



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Pulmonary Function Testing

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- Cornell (Weill) Medical College
- Internal Medicine Residency and Global Health Residency @ Brigham and Women's Hospital
- Pulmonary and Critical Care Fellowship @Penn and BWH
- Instructor of Medicine @ HMS
- Director, Pulmonary Rehabilitation Program
- Associate Director, PFT laboratory @BWH
 - Clinical focus: Severe Asthma, pulmonary medicine
 - Research focus: Asthma

DISCLOSURES

- UpToDate

OBJECTIVES

- Basics of pulmonary function testing:
 - why / what / how
- Interpretation algorithm, with recent updates (2022)
 - Grading severity
 - “non-specific” impairment
 - Bronchodilator response definition
 - (Removal of race adjustment)
- Examples

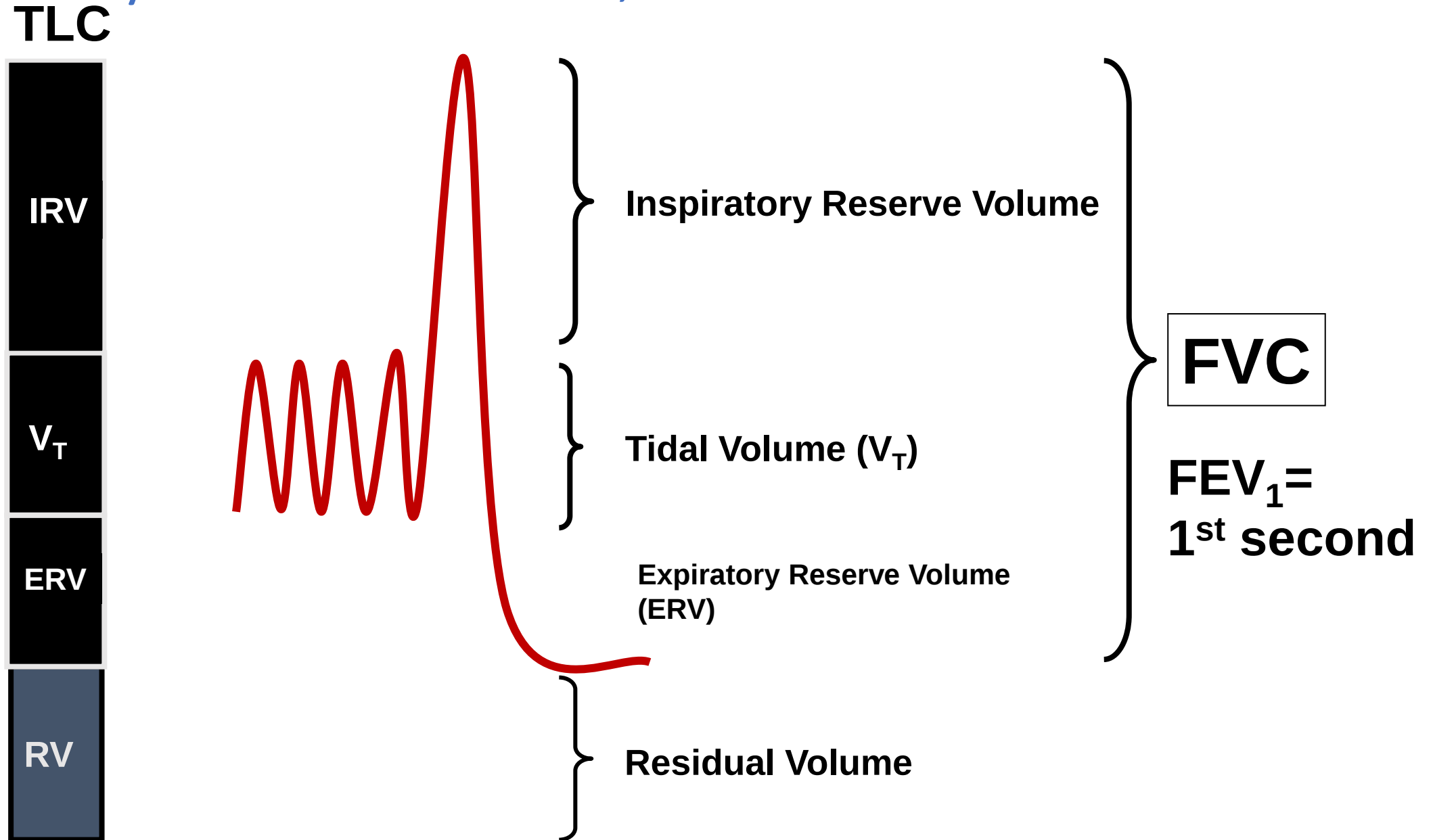
Purpose of PFTs

- Aid in diagnosis of lung disease
- Evaluate patients with dyspnea
- Monitor disease progression, treatment response, toxicity
- Estimation of risk
 - Peri operative
 - Occupational

Pulmonary Function Testing

- Spirometry
- Lung volumes
- Diffusing capacity (DLCO)

Spirometry: how to do it, what we measure



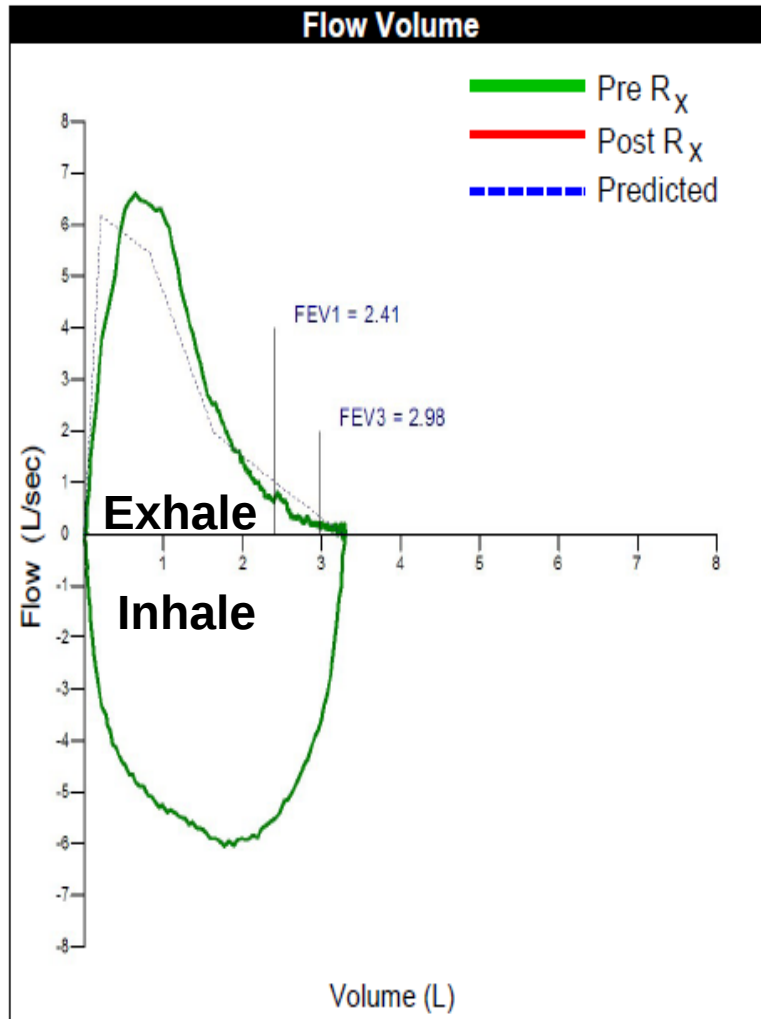
Spirometry: results

New Z score column

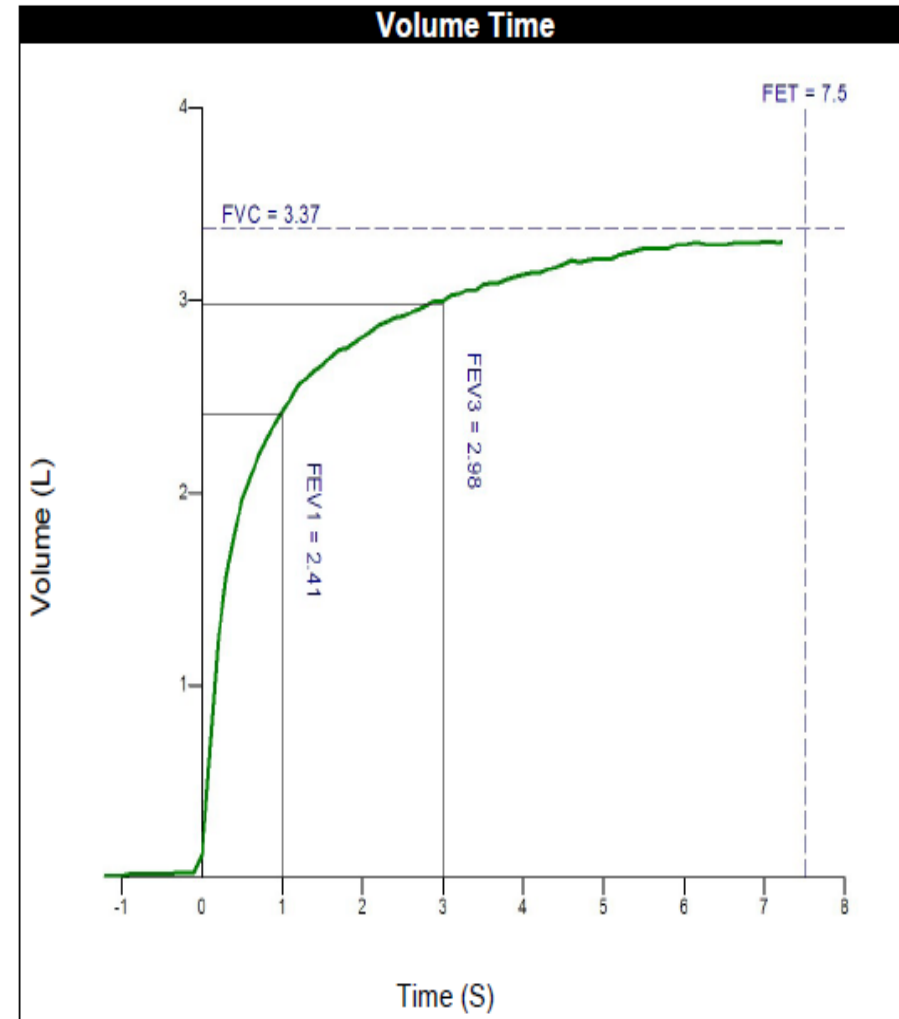


Spirometry (BTPS)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
FEV ₁	L	2.48	1.92	2.41	97
FVC	L	3.27	2.59	3.37	103
FEV ₁ / FVC	%	75	66	72	96

Spirometry: graphics



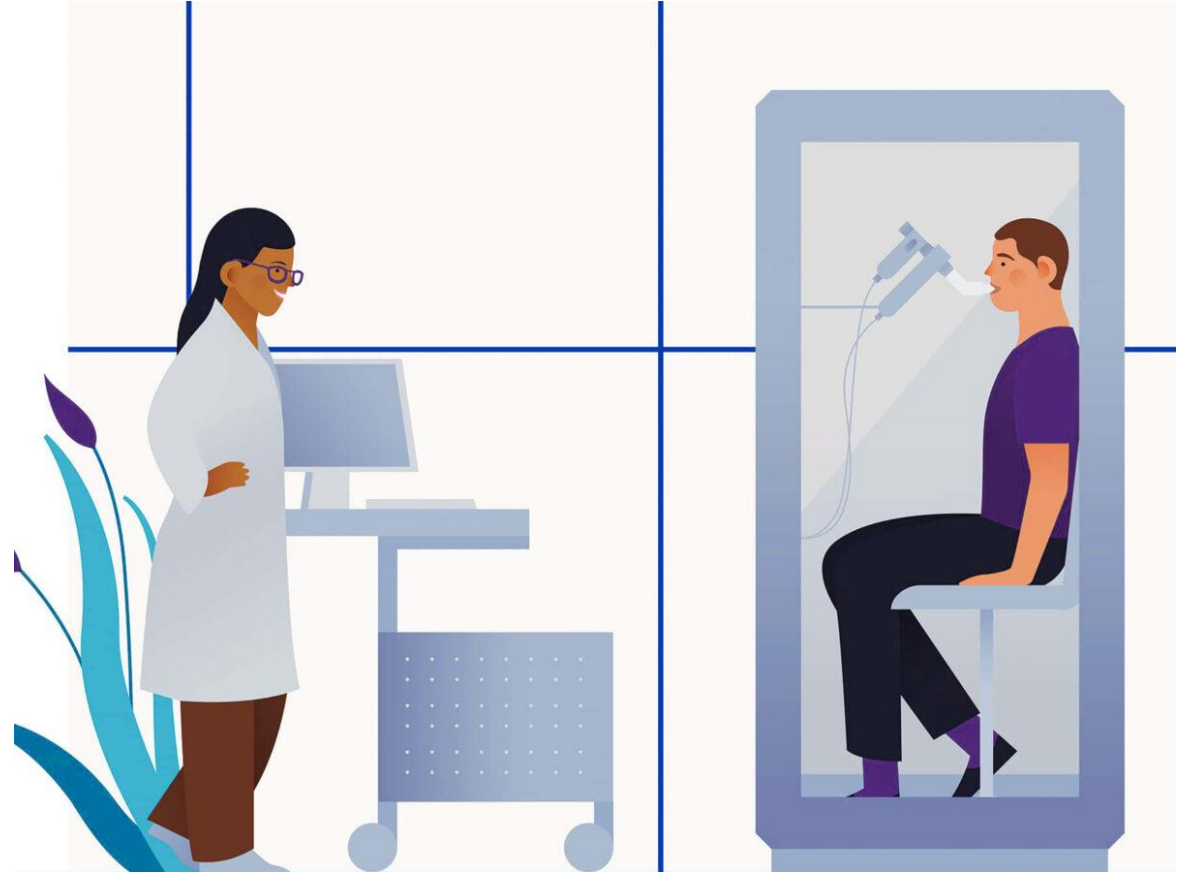
FV loop: Flow vs Volume



VT curve: Volume vs Time

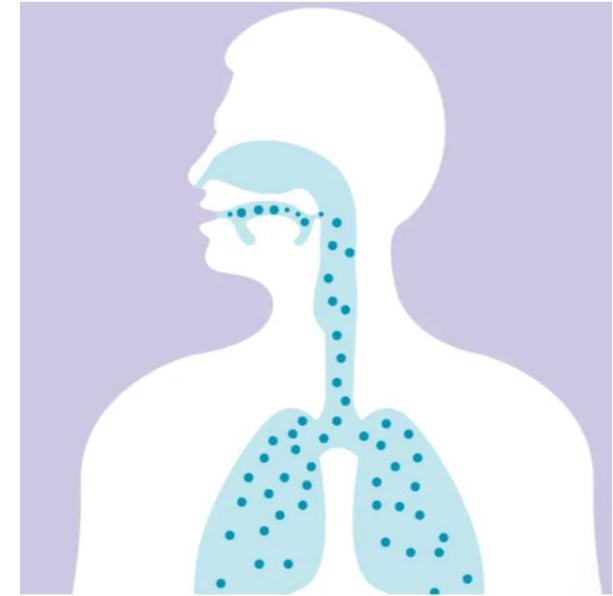
Lung volumes

- Plethysmography “body box”
- Helium dilution
- Nitrogen washout
- **TLC (total lung capacity)**
- Also information from:
 - RV
 - RV/TLC
 - FRC



Diffusing Capacity

- Patient breathes in a gas mixture that includes 0.3% CO
 - Binds 250x more avidly to Hgb than oxygen
 - Hold breath for approximately 10 sec, exhale
- Machine measures the *change in concentration of CO* and the *volume exhaled* to determine diffusing capacity (amount of CO bound to Hgb)



Types of deficits

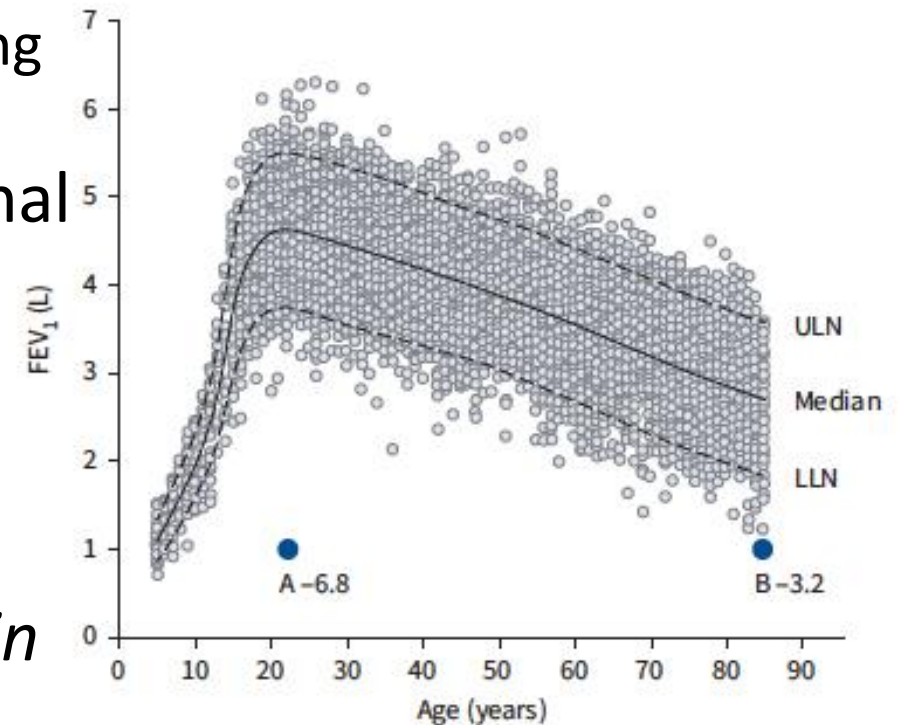
- Obstructive
 - $FEV_1/FVC < LLN$
- Restrictive
 - $TLC < LLN$
- Combined obstructive and restrictive
 - $FEV_1/FVC < LLN$, +/- $FVC < LLN$ AND $TLC < LLN$
- “Non-specific” impairment
 - $FEV_1/FVC > LLN$, FEV_1 or $FVC < LLN$ AND $TLC > LLN$
- With or without diffusion abnormalities
 - $DLCO < LLN$
- Additional considerations:
 - Hyperinflation $TLC > ULN$
 - Air trapping RV , $RV/TLC > ULN$
 - Always compare to priors when available!

Reminder: meaning of LLN

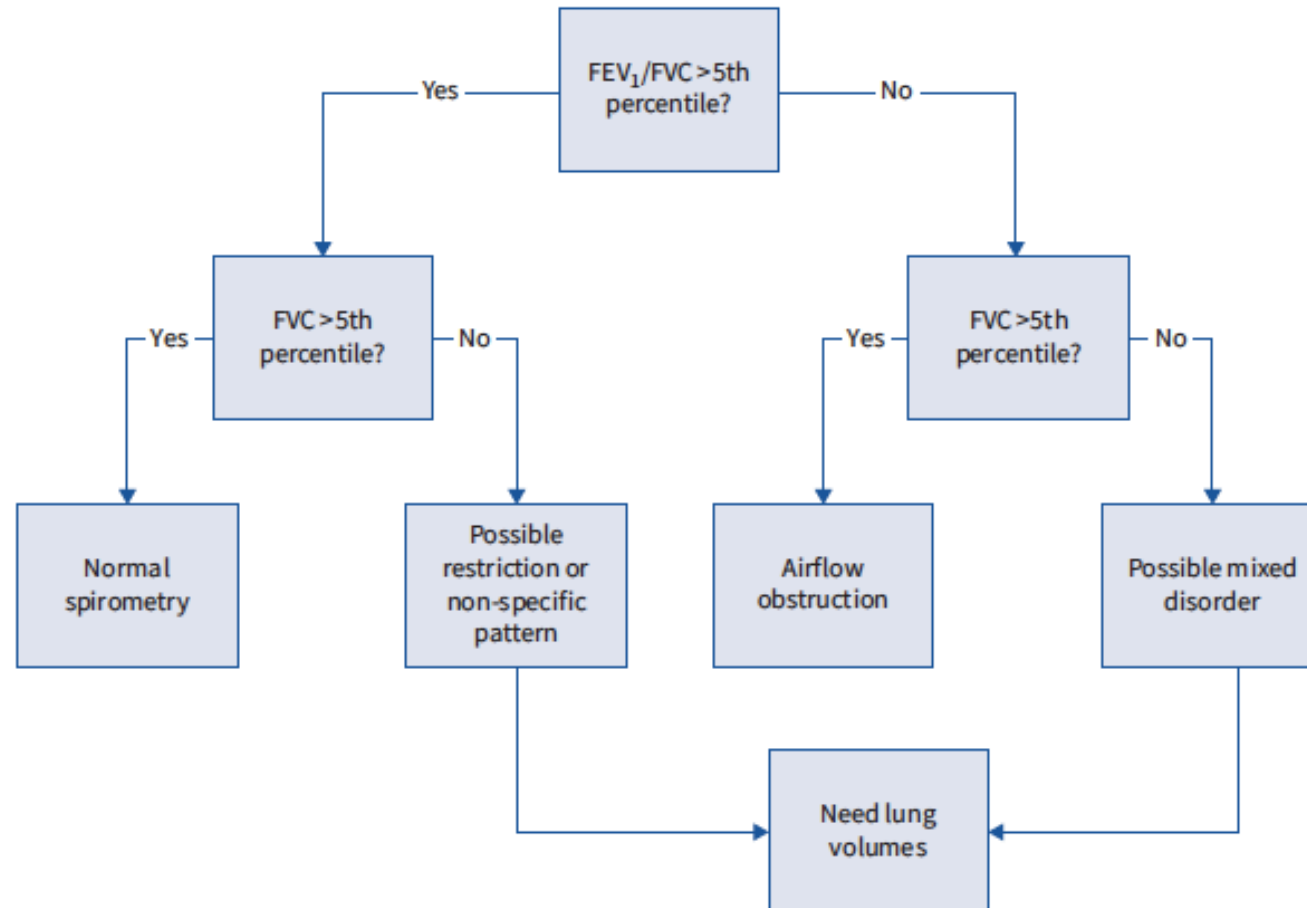
- Threshold, but not necessarily clinically meaningful
 - Does not necessarily define presence or absence of lung disease
- Low(er) chance ($\leq 5\%$) this number is within normal range (based on the reference population)
 - Continuum

Also

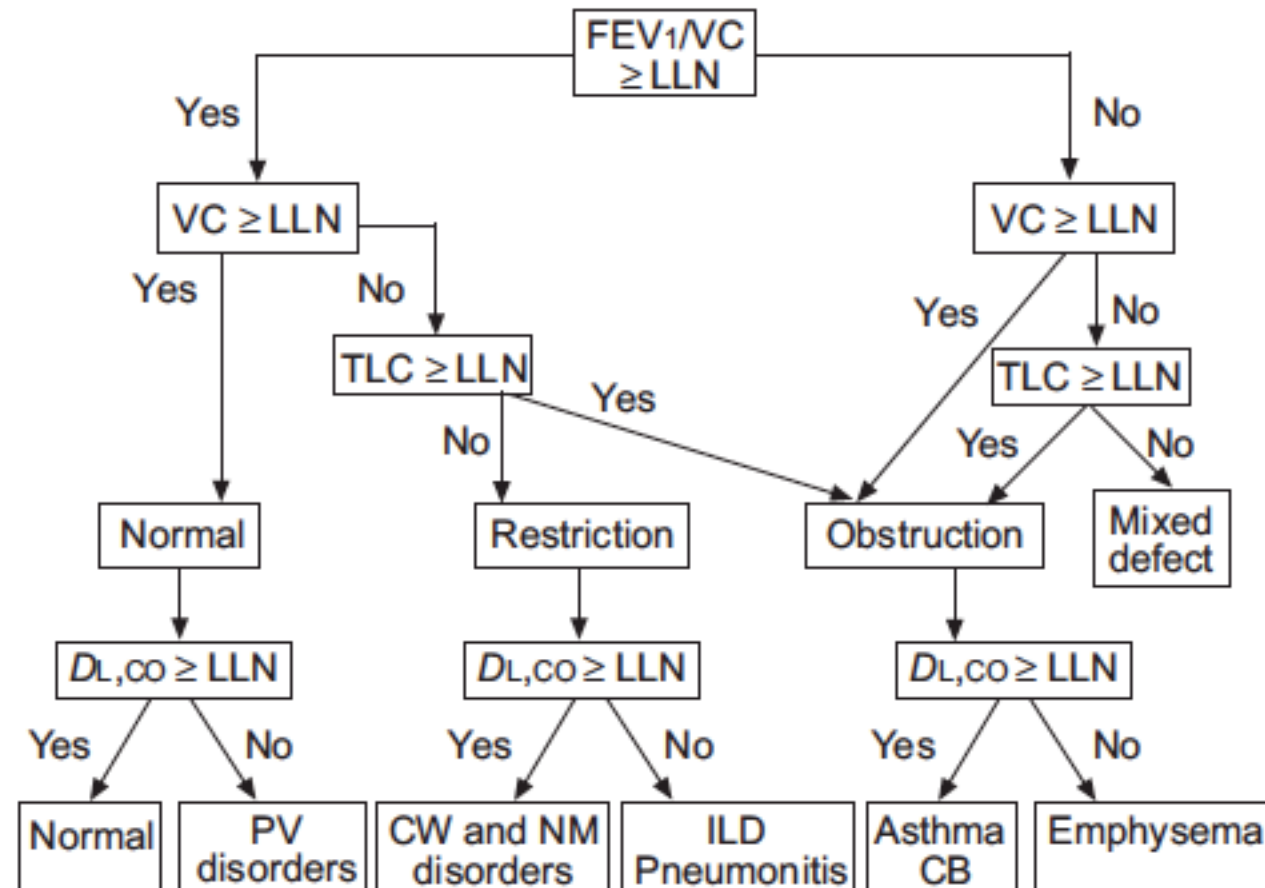
- Changes in lung function *even if they remain within normal limits* can still be pathologic / clinically meaningful
 - Example: 95% predicted $\rightarrow$ 80% predicted



Spirometry interpretation



Interpretation Algorithm





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

Sanja Stanojevic ¹, David A. Kaminsky², Martin R. Miller ³, Bruce Thompson⁴, Andrea Aliverti⁵, Igor Barjaktarevic⁶, Brendan G. Cooper⁷, Bruce Culver⁸, Eric Derom⁹, Graham L. Hall¹⁰, Teal S. Hallstrand⁸, Joerg D. Leuppi^{11,12}, Neil MacIntyre¹³, Meredith McCormack¹⁴, Margaret Rosenfeld¹⁵ and Erik R. Swenson^{8,16}

Important Take Home Point:

Recent updates may change the interpretation of your patients' results with ***NO ACTUAL CHANGE*** in the measurement of their lung function

Grading Severity of Impairment:

FEV₁ **Z score** instead of % predicted

OLD: FEV₁ % predicted

NEW: FEV₁ Z score

TABLE 6 Severity of any spirometric abnormality based on the forced expiratory volume in one second (FEV ₁)	
Degree of severity	FEV ₁ % pred
Mild	>70
Moderate	60–69
Moderately severe	50–59
Severe	35–49
Very severe	<35
% pred: % predicted.	

Z-score	Severity
> -1.645	Normal
-1.65 to -2.5	Mild
-2.5 to -4	Moderate
< -4	Severe

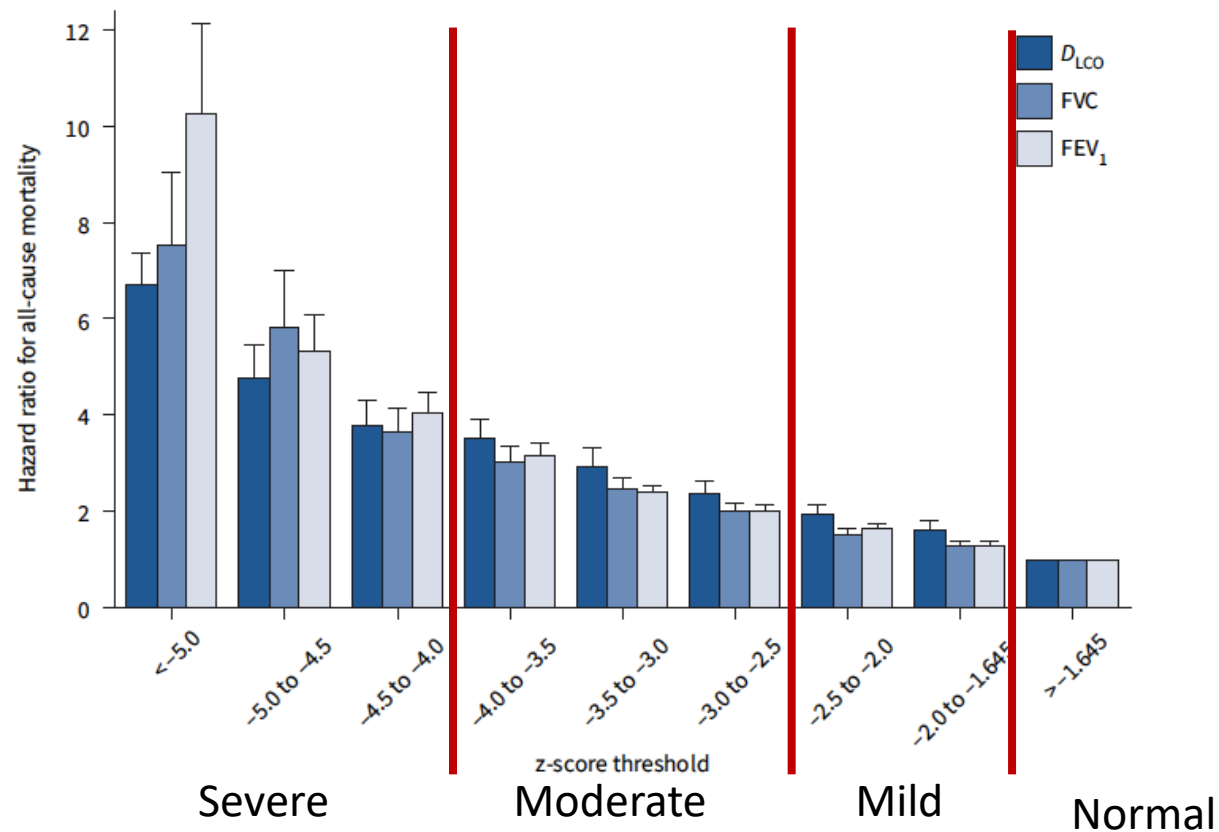
*This also applies for grading severity of diffusing capacity deficit (DLCO)

Severity of physiologic impairment NOT disease severity

Quality of life, functional impairment, symptoms etc.

Lung function and overall mortality

Z score has better correlation with mortality compared to percent predicted



FEV₁ Z score

(NOT FEV₁/FVC, TLC or FVC!)

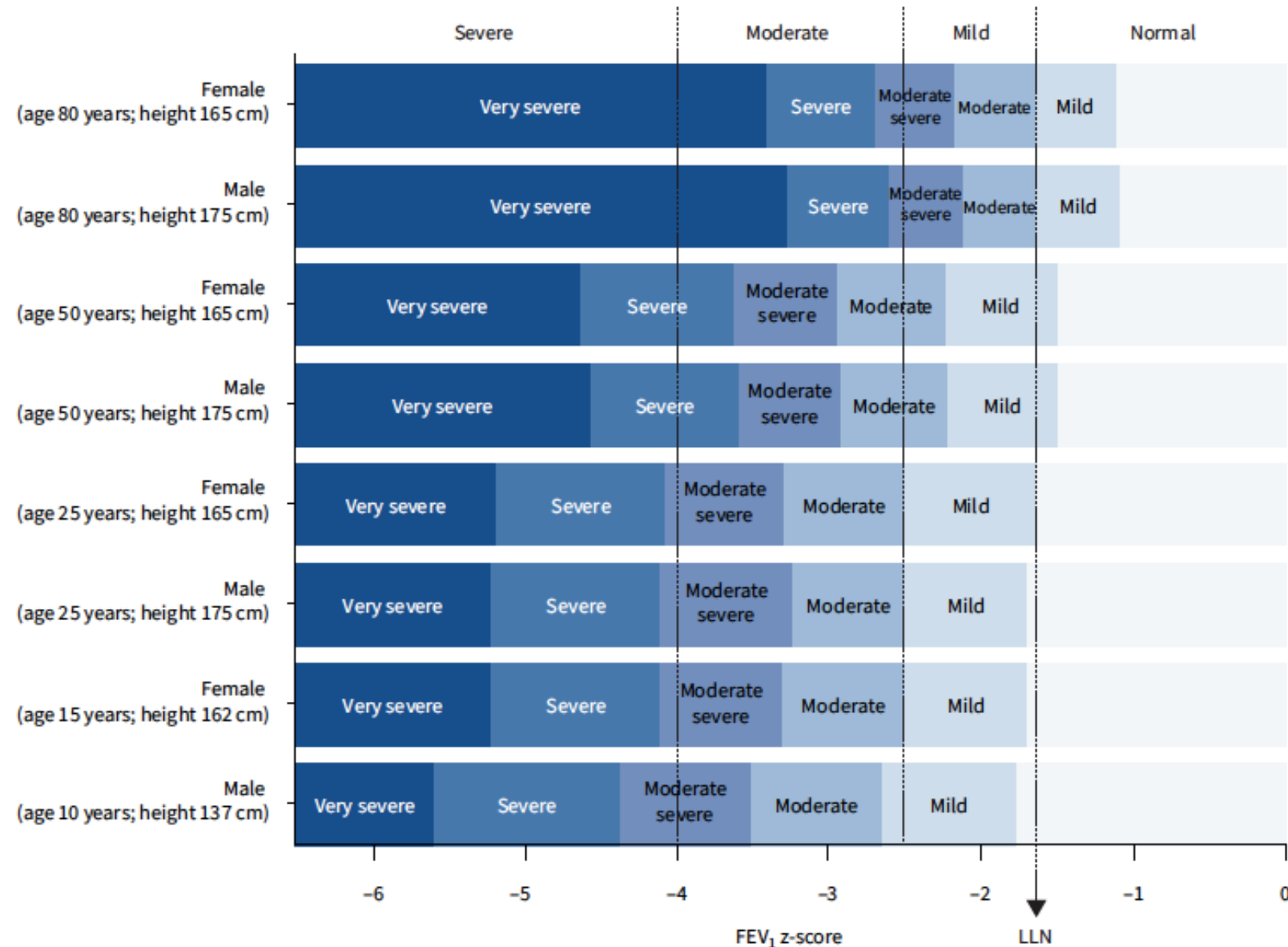
to grade severity

for any type of impairment

(obstruction, restriction, mixed,
non-specific etc.)

How might this affect your patient's results?

- **Older subjects:**
 - results may ↓ in severity
- **Younger subjects**
 - Grouping more stable
 - Mod / mod severe merged

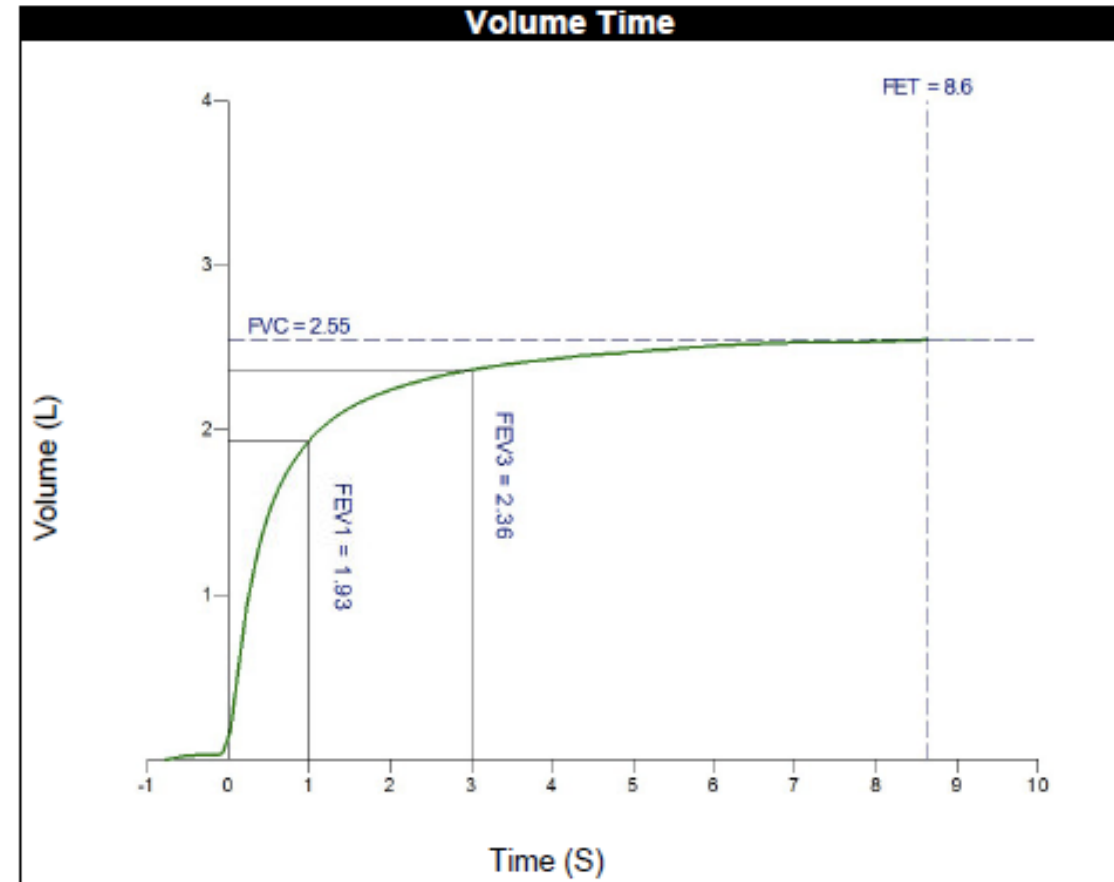
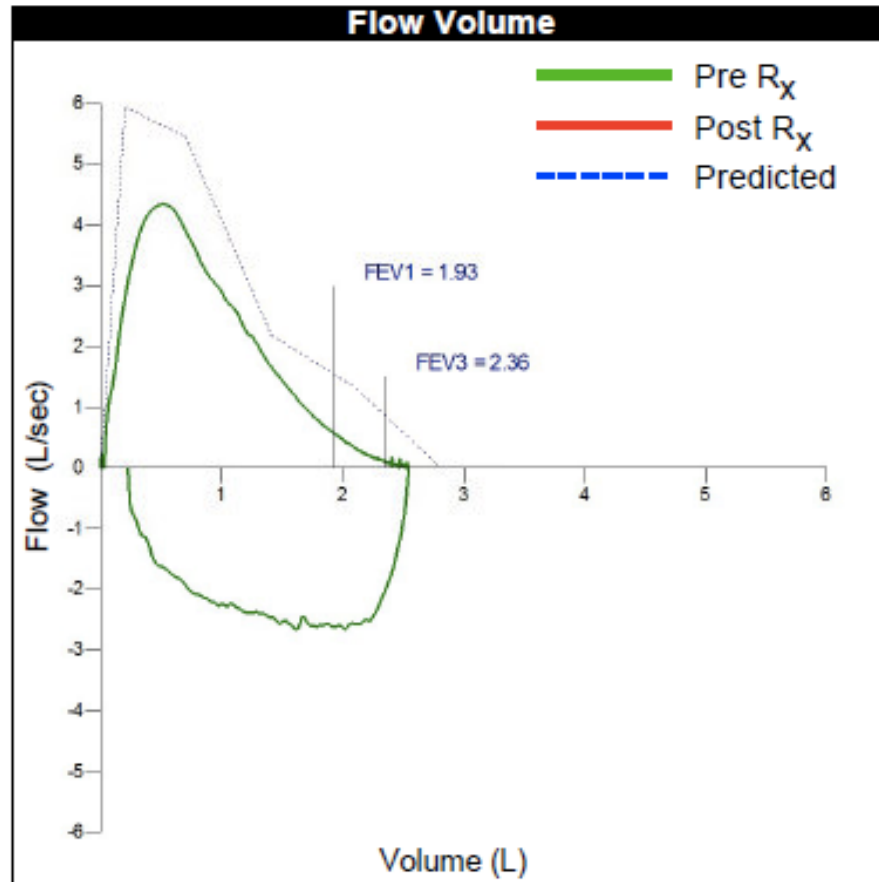


PFT Examples

Example 1

Spirometry (BTPS)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
FVC Effort Time		----	----	15:30	----
FEV ₁	L	2.26	1.70	1.93	85
FVC	L	2.81	2.14	2.55	91
FEV ₁ / FVC	%	81	70	76	94
FEV ₆	L	2.66	1.98	2.51	94
FEV ₁ / FEV ₆	%	83	73	77	93
FEF ₂₅₋₇₅	L/s	2.28	1.09	1.60	70
PEFR	L/s	5.93	3.99	5.31	90
FET	sec	----	----	8.63	----
MWV	L/m	79.9	28.9	----	----

Example 1

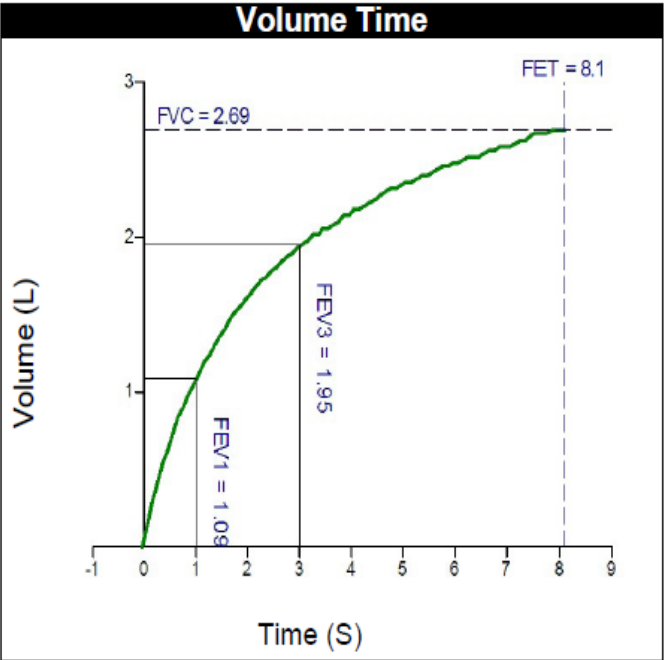
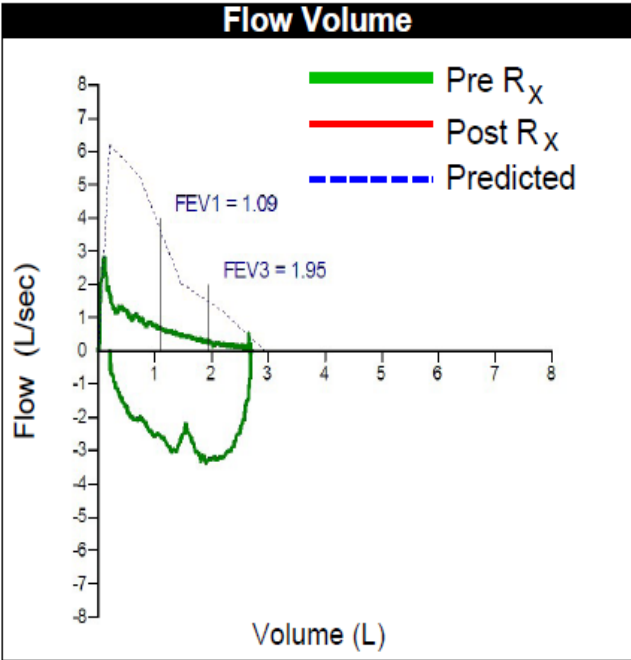
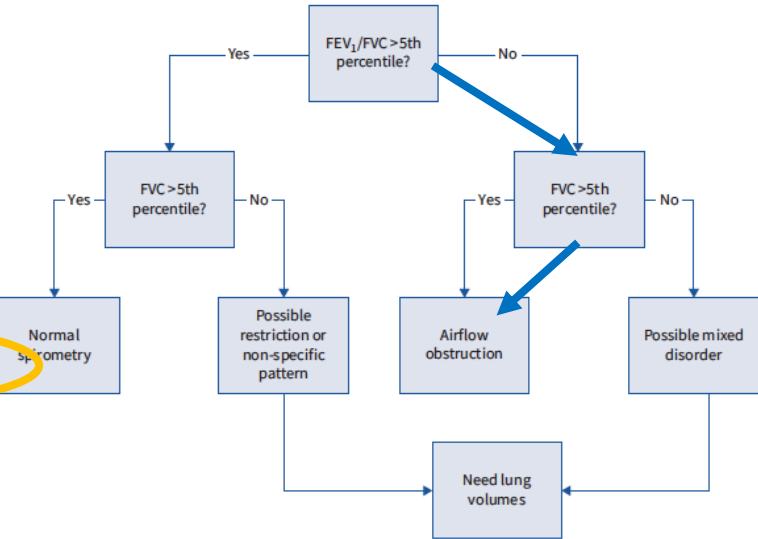


Result: Normal spirometry

Example 2

Spirometry

		Predicted Range		Pre Bronchodilator		
		Mean	95%	Actual	% Pred	Z score
FEV ₁	L	2.39	1.83	1.09	46	-4.25
FVC	L	2.93	2.25	2.69	92	
FEV ₁ / FVC	%	81	72	41	51	



Z-score	Severity
> -1.645	Normal
-1.65 to -2.5	Mild
-2.5 to -4	Moderate
< -4	Severe

Severe Obstruction

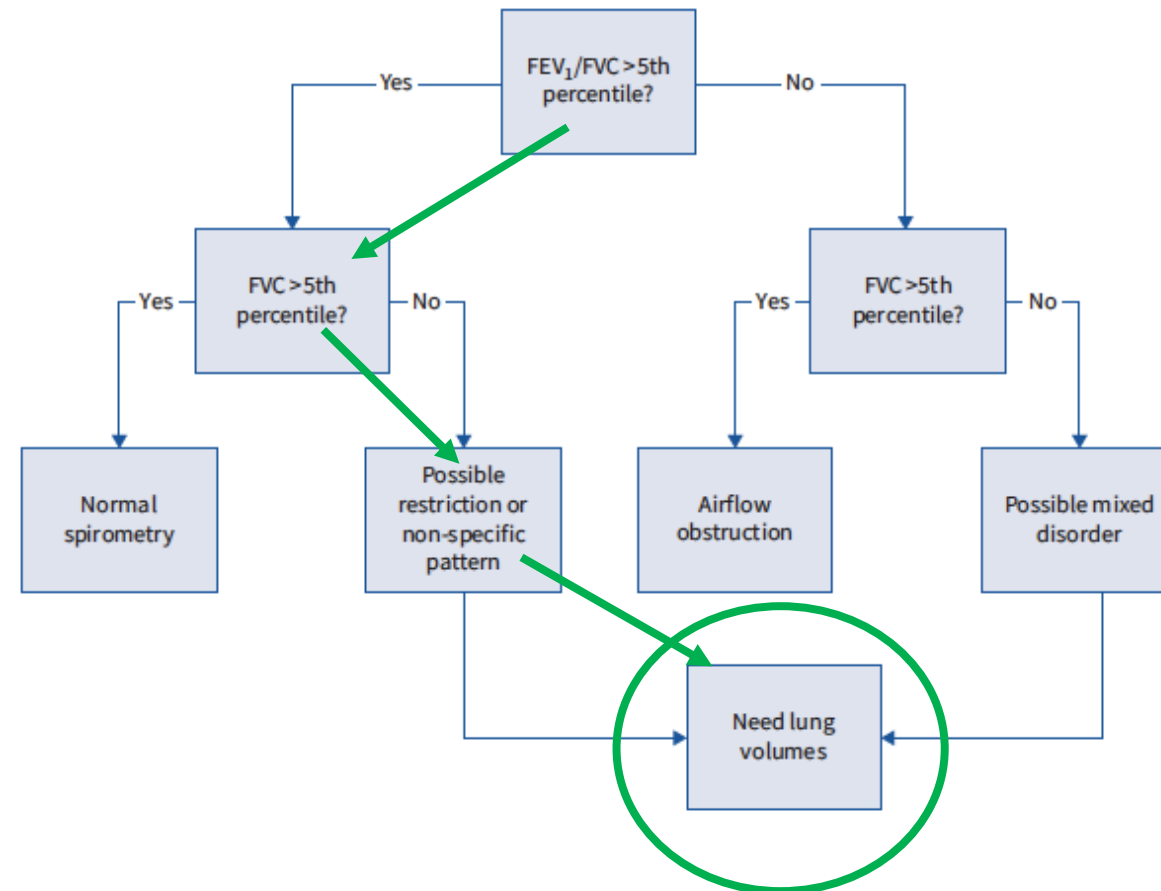
PFT's: define "normal"

- 95% confidence interval / LLN or ULN → Normal vs. Abnormal but....
- Use **FEV₁** Z score → HOW SEVERE impairment is

Example 3

Spirometry

Pre Bronchodilator							
		FVC A	Spirometry Grading				
		FEV1 A					
		Actual	Pred	% Pred	Lower	Upper	Z-Score
FEV ₁	L	1.06	1.48	72	1.01	1.93	-1.48
FVC	L	1.29	1.89	68	1.31	2.50	-1.69
FEV ₁ / FVC	%	82	80	102	68	91	0.27
FEF ₂₅₋₇₅ [ISO]	L/s	1.36	1.33	102	0.56	2.50	---
PEFR	L/s	2.88	3.84	75	2.48	5.20	---
FET	s	10.03	0.00	---	6.00	0.00	---



- Low FVC → need lung volumes

Example 3

- Mild /minimal RESTRICTION
- WITH moderately reduced diffusing capacity

Spirometry

		Pre Bronchodilator							
		FVC A	FEV1 A	Spirometry Grading					
		Actual	Pred	% Pred	Lower	Upper	Z-Score		
FEV ₁	L	1.06	1.48	72	1.01	1.93	-1.48	N	
FVC	L	1.29	1.89	68	1.31	2.50	-1.69	A	m
FEV ₁ / FVC	%	82	80	102	66	91	0.27	N	
FEF ₂₅₋₇₅ [ISO]	L/s	1.36	1.33	102	0.56	2.50	---		
PEFR	L/s	2.88	3.84	75	2.48	5.20	---		
FET	s	10.03	0.00	---	6.00	0.00	---		

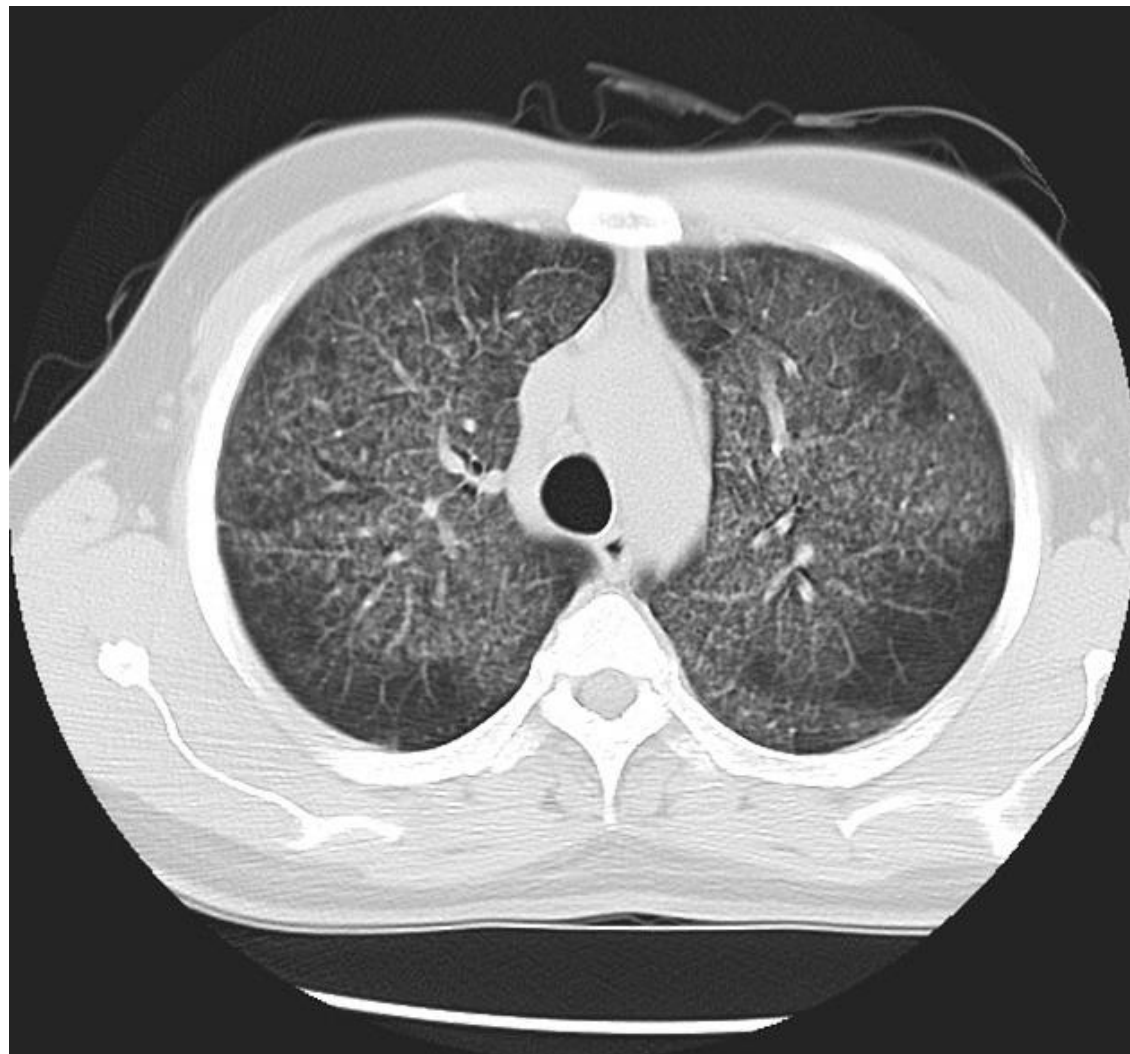
Lung Volumes Box

		Pre Bronchodilator							
		Actual	Pred	% Pred	Lower	Upper	Z-Score		
TLC	L	2.62	3.76	70	2.92	4.72	-2.29	A	m
VC	L	1.37	2.04	67	1.58	2.50	-2.38	A	m
RV	L	1.25	1.70	74	0.98	2.65	-0.97	N	
RV/TLC	%	48	45	107	31	60	0.34	N	
FRC	L	1.27	2.11	60	1.50	2.87	-2.41	A	m
IC	L	1.35	1.52	89	1.00	2.05	-0.53	N	
ERV	L	0.02	0.46	4	0.09	1.07	-2.35	A	m

Diffusing Capacity

		Pre Bronchodilator							
		Actual	Pred	% Pred	Lower	Upper	Z-Score		
DLCO [Unc]	mL/min/mmHg	7.33	15.22	48	11.26	20.15	-3.79	A	M
DLCO [Cor]	mL/min/mmHg	7.92	15.22	52	11.26	20.15	-3.42	A	M
KCO	mL/min/mmHg/L	4.19	4.40	95	3.32	5.62	-0.30	N	
VA [BTPS]	L	1.89	3.46	55	2.74	4.26	-3.88	A	M
VI [BTPS]	L	1.26	2.04	62	1.58	2.50	---		
Diffusion Time	s	9.37	0.00	---	0.00	0.00	---		

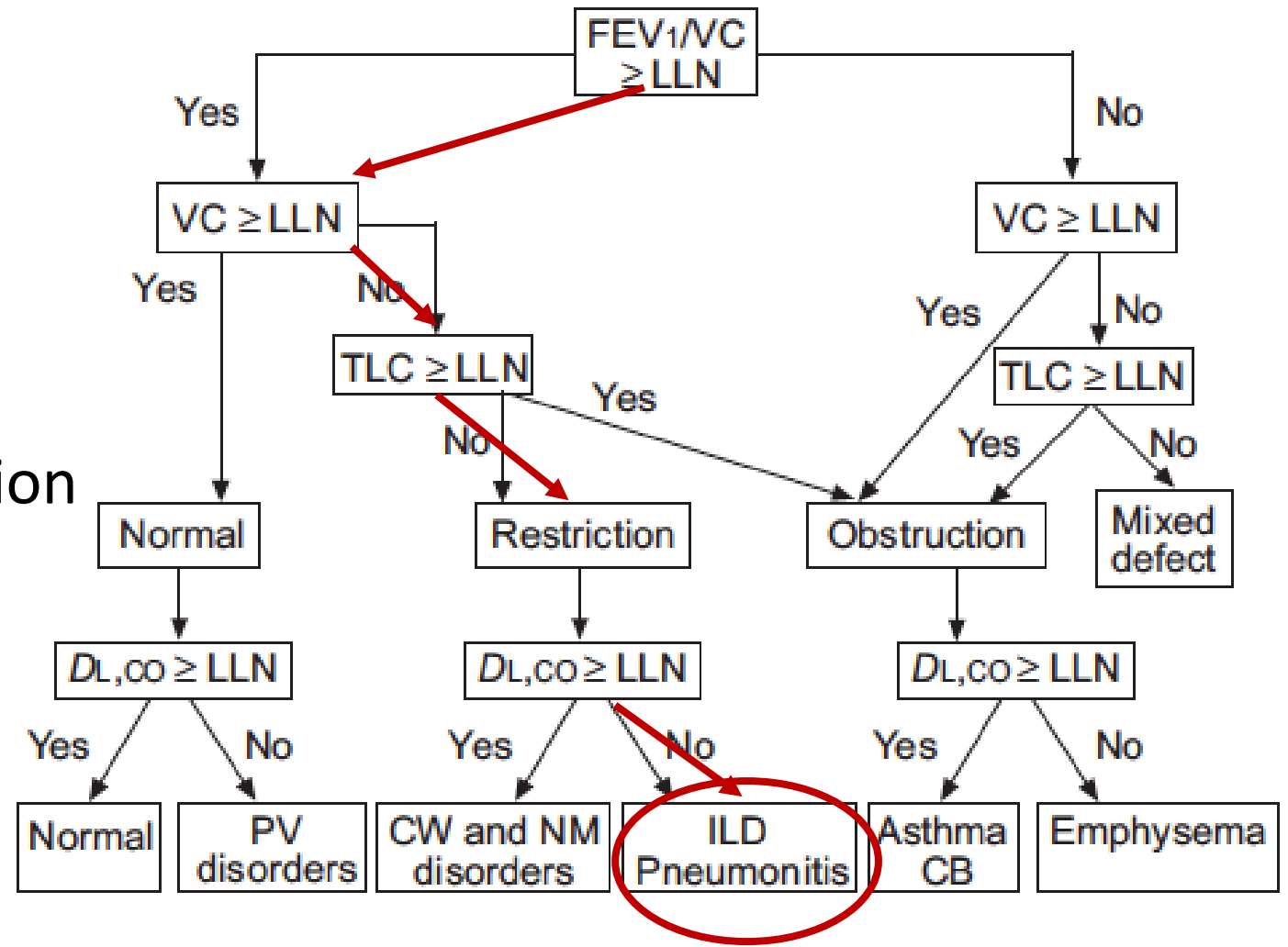
CT scan: NSIP



PFTs in ILD

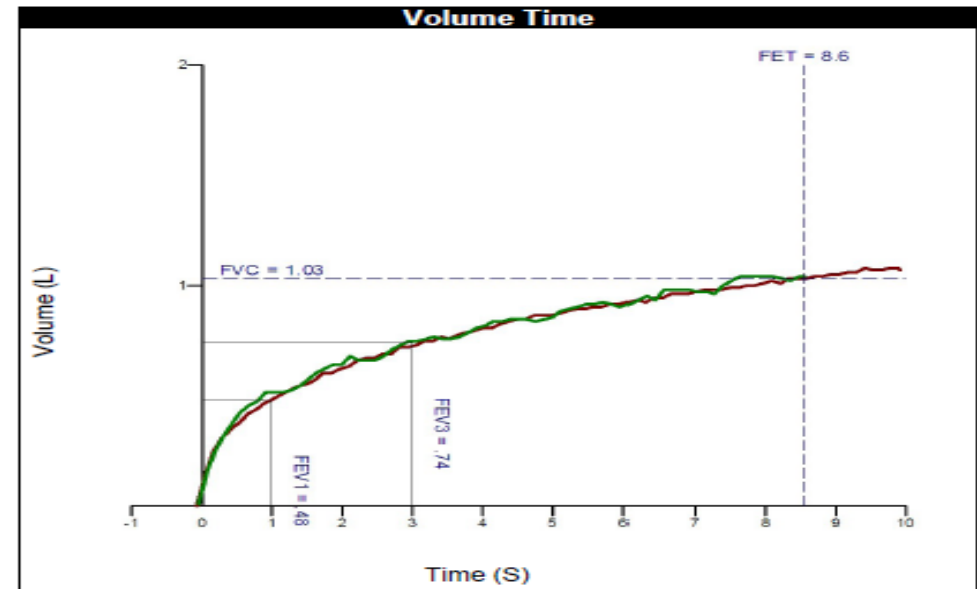
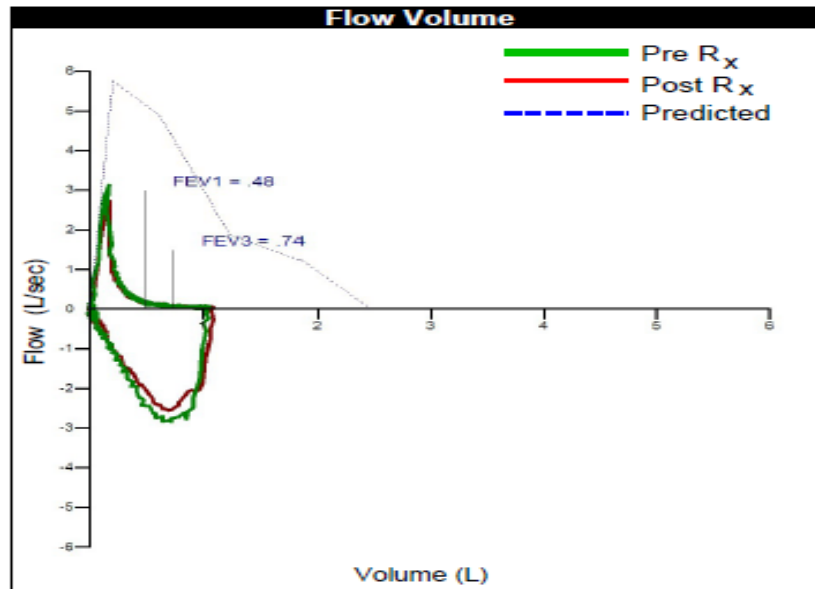
Typical pattern for ILD

- Normal (or high) ratio
- Low FVC → lung volumes!
- Low TLC → confirms restriction
- Low DLCO



Example 4

Spirometry (BTPS)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
FEV ₁	L	2.13	1.57	0.48	23
FVC	L	2.47	1.79	1.03	42
FEV ₁ / FVC	%	85	76	47	55

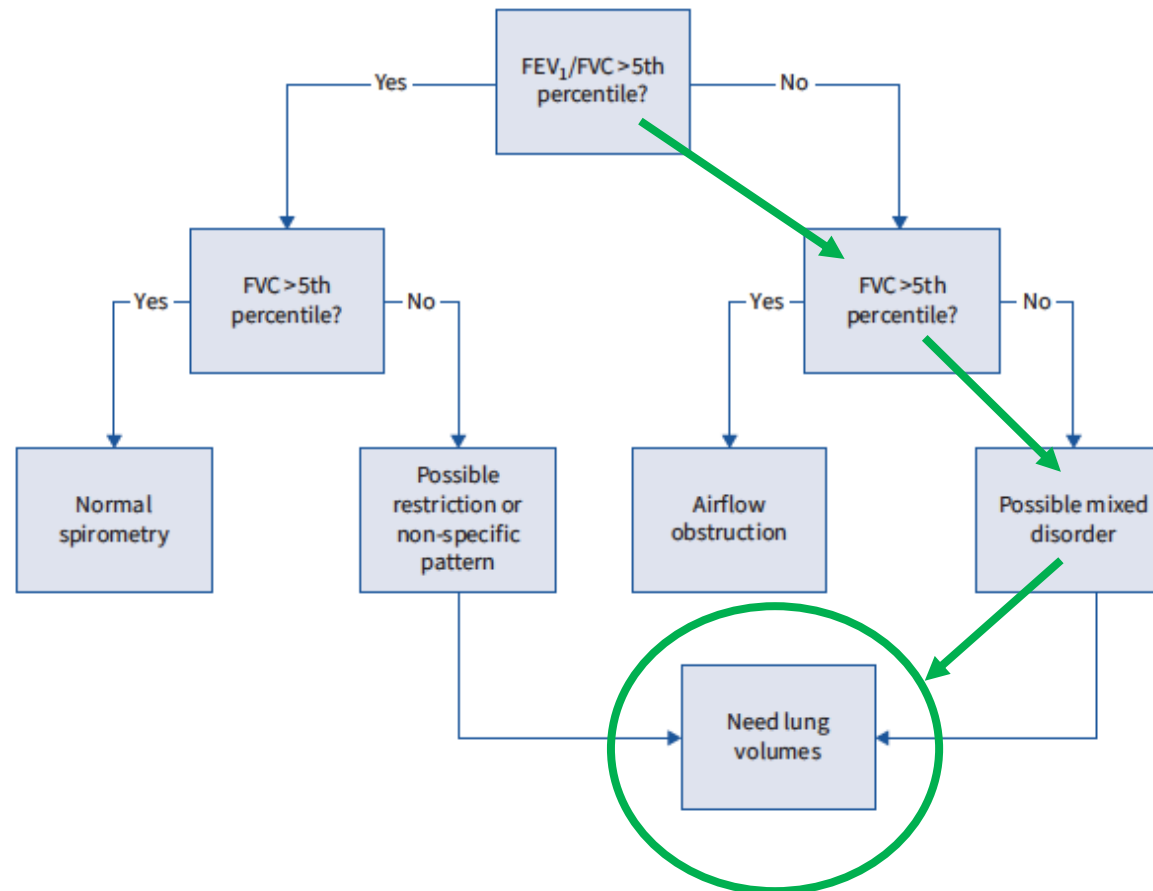


Interpret patient's spirometry result:

Low ratio, Low FEV₁, Low FVC

- A) Obstruction
- B) Restriction
- C) Non-specific respiratory deficit
- D) Obstruction and possible restriction
- E) Combined obstruction and restriction

Low ratio, Low FVC



Interpret patient's spirometry result:

- A) Obstruction
- B) Restriction
- C) Non-specific respiratory deficit
- D) Obstruction and possible restriction
- E) Combined obstruction and restriction

If FVC is low: **lung volumes are necessary** to confirm (or rule out) restriction

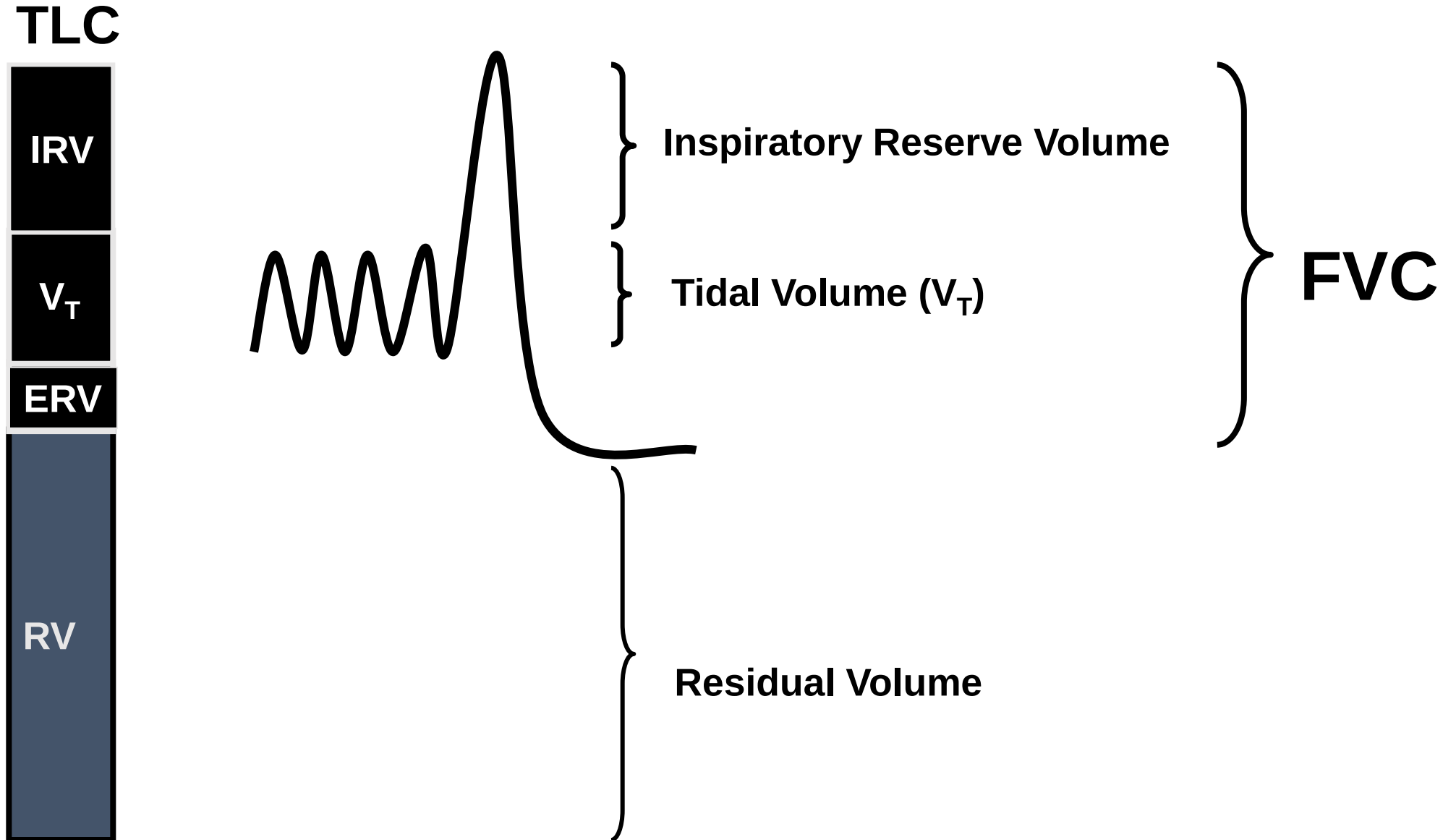
Lung Volumes

Spirometry (BTPS)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
FEV1	L	2.13	1.57	0.48	23
FVC	L	2.47	1.79	1.03	42
FEV1 / FVC	%	85	76	47	55

Lung Volumes (Box)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
TLC	L	4.23	3.15	4.38	104
FRC	L	2.38	1.32	3.76	158
IC	L	1.85	----	0.62	34
ERV	L	0.80	----	0.06	8
RV	L	1.58	0.81	3.70	234
RV/TLC	%	36	25	84	233

- $\uparrow$ RV, RV/TLC >ULN $\rightarrow$ air trapping
- If TLC >ULN $\rightarrow$ hyperinflation (not in this case)

In Obstruction, FVC can be LOW Due to Trapped Gas at End-Exhalation ($\uparrow$ RV)



Interpret patient's full PFT result:

- A) Obstruction *(with air trapping)*
- B) Restriction
- C) Non-specific respiratory deficit
- D) Obstruction and possible restriction
- E) Combined obstruction and restriction

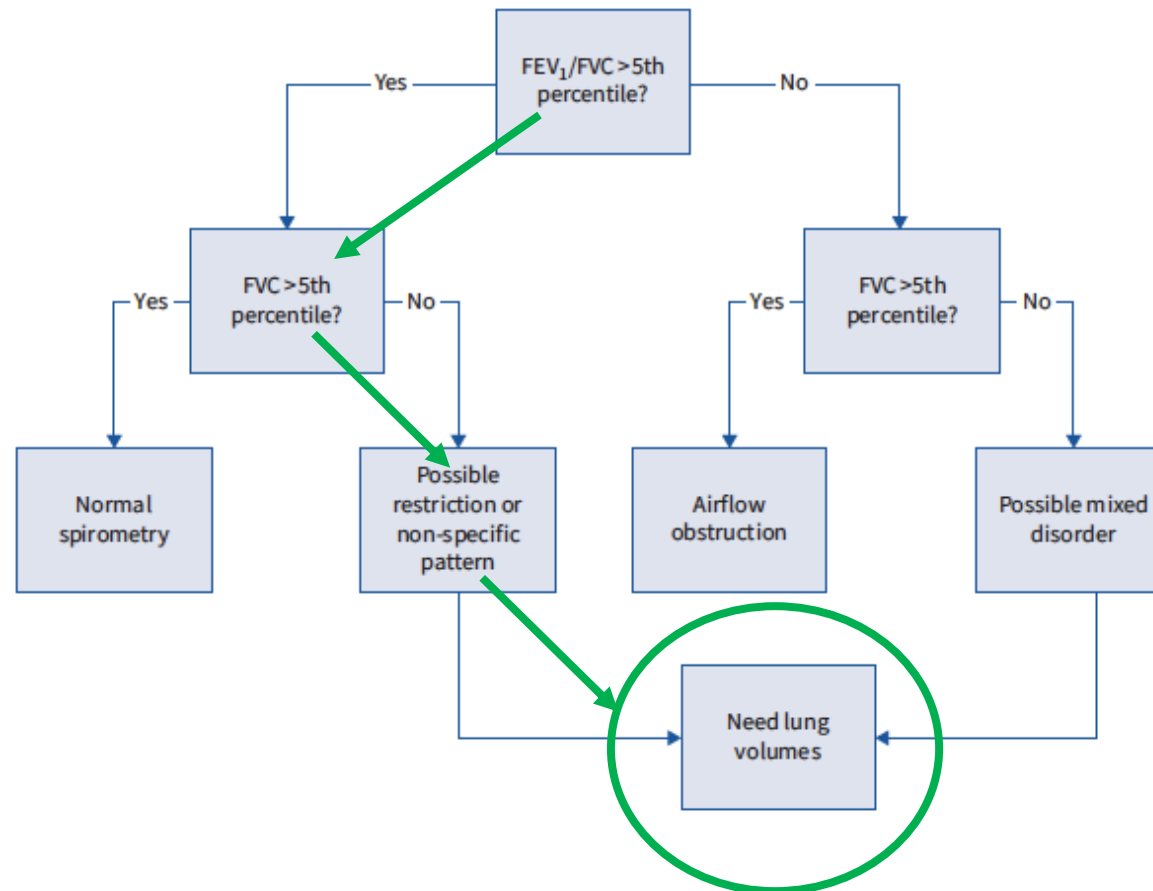
Despite low FVC, **normal TLC rules out restriction**

Example 5

Spirometry (BTPS)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
FVC	Effort Time	----	----	14.29	----
FEV ₁	L	2.36	1.80	1.06	45
FVC	L	2.97	2.29	1.38	46
FEV ₁ / FVC	%	79	70	77	97
FEV ₆	L	3.07	2.41	1.33	43
FEV ₁ / FEV ₆	%	81	72	80	99
FEF ₂₅₋₇₅	L/s	2.39	1.03	0.86	36
PEFR	L/s	6.14	4.48	4.59	75
FET	sec	----	----	9.74	----
MVV	L/m	89.4	38.4	----	----

- Ratio: NORMAL
- FEV₁: low
- FVC: low

Obstruction or Restriction? → Need lung volumes



Lung volumes

Lung Volumes (Box)		Predicted Range		Pre Bronchodilator	
		Mean	95%	Actual	% Pred
VTG Effort Time		----	----	10:38	----
TLC	L	6.77	5.16	5.49	81
FRC	L	3.54	2.08	3.12	88
IC	L	3.23	----	2.37	73
ERV	L	1.31	----	0.63	48
RV	L	2.23	1.47	2.49	112
RV/TLC	%	33	22	45	136
VC	L	4.54	3.42	3.00	66

- TLC: normal → NOT restriction
- RV, RV/TLC: high = AIR TRAPPING

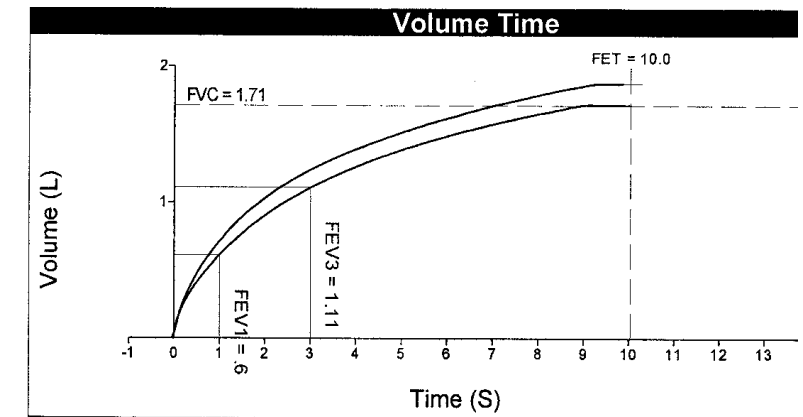
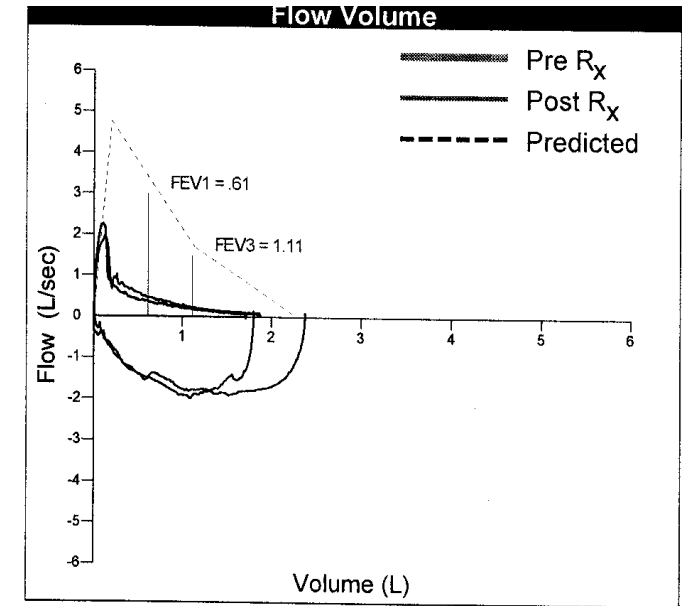
“non-specific” impairment

Reduced FEV_1 and FVC, normal FEV_1/FVC , normal TLC

- Poor effort
 - Failure to inhale or exhale completely “falsely low” FEV_1 and FVC
- Severe Obstruction
 - Flow reduced cannot exhale long enough to get to RV, should appear concave
- Early obstruction
 - Small airway collapse → reduced FVC, increased RV but ratio still normal
- Early restrictive pattern
 - FVC reduction not yet RV reduction
- In current or former smokers
 - Preserved Ratio Impaired Spirometry or PRISm
- 3 year follow up of non-specific pattern
 - 1/3 develop overt obstruction or restriction
 - 2/3 remain with this pattern

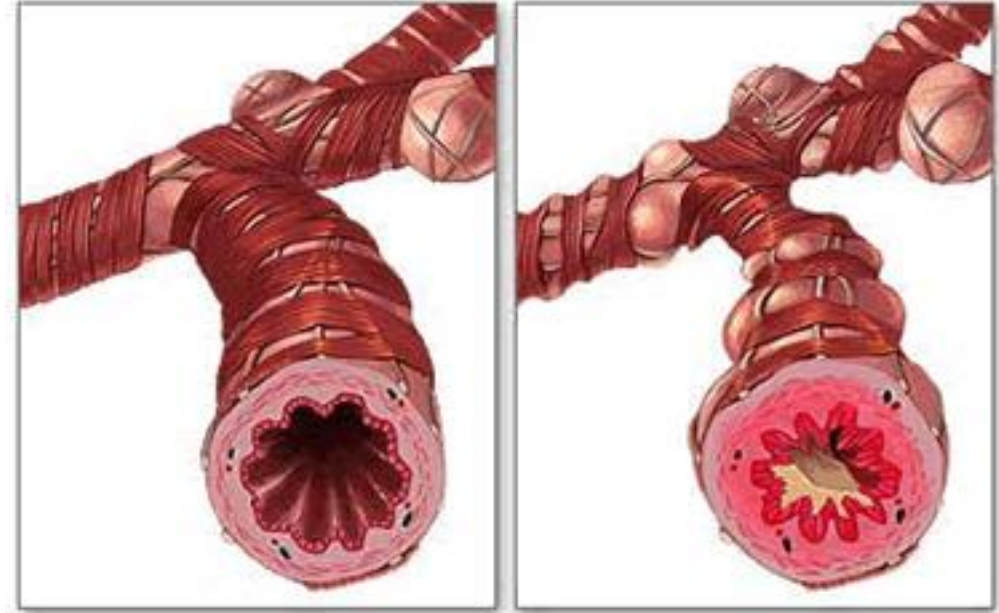
Non-specific pattern: other clues

- Obtain lung volumes
 - → if reduced then restriction
- Look at FV loop, VT curve
 - Concave, failure to reach plateau suggestive of obstruction
 - Air trapping or hyperinflation?
 - RV, RV/TLC, or TLC > ULN
- Compare FVC to SVC
 - $\Delta > 100\text{cc}$: airway collapse during forced exhalation
- Assess BD response
 - If + suggestive of airways disease



Bronchodilator response

- 2-4 puffs albuterol MDI or nebulizer, wait 15 min
- **Hold** short-acting and long-acting bronchodilators 4 hours and 12 hours, respectively, prior to testing



BDR: bronchodilator response

- Old:
 - 12% **AND** 200cc
 - relative to measured baseline FEV₁ or FVC
- New
 - 10% change
 - relative to ***predicted*** value of FEV₁ or FVC
- Minimizes effect of height/age/sex and baseline value in assessing BDR
- Based on studies of healthy subjects showing 10% to be ULN
- Better prediction / separation of subjects with asthma from normal or other lung diseases
- “Over-reliance on strict cut-offs for BDR should be avoided”
 - Not dichotomous trait

BDR: bronchodilator response

- Absolute change expressed as a percentage of predicted value
- >10% considered significant

BOX 1 Determination of a bronchodilator response

$$\text{Bronchodilator response} = \frac{(\text{post-bronchodilator value (L)} - \text{pre-bronchodilator value (L)}) \times 100}{\text{predicted value (L)}^\#}$$

A change of >10% is considered a significant bronchodilator response.

"#": predicted value should be determined using the appropriate Global Lung Function Initiative (GLI) spirometry equation.

For example, a 50-year-old male, height 170 cm, has a pre-bronchodilator forced expiratory volume in 1 s (FEV₁) of 2.0 L and a post-bronchodilator FEV₁ of 2.4 L. The predicted FEV₁ is 3.32 L (GLI 2012 "other" equation).

$$\text{Bronchodilator response} = \frac{(2.4 - 2.0) \times 100}{3.32} = 12.1\%$$

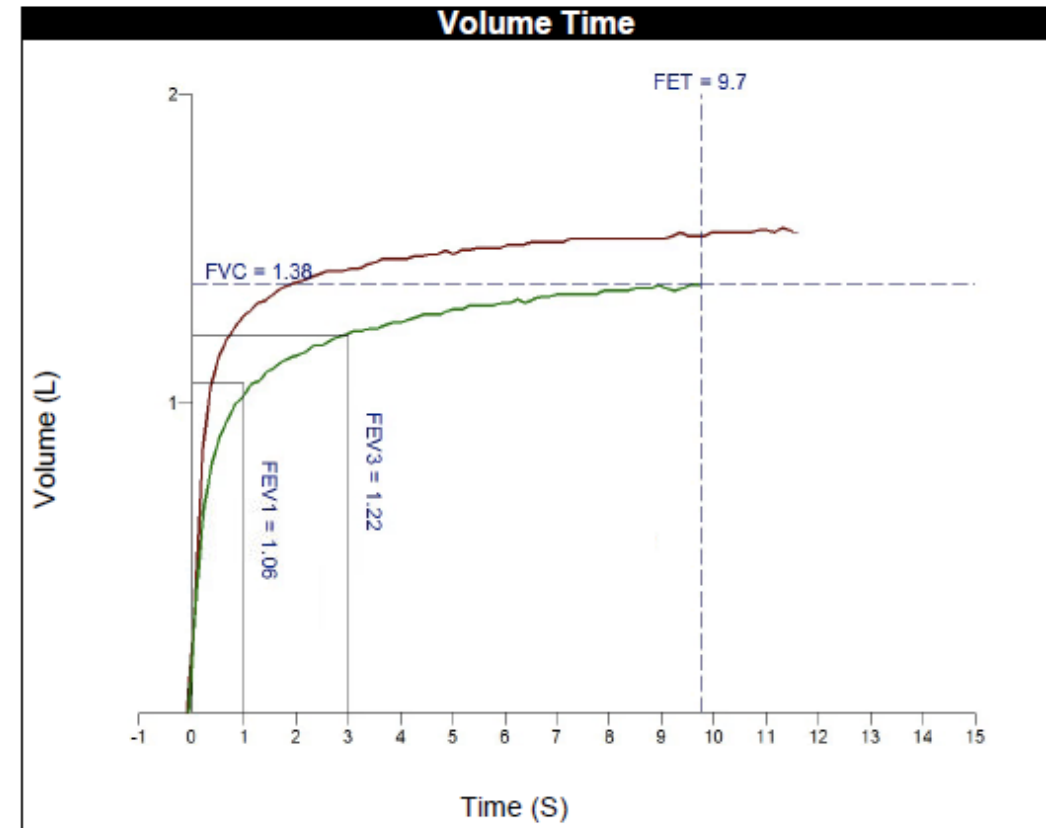
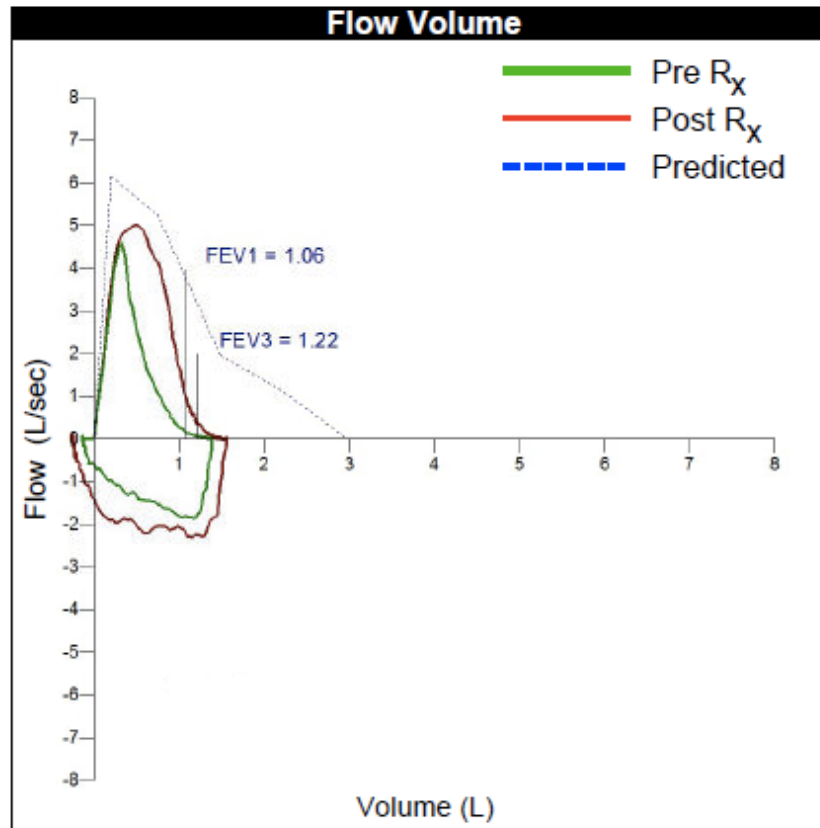
Therefore, their bronchodilator response is reported as an increase of 12.1% of their predicted FEV₁ and classified as a significant response.

Example 5 cont: bronchodilator testing

Spirometry (BTPS)		Predicted Range		Pre Bronchodilator		Post Bronchodilator		Percent Change
		Mean	95%	Actual	% Pred	Actual	% Pred	
FVC Effort Time		----	----	14:29	----	15:29	----	--
FEV ₁	L	2.36	1.80	1.06	45	1.28	54	21
FVC	L	2.97	2.29	1.38	46	1.57	53	14
FEV ₁ / FVC	%	79	70	77	97	82	104	6
FEV ₆	L	3.07	2.41	1.33	43	1.50	49	13
FEV ₁ / FEV ₆	%	81	72	80	99	85	105	6
FEF ₂₅₋₇₅	L/s	2.39	1.03	0.86	36	2.05	86	138
PEFR	L/s	6.14	4.48	4.59	75	6.26	102	36
FET	sec	----	----	9.74	----	11.53	----	18
MVV	L/m	89.4	38.4	----	----	----	----	--

- Old BDR criteria: FEV₁ 220cc and 21% = **YES**
- New BDR criteria: $(1.28 - 1.06) \times 100 / 2.36 = 9.3\%$ **NO... but almost**

FV loop: Bronchodilator response



Example 6

Spirometry

Pre Bronchodilator

		Actual	Pred	% Pred	Lower	Upper	Z-Score		
FEV ₁	L	2.33	2.13	109	1.52	2.71	0.56	N	
FVC	L	3.21	2.78	115	1.99	3.62	0.86	N	
FEV ₁ / FVC	%	73	77	95	64	90	-0.50	N	
FEF ₂₅₋₇₅	L/s	1.74	1.74	100	0.76	3.16	—		
PEFR	L/s	3.84	5.38	71	3.62	7.14	—		

Multiple Breath N2

Pre Bronchodilator

		Actual	Pred	% Pred	Lower	Upper	Z-Score		
TLC	L	4.70	5.09	92	3.99	6.34	-0.58	N	
VC	L	3.21	2.88	111	2.23	3.52	0.85	N	
RV	L	1.49	2.14	70	1.26	3.30	-1.16	N	
RV/TLC	%	32	42	76	29	56	-1.24	N	
FRC	L	—	2.93	—	2.09	4.00	-0.36	N	
IC	L	1.97	2.13	92	1.40	2.85	-0.36	N	

Diffusing Capacity

Pre Bronchodilator

		Actual	Pred	% Pred	Lower	Upper	Z-Score		
DLCO [Unc]	mL/min/mmHg	13.41	19.10	70	14.25	25.13	-1.97	A	m
KCO	mL/min/mmHg/L	3.28	4.07	81	3.09	5.18	-1.31	N	
VA [BTPS]	L	4.10	4.65	88	3.70	5.71	-0.93	N	
VI [BTPS]	L	3.01	2.88	105	2.23	3.52	—		
Diffusion Time	s	9.32	0.00	—	0.00	0.00	—		

This pattern is consistent with any of the following except:

- A) Interstitial lung disease
- B) Emphysema
- C) Neuromuscular weakness
- D) Anemia
- E) Pulmonary hypertension

CT chest



Echocardiogram



Isolated decrease in DLCO

- Emphysema
- Anemia (if not corrected for hemoglobin level)
- Early interstitial lung disease
- Pulmonary edema
- Pulmonary vascular disease (pulmonary hypertension)

NOT neuromuscular disease

Example 7

Spirometry

Pre Bronchodilator

		Actual	Pred	% Pred	Lower	Upper	Z-Score		
FEV ₁	L	1.56	2.76	57	2.11	3.38	-2.97	A	M
FVC	L	2.07	3.50	59	2.68	4.35	-2.93	A	M
FEV ₁ / FVC	%	75	79	95	68	89	-0.60	N	
FEF ₂₅₋₇₅	L/s	1.20	2.52	48	1.33	4.08	-1.87	A	m
PEFR	L/s	7.05	6.79	104	4.96	8.62	---		
FET	s	7.94	0.00	---	6.00	0.00	---		

Lung Volumes Box

Pre Bronchodilator

		Actual	Pred	% Pred	Lower	Upper	Z-Score		
TLC	L	3.53	5.50	64	4.47	6.66	-3.32	A	M
VC	L	2.07	3.74	55	2.95	4.53	-3.44	A	M
RV	L	1.46	1.77	82	1.08	2.68	-0.67	N	
RV/TLC	%	41	32	128	21	43	1.30	N	
FRC	L	1.90	2.92	65	2.07	3.98	-2.04	A	m
IC	L	1.63	2.67	61	1.81	3.54	-1.99	A	m
ERV	L	0.44	0.97	45	0.36	1.87	-1.36	N	

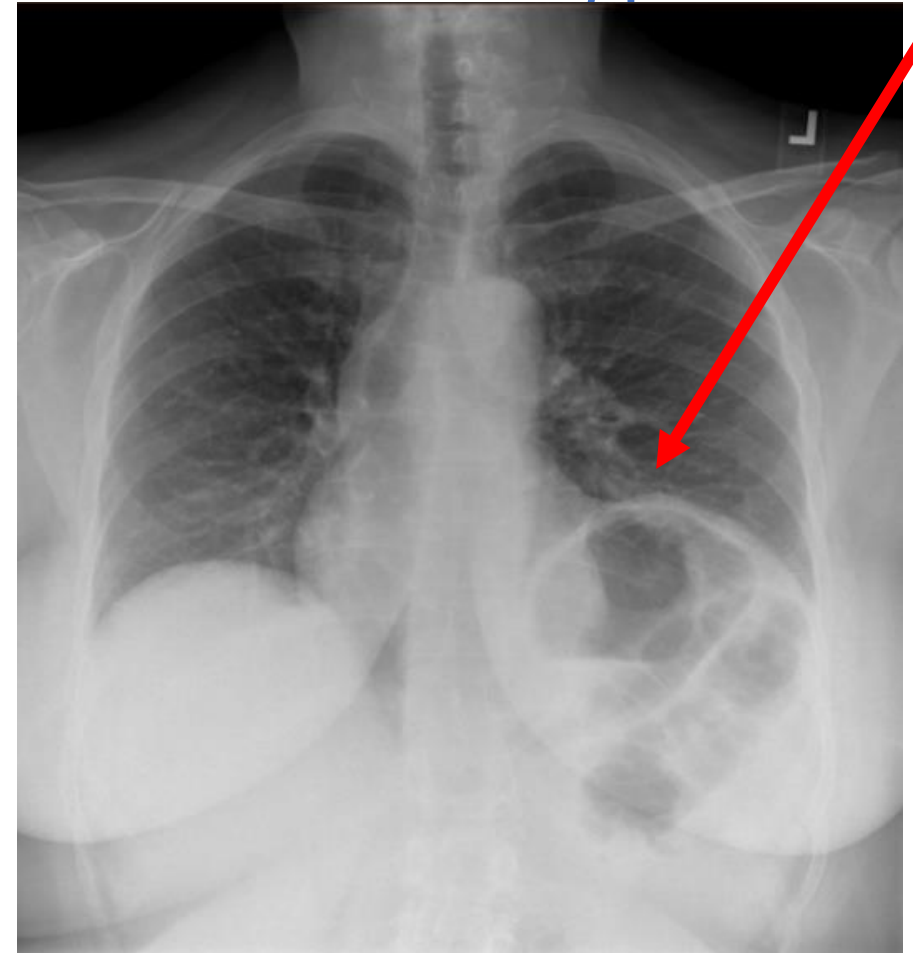
DLCO: normal

Case 3 (cont): Respiratory muscle strength

- MIP: maximal inspiratory pressure
- MEP: maximal expiratory pressure

Respiratory Muscle		Pre Bronchodilator				
		Actual	Pred	% Pred	Lower	Upper
MIP	cmH ₂ O	36	76	47	50	102
MEP	cmH ₂ O	75	96	78	56	136

- MIP: primarily diaphragm
- MEP: intercostal and abdominal muscles



PFT patterns in neuromuscular weakness

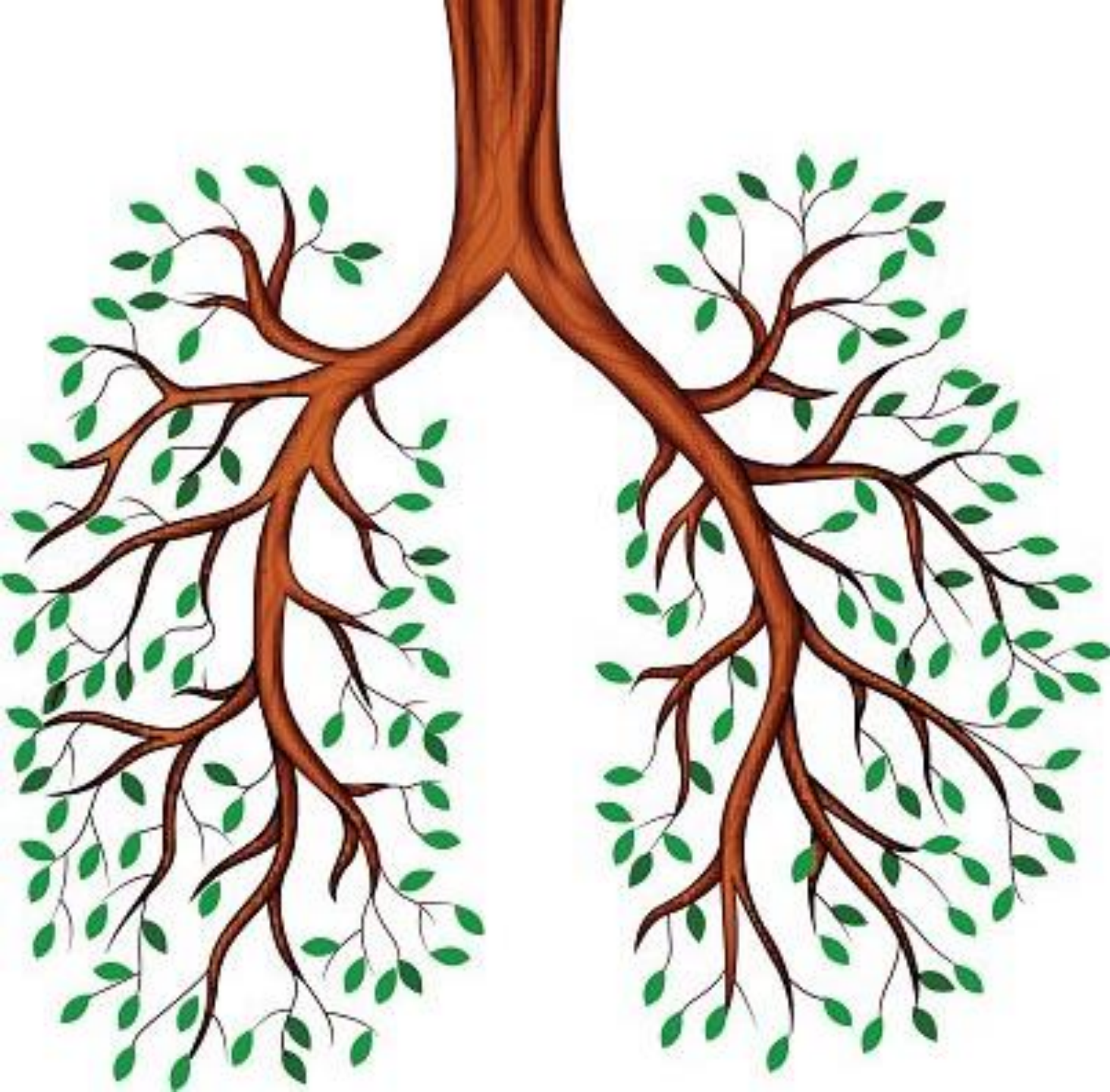
- Restriction
- Normal DLCO
- Not all volumes down the same (vs. ILD)
 - RV, FRC often normal or not as low
 - RV/TLC may be elevated– **NOT due to air trapping** but bc RV is normal while TLC low
- Reduced PEFr (in systemic disorders)
- **FVC**
 - Seated / supine spirometry: 20% decline suggestive of diaphragmatic weakness
 - Often followed over time
 - Used to predict need for nocturnal ventilation (<50%)
 - Daytime ventilation (<20%)

Summary /MOC REFLECTIVE STATEMENT

- PFTs can be very useful in defining physiology in patients with respiratory symptoms
- Use LLN / 95% CI to define normal/abnormal
 - But remember it is a continuum!
- Use FEV_1 to **grade severity** of *ANY* respiratory deficit
- $FEV_1/FVC < LLN$ defines obstruction
 - But can see other patterns in obstructive lung disease
- Consider lung volumes
 - Necessary to define or rule out restriction
 - Delineate other patterns

Selected References

- Pellegrino *et al* ATS/ERS Task force: Interpretive strategies for lung function tests. ERJ 2005;26:948-968
- Stanojevic *et al* ERS/ATS technical standard on interpretive strategies for routine lung function tests. ERJ 2022;60:2101499



Thank you!

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