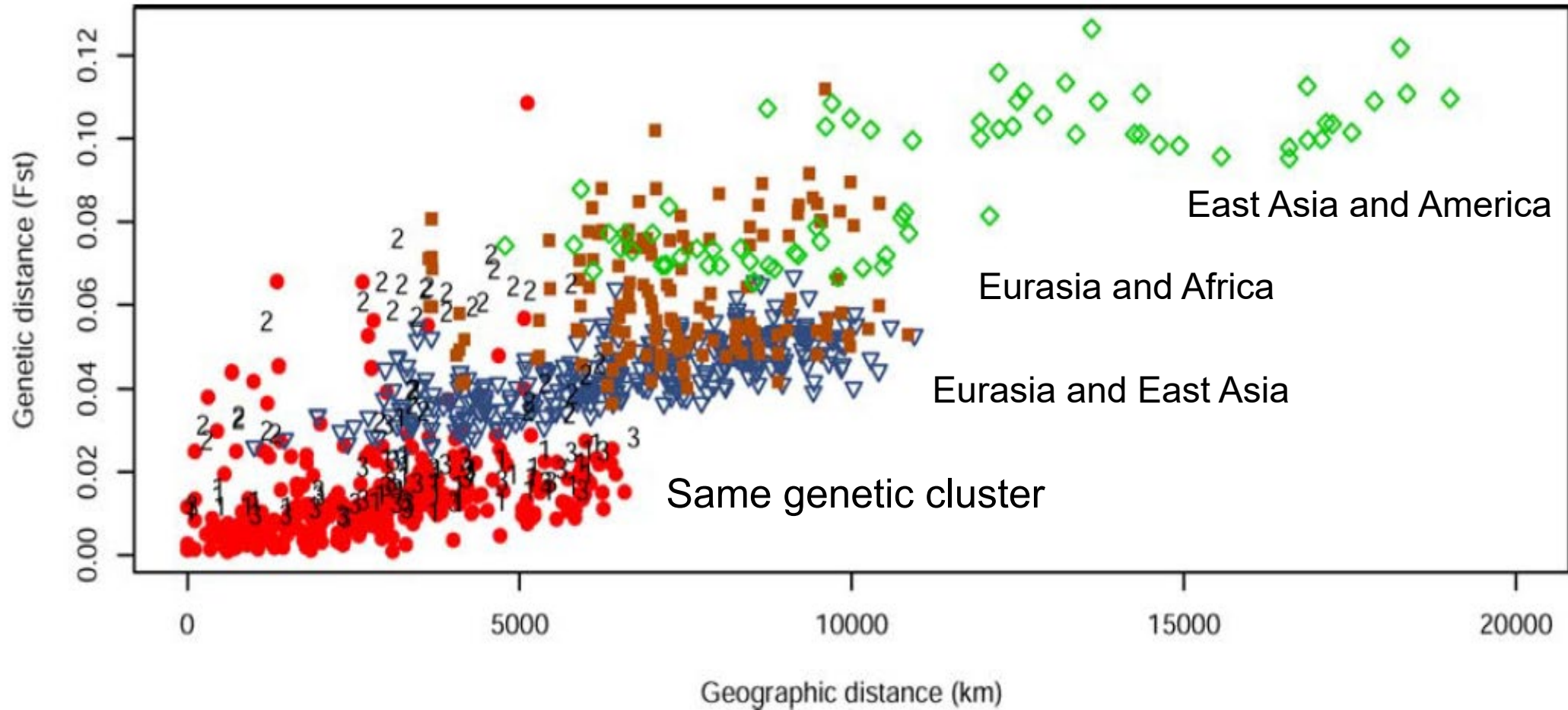
Becklake MR. Am J Med 1986; 80: 1158-1164
 Quanjer PH et al. Eur Respir J 2012; 40: 1324-43

LUNG FUNCTION DIFFERENCES BY ANCESTRAL ORIGIN

Pulmonary Function Differences by Sex, Ethnic Group (% Δ vs Caucasians)						
	Male			Female		
	FEV ₁	FVC	FEV ₁ /FVC	FEV ₁	FVC	FEV ₁ /FVC
African American	-13.8	-14.4	0.6	-14.7	-15.5	0.8
North East Asian	-0.7	-2.1	1.1	-2.7	-3.6	0.9
South East Asian	-13.0	-15.7	2.9	-9.7	-12.3	2.8

American Thoracic Society. Am Rev Respir Dis 1991; 144: 1202-18
 Quanjer PH et al. Eur Respir J 2012; 40: 1324-43

RACE, ETHNICITY, AND LUNG FUNCTION



Rosenberg NA et al. PLoS Genetics 2005; 1(6): e70

ANCESTRAL ORIGIN AND LUNG FUNCTION

- Standing vs sitting height impacted by socioeconomic status, education, nutrition, exposures
- Survival similar for same absolute FEV₁ in Caucasians, Blacks
 - Caucasians with better survival using adjusted % predicted
- Race adjusted equations may lead to underestimation of lung function impairment, limiting access to therapies
- “Race-neutral” GLI Global equations recommended by ATS/ERS

Harik-Khan RK et al. Am J Respir Crit Care Med 2001; 164: 1647-54

Jones RL et al. Chest 2006; 130: 827-33

Burney PG et al. Int J Epidemiol 2012; 41: 782-790

Hill NS. Proc Am Thorac Soc 2006; 3: 66-74

Kaminsky DA. Am J Respir Crit Care Med 2022; 205: 746-48

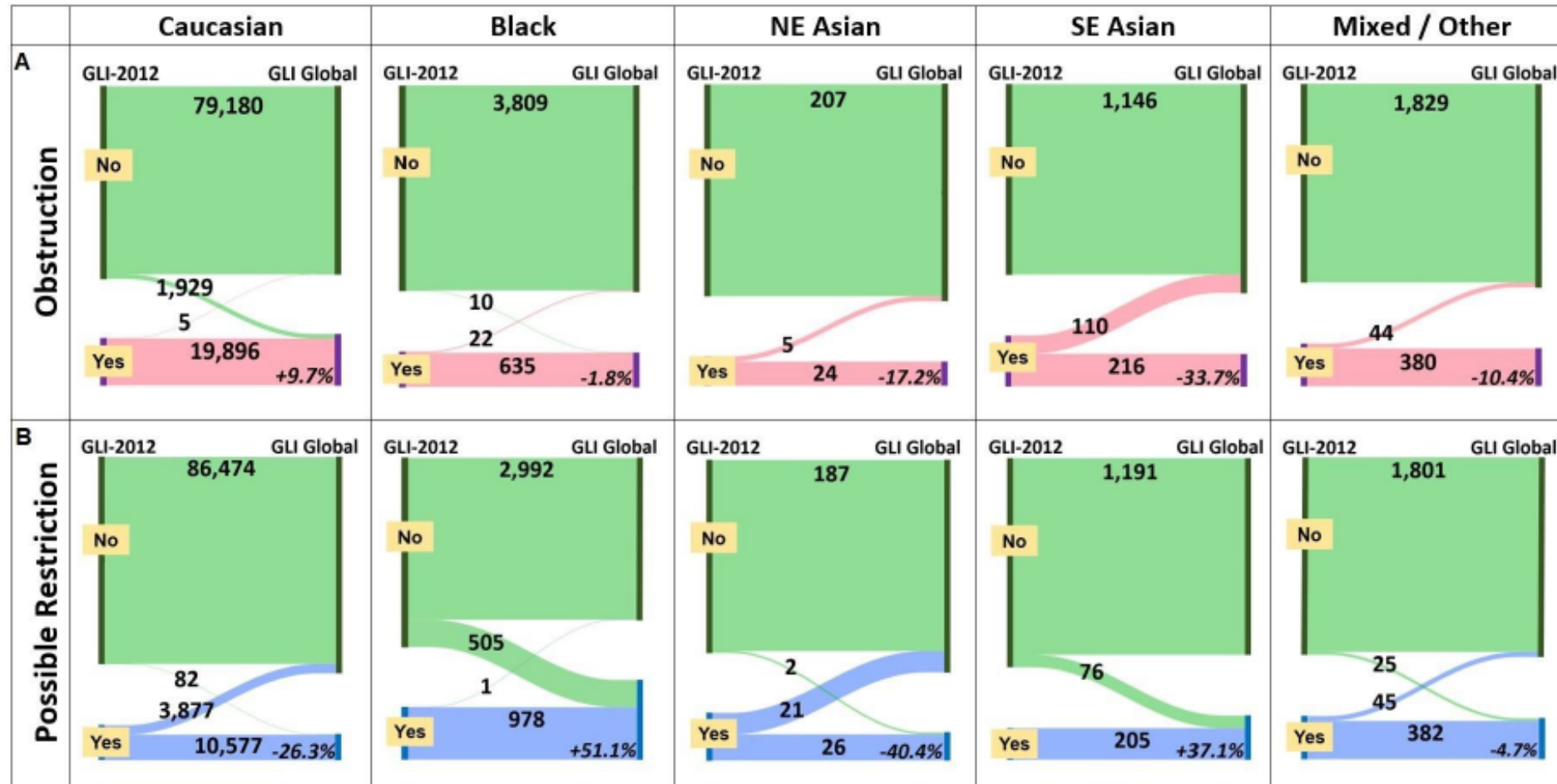
McCormack MC et al. Am J Respir Crit Care Med 2022; 205: 723-24

Bowerman C et al. Am J Respir Crit Care Med 2023; 207(6): 768-74

Bhakta NR et al. Am J Respir Crit care Med 2023; 207(8): 978-95

IMPACT OF GLI GLOBAL TRANSITION

- 109,447 patients (Mayo Clinic Rochester, Jacksonville, Eau Claire)



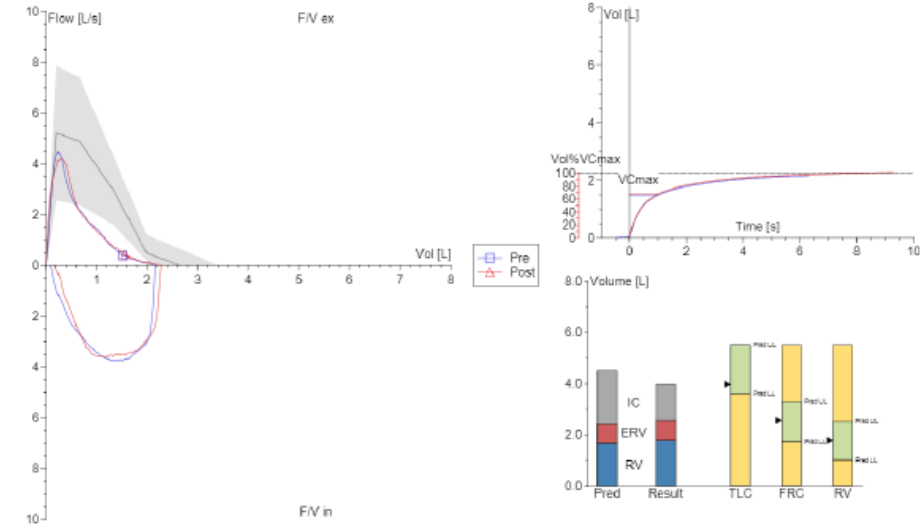
65 year old woman

Ht 154.6 cm

Wt 60.0 kg

BMI 25 kg/m²

	Measured	% Predicted	Z score	Post-BD
TLC (L)	3.96	88%	-0.93	
RV (L)	1.77	106%	0.23	
RV/TLC	44	122%		
FVC (L)	2.21	83%	-1.07	2.26 (2%)
FEV ₁ (L)	1.49	71%	-1.83	1.52 (2%)
FEV ₁ /FVC	67.5		-1.53	
DLCO (adj)	16.1	90%	-0.61	



What is Your Interpretation?

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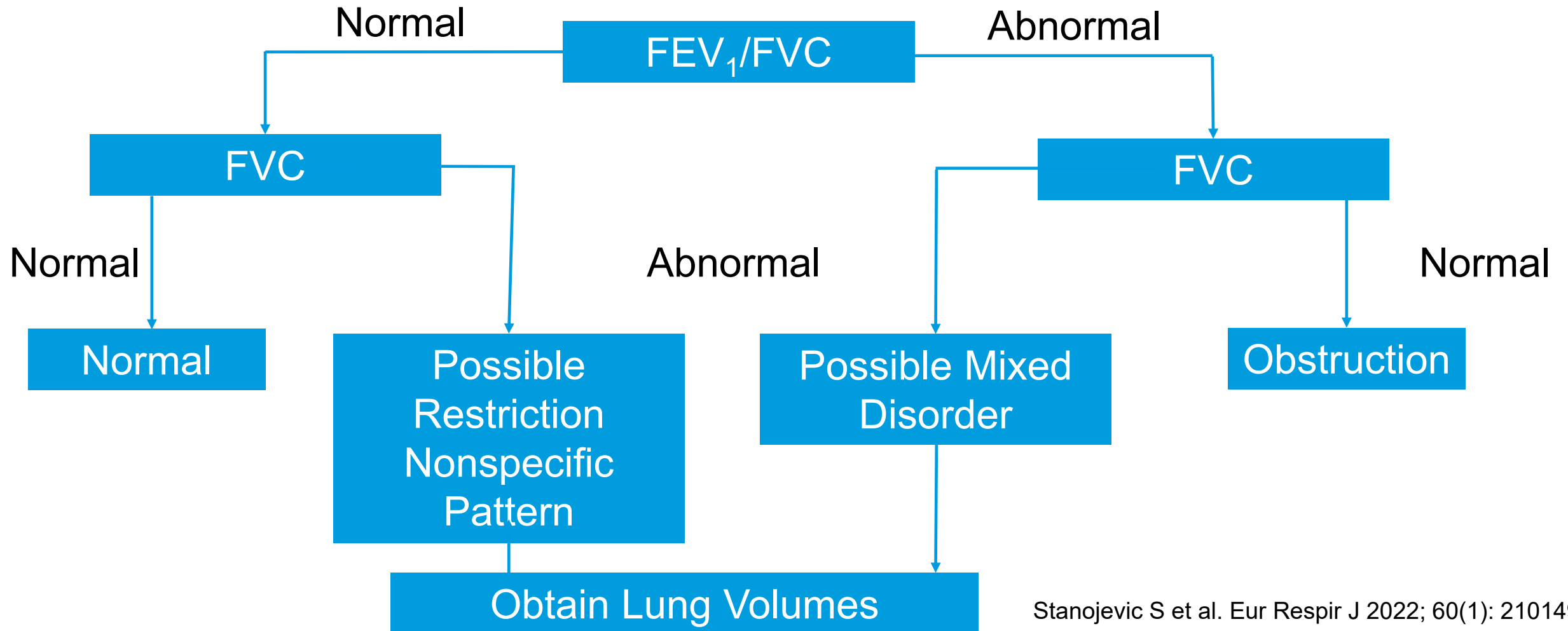
- A. Poor effort
- B. Non-specific
- C. Obstruction
- D. Restriction

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ERS/ATS INTERPRETIVE STRATEGIES



Stanojevic S et al. Eur Respir J 2022; 60(1): 2101499

NONSPECIFIC PATTERN

- Normal TLC_{pleth}
- Normal FEV_1/FVC ratio
- Low FVC, FEV_1 , or both
- $DLCO > LLN^*$
- 9.5% prevalence
 - 1991-2000
 - 80,929 subjects

Diagnosis	Men (n = 62)	Women (n = 38)	Combined (n = 100)
Airway hyperreactivity (AHR)	11 (18)	10 (26)	21 (21)
AHR with obesity	16 (26)	15 (40)	31 (31)
Chronic lung disease	13 (21)	3 (8)	16 (16)
Obesity	7 (11)	0 (0)	7 (7)
Other Chest wall / Neuromuscular (9) Parenchymal lung disease (6) CHF (5) S/P CABG, AAA (3)	15 (24)	10 (26)	25 (25)

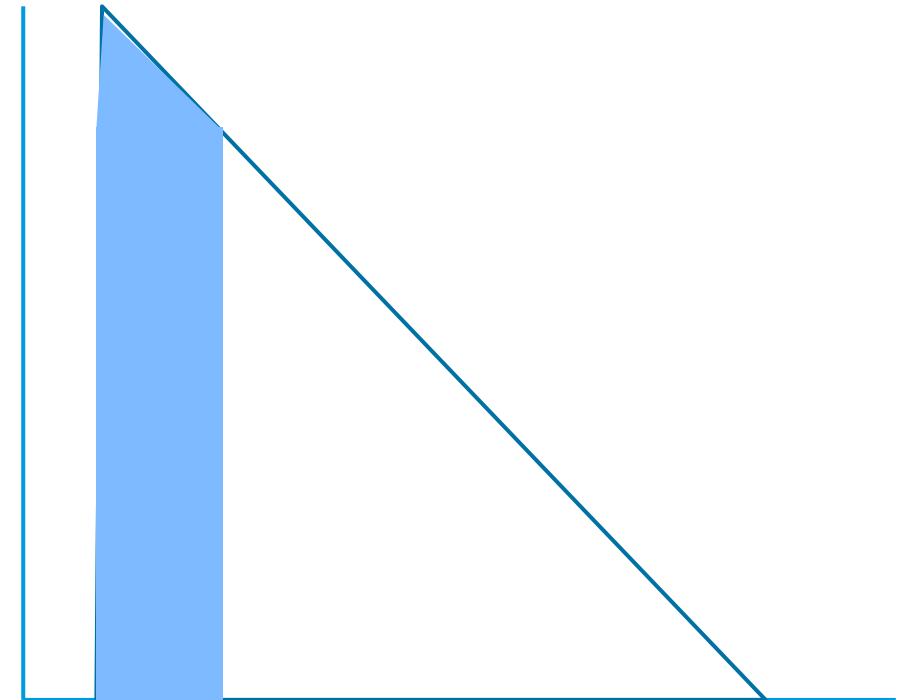
*Not included in subsequent studies

Hyatt RE et al. CHEST 2009; 135(2): 419-24

PHYSIOLOGIC CONSIDERATIONS

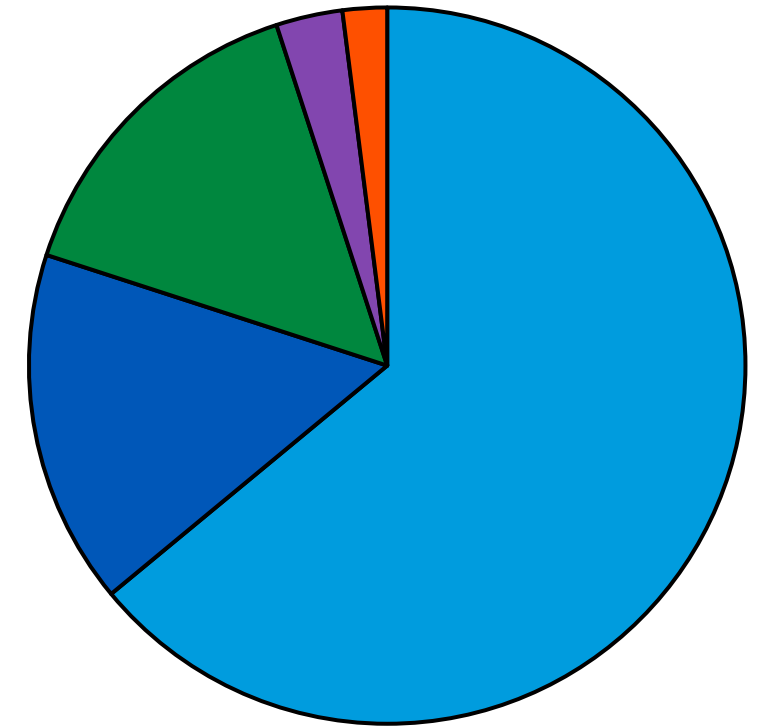
- Thoracic, neuromuscular impairment, obesity
- Volume de-recruitment, airway closure
- Inadequate inflation to TLC

BMI (kg/m ²)	Men (n,%)	Women (n,%)	Total (n,%)
< 25	10 (16.1)	13 (34.2)	23 (23)
25 – 29.9	20 (32.2)	7 (18.4)	27 (27)
30 – 34.9	16 (25.8)	9 (23.7)	25 (25)
35 – 39.9	12 (19.4)	6 (15.8)	18 (18)
≥ 40	4 (6.5)	3 (7.9)	7 (7)



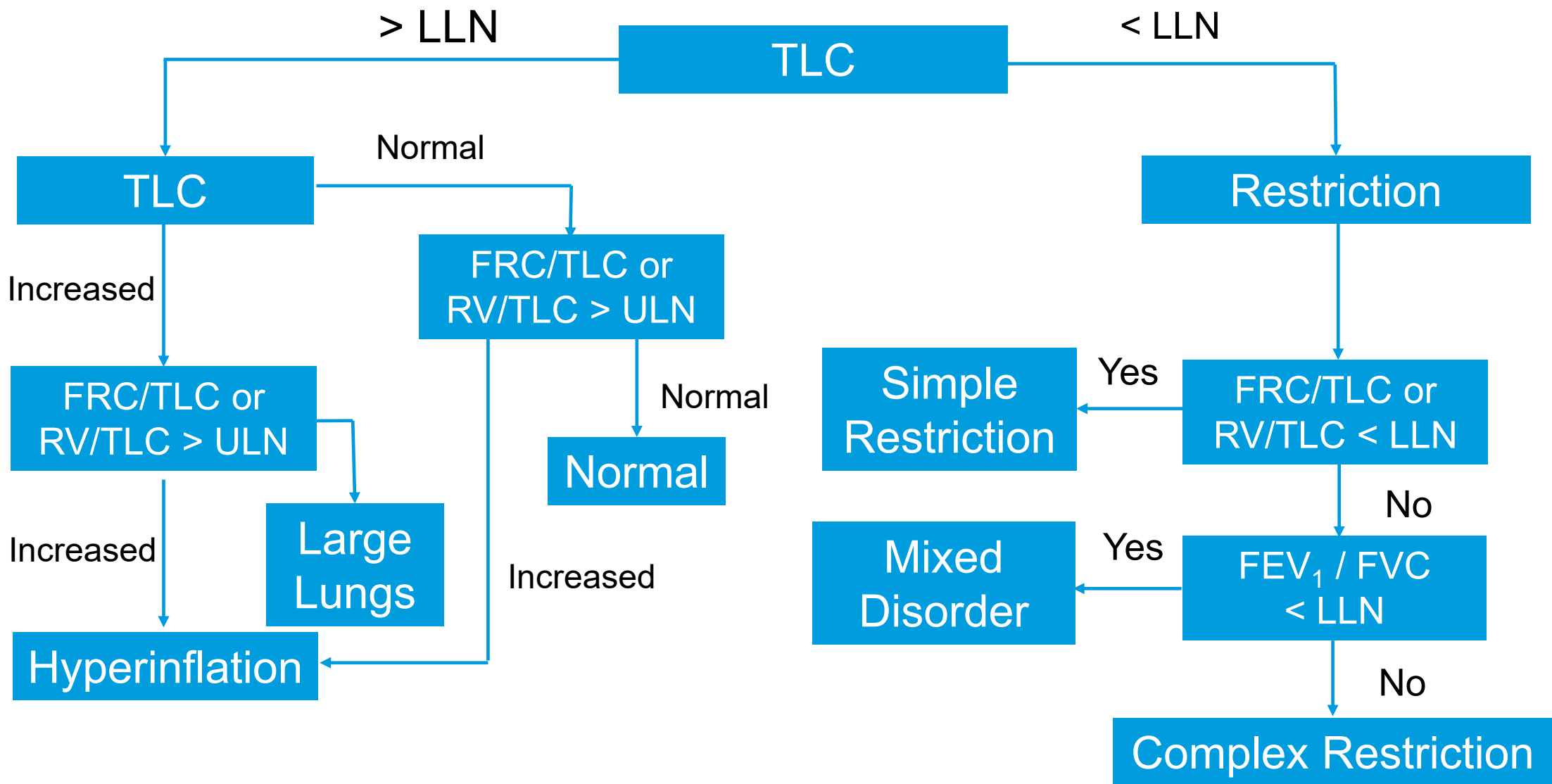
NONSPECIFIC PATTERN OVER TIME

- 1,284 patients
 - Normal / abnormal DLCO, ≥ 6 months f/u
 - Age, smoking status, BMI
 - BD response, sRaw, TLC- V_A , SVC-FVC
- 55% with bronchodilator response
 - 24% developed obstruction ($p = 0.04$)
 - Stratification using sRaw, TLC – V_A
- Similar FEV₁ decline (Lung Health Study)



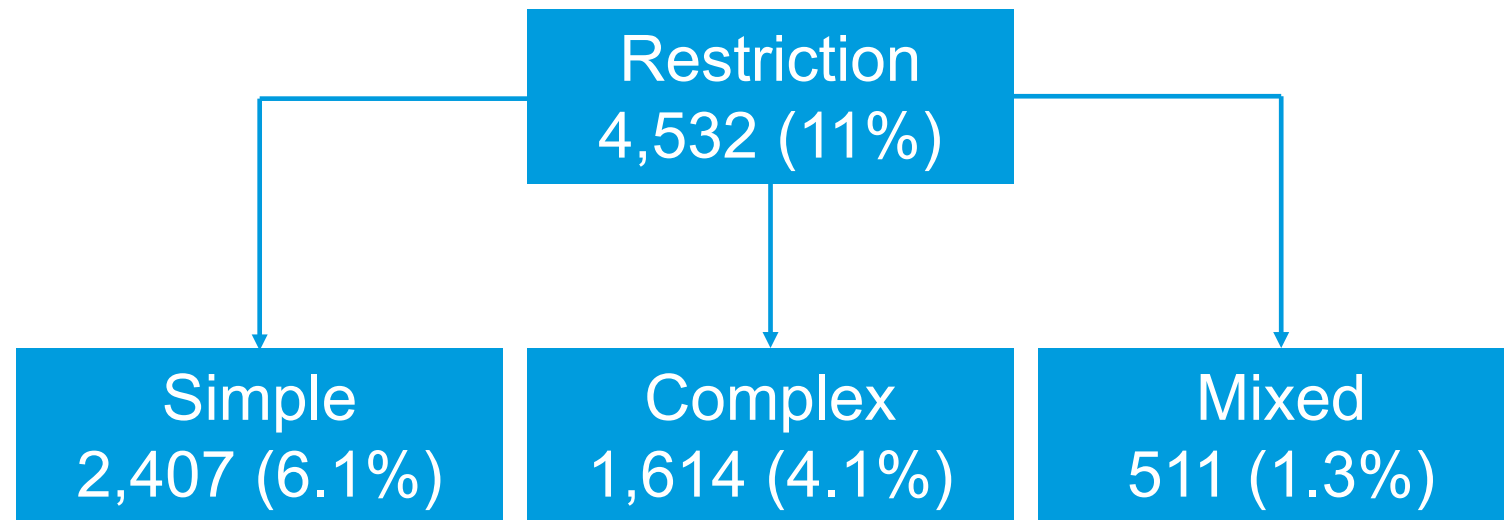
■ Nonspecific ■ Restrictive ■ Obstructive
■ Normal ■ Mixed

ERS/ATS INTERPRETIVE STRATEGIES



COMPLEX RESTRICTION

- Disproportionate reduction in FVC_{pp} relative to TLC_{pleth}



COMPLEX RESTRICTION ($TLC_{PP} - FVC_{PP} > 10\%$)

	Simple Restriction	Complex Restriction*			
		> 10% to ≤ 15%	> 15% to ≤ 20%	> 20% to ≤ 25%	> 25%
Age (mean, y)	80	69	67	64	68
Female, %	17	22	56	46	54
BMI, kg/m ²	29.0	29.6	30.1	29.5	32.0
BMI < 18.5 kg/m ² , %	1	0	4	12	8

Patients with complex restriction had

*p < 0.001 or greater

- Less interstitial lung disease (8-24% vs 59%)
- More neuromuscular disease, pulmonary hypertension
- High RV_{pp} , RV/TLC ratio

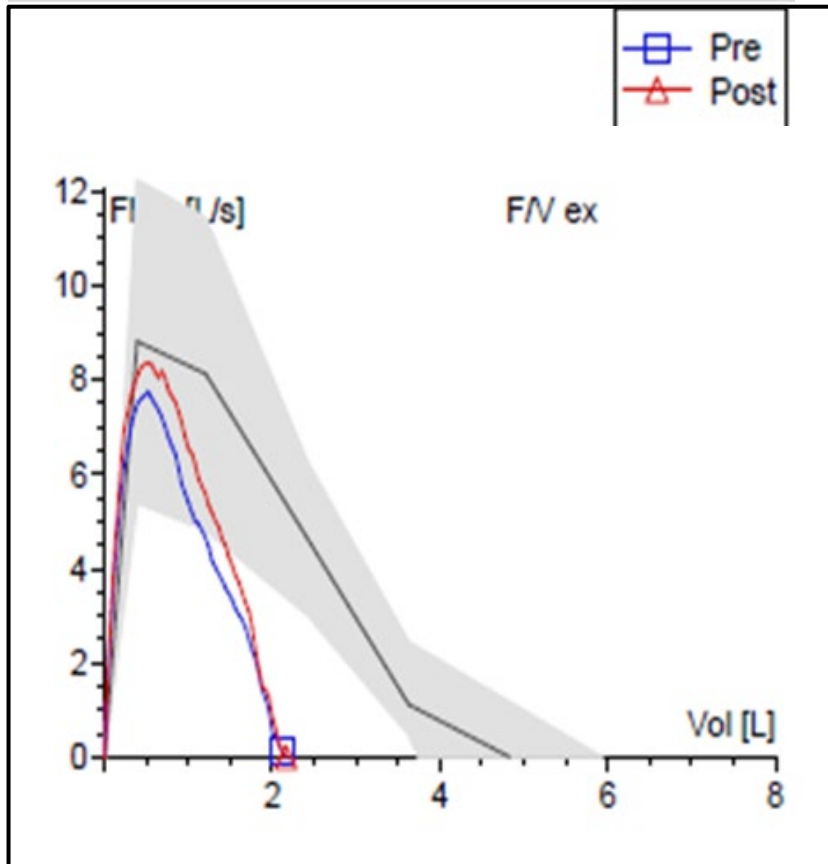
Clay RD. Chest 2017; 152(6): 1256-1265

53 YEAR OLD MALE S/P BLUNT THORACIC TRAUMA

HT 117.2 CM

WT 70 KG

BMI 22 KG/M₂



	Measured	% Predicted	Post-BD
TLC	4.83	68%	
RV	2.79	124%	
RV/TLC	57.8	167%	
FVC	2.16	45%	- 0.03 (-1%)
FEV ₁	2.11	56%	0.01 (<1%)
FEV ₁ /FVC	97.9		
DLCO (adj)	16.6	56%	

PF LAB INFECTION CONTROL STRATEGIES

Minimize
pre-test
probability

Can we differentiate
acute on chronic
respiratory symptoms?

Minimize
particle
generation

V_E , nebulizer use
primary risks

Enhance
containment,
clearance

Increase environmental
air exchanges

Increase
Protective
Measures

What level of PPE is
prudent?

PARTICLE GENERATION WITH COMMON PF PROCEDURES

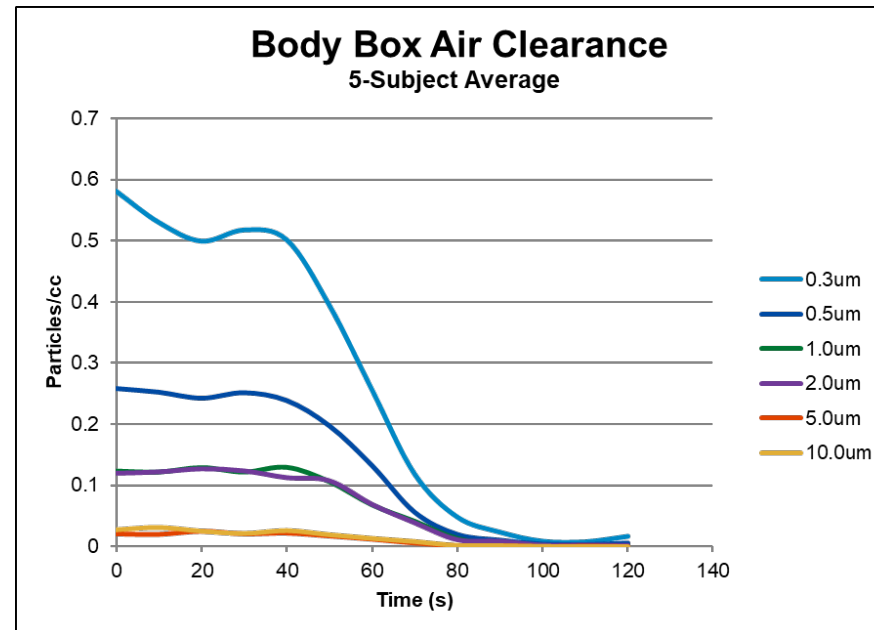
Procedure	Particles/cc (0.02 – 1 μm)
Masked tidal breathing	0.40 ± 0.33
Spirometry with MVV (viral filter)	1.56 ± 0.79
Bronchodilator testing	
MDI	23.36 ± 26.61
Monaghan BAN nebulizer + viral filter	851 ± 867
Hudson Micromist nebulizer	35,906 ± 1010
Bronchoprovocation testing (methacholine)	
Koko dosimeter + Hudson Micromist + filter	1258 ± 1644
Ombra + Monaghan BAN nebulizer + filter	2356 ± 1267
Ombra + Hudson Micromist nebulizer	47,078 ± 14204
Cardiopulmonary exercise testing	10,100 ± 15875

← 85.10 ± 9.33
Ambient air
PF Lab

Particle characteristics, infectious dose not known

ENHANCE CLEARANCE (AND CONTAINMENT?)

Building	Floor	Room	Area (Square feet)	Ceiling Height (Feet)	Volume (Cubic feet)	Original State			New State		
						Supply CFM	Return or Exhaust CFM	Air Changes Per Hour (ACH)	Supply CFM	Return Exhaust CFM	Air Changes per hour (ACH)
Gonda	18	172 PFT 7	146	8.5	1,241	210	210	10.2	310	310	15
Gonda	18	174 PFT 6	150	8.5	1,275	210	210	9.9	320	320	15.1



SUMMARY

- Acceptability, repeatability first!
 - New end of test, FIVC criteria
- Z scores help normalize impact of lung age, standardize impairment assessment
- GLI Global will significantly impact interpretation
 - Patient outcomes data needed
- Nonspecific, complex restriction
- Enhanced PF infection control – but how much?



Questions