Updates in Respiratory Medicine: **Pulmonary Function Testing**

Developed for The *Australian Medical Forum* and
The Royal Australian College of General Practitioners

Sam Kim MBBS (UQ) FRACP MPH MBA MMED (USyd)
Spring Hill BRISBANE QLD
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Overview

- Basis for spirometry
- Techniques
- Diagnostic features of common diseases
- Cases (Q & A)

Indications

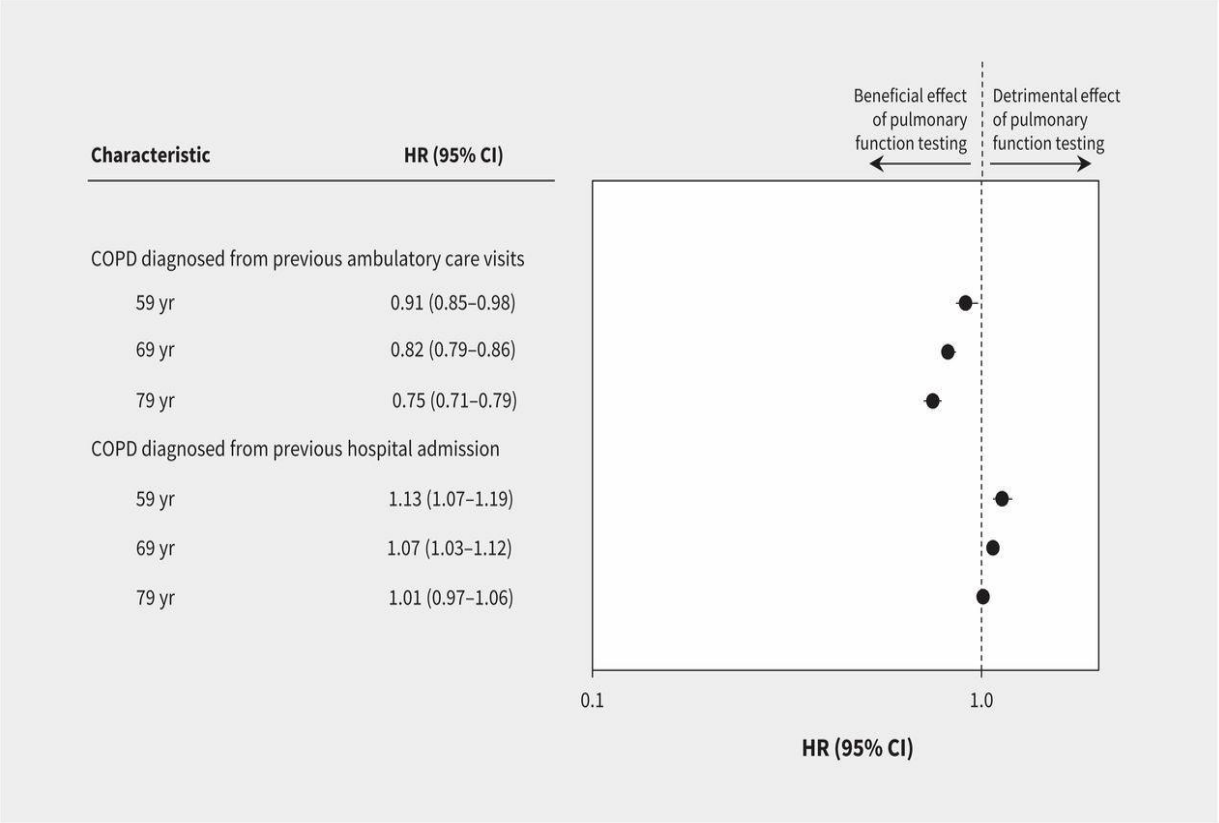
Whenever feasible, patients should have lung function measured and diagnosis confirmed

- Assessment of breathless (out-)patient (see Gershon *et al*, 2017).
- Monitoring pre-existing lung disease.
- Preoperative assessment.
- Occupational screening.
- Post-transplant monitoring.
- Medicolegal (see AMA Table 5.12).
- Research.

Outcomes of patients with COPD diagnosed with or without pulmonary function testing[1]

N=68,898 patients, 41.2% completed pulmonary function testing (2005-2012, Ontario)

https://jamanetwork.com/journals/jama/fullarticle/1904829



Reduced risk in ambulatory patients of hospital admission and death from lung function group

For hospital patients, greater use of ICS (30.1% v 18.7%) and LAMA (44.5% v 25.4%)

Reference:

[1]Gershon A, Mecredy G, Croxford R et al, 'Outcomes of patients with chronic obstructive pulmonary disease diagnosed with or without pulmonary function testing', 189 (2017) *CMAJ* E530.

Contra-Indications

Whenever feasible, common sense apply in performing/requesting lung function testing

- Recent eye, thoracic, abdominal or pelvic surgery (<6 weeks).
- Acute or recent pneumothorax (<4 weeks).
- Myocardial infarction (<4 weeks).
- Active infection.
- Child less than age of 3 years (i.e. exceptions).
- Tracheostomy (i.e. exceptions).

Concept of "Normal"

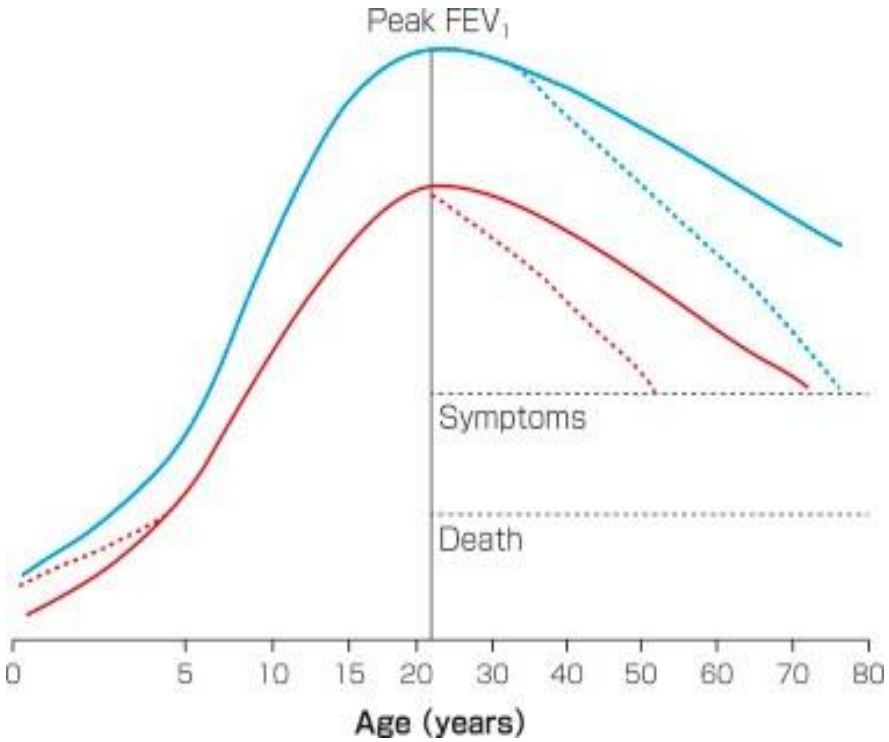
Whenever feasible, adjust for height, weight, age and ethnicity

- Caucasians have greater trunk-to-leg ratio, so bigger lungs.
- However, >70% of parameters depend on **height, weight and age.**[1]
- **"percentage predicted"** is arbitrary, i.e. no scientific basis.[2]
- **"80% or more"** does not mean "no lung disease".[3]
- Your overall clinical assessment is the key.

Reference:
[1]Miller MR *et al*, 'General considerations for lung function testing' (2005) 26(1) *Eur Resp J* 153; [2]MiPellegrino et al, 'Interpretative strategies for lung function testings' (2005) 26(5) *Eur Resp J* 948; [3]Miller MR *et al*, 'Standardisation of spirometry' (2005) 26(3) *Eur Resp J* 319

Early origin of lung disease: Age-related FEV_1 decline

Note: effects of intrauterine and/or post-natal insults (first 5 years of life)[1]



Blue – maximum lung function for normal birth

Red – intrauterine and/or postnatal insults (first 5 years of life)

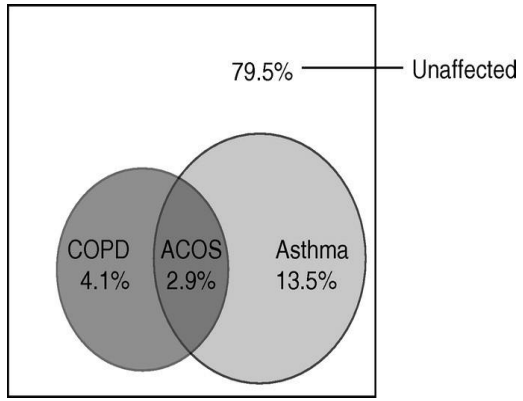
Reference:

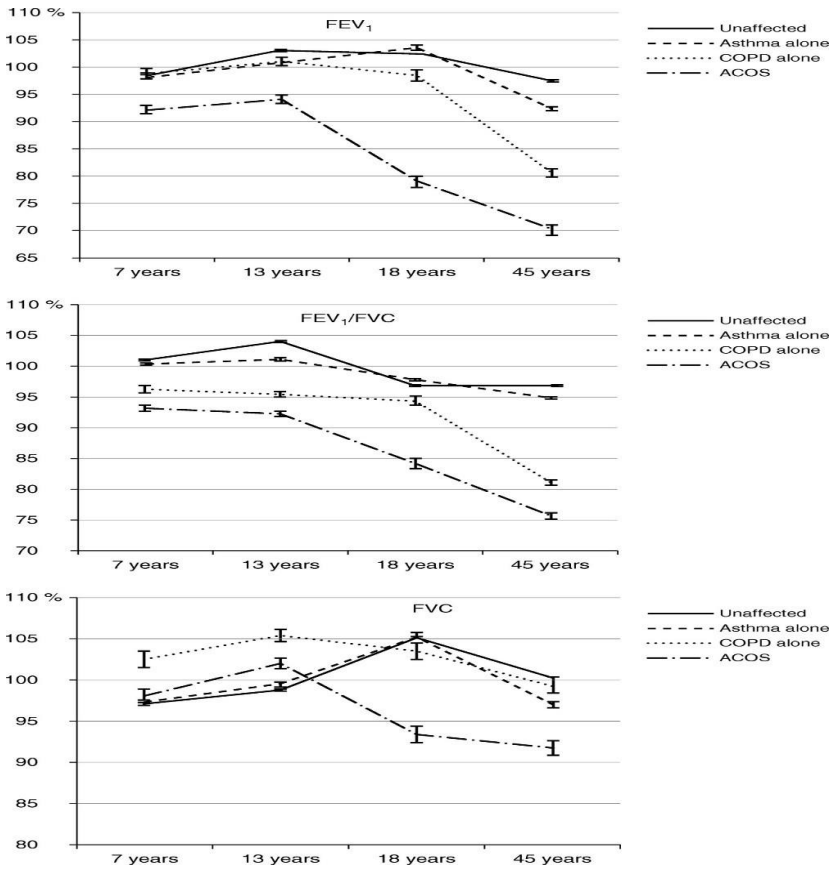
[1]Stocks J, Hislop A, Sonnappa s, 'Early lung development: lifelong effect of respiratory health and disease', 1 (2013) *Lancet Respir Med* 728.

Cross-sectional comparison of prebronchodilator lung function (mean and 95% confidence interval of % predicted values) for the four designated groups.

ACOS = asthma–COPD overlap syndrome; COPD = chronic obstructive pulmonary disease.[1]

[1]Dinh S. Bui, DS, Burgess JA, Lowe, AJ *et al*,
'Childhood lung function predicts adult chronic obstructive pulmonary disease and asthma-chronic obstructive pulmonary disease overlap syndrome' (2017) 196 *Am J Respir Crit Care Med* 39.





Study of sub-sample (n=1,389) of Tasmanian 7 year old cohort at age of 45 years (n=8,583)

Quality Control

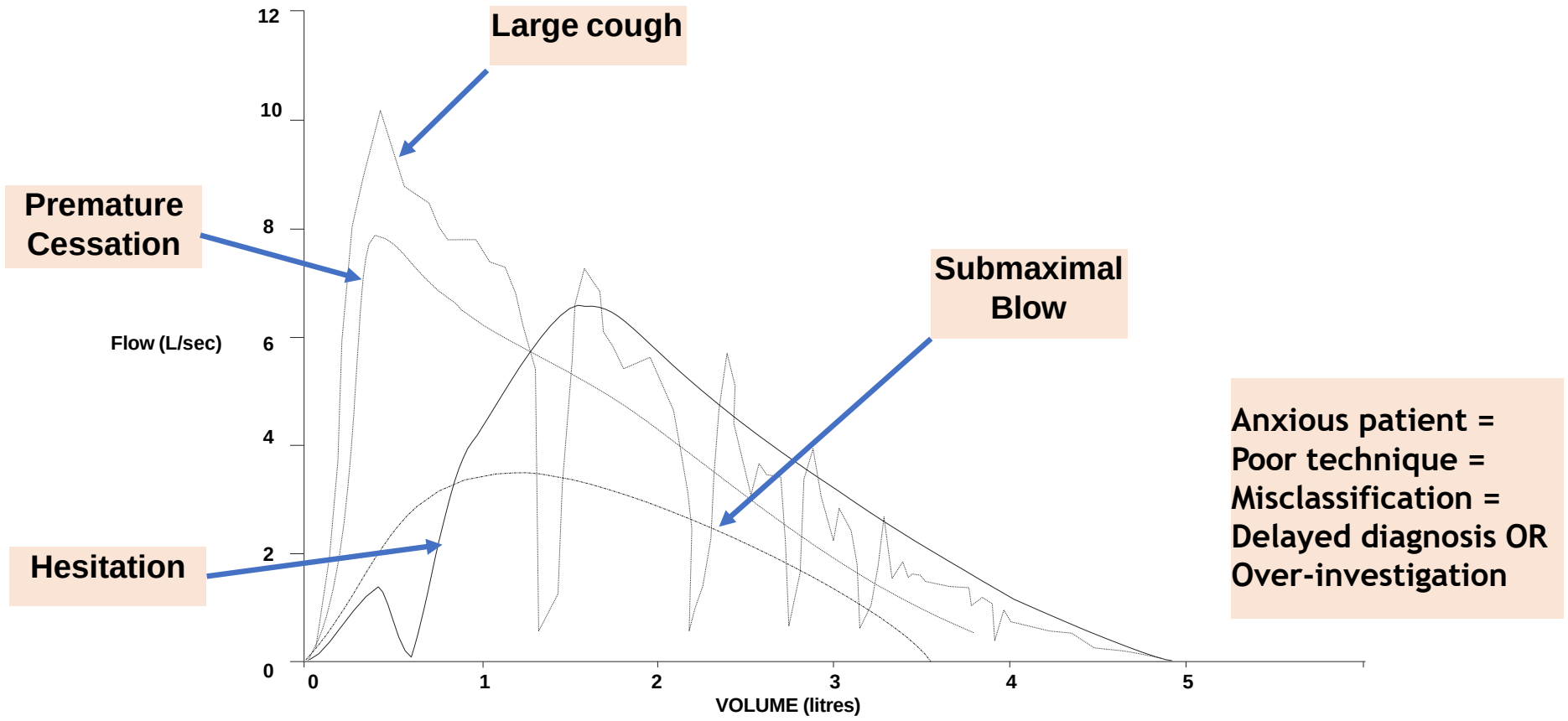
3 manoeuvres with the best 2 reproducible are unhelpful;

Whenever feasible, look at the overall pattern, see the numbers and apply pattern recognition

- Significant variability in outpatient setting (18-30%).[1]
- Up to 20% did not meet "Gold standard".[2]
- Accept uncertainty even at "cut-off" FEV_1/FVC of 70%.[3]

Reference:
[1]American Thoracic Society, 'Standardisation of spirometry: 1994 update' (1995) 152 *Am J Resp Crit Care Med* 1107; [2]MiSchermer *et al*, 'Validity of spirometric testing in a general practice population of patients with COPD' (2003) 58 *Thorax* 861; [3]Fabbri LM, Hurd SS, for the GOLD Scientific Committee, 'Global strategy for the diagnosis, management and prevention of COPD: 2003 update' (2003) Eur Resp J 1.

Common spirometric errors causing misclassification[1]

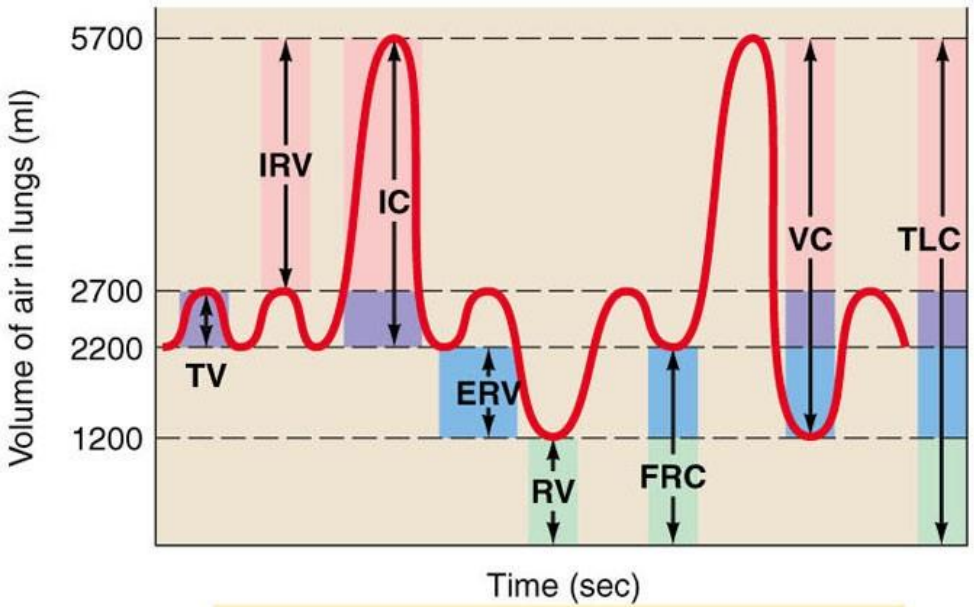


Reference:
[1]Enright PL, Studnicka M, Zielinski J, '*Spirometry to detect and manage chronic obstructive pulmonary disease and asthma in the primary care setting*' in Gosselink R, Stam H (eds.) Lung Function Testing (2005) vol. 10. Monograph 31, European Respiratory Society Journals Ltd, The Charlesworth Group, Wakefield, UK.

COPD screening devices available in australia

Lung function set-up

Performing dynamic spirometry

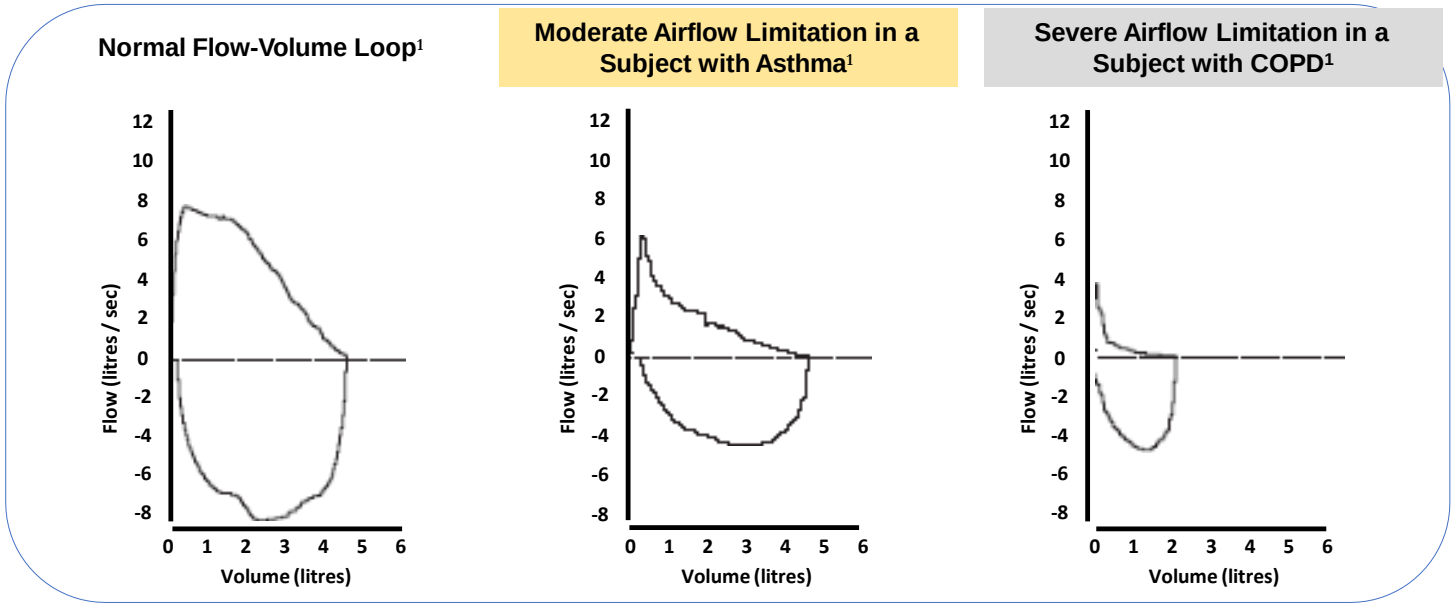


TV = Tidal volume (500 ml)
IRV = Inspiratory reserve volume (3000 ml)
IC = Inspiratory capacity (3500 ml)
ERV = Expiratory reserve volume (1000 ml)
RV = Residual volume (1200 ml)
FRC = Functional residual capacity (2200 ml)
VC = Vital capacity (4500 ml)
TLC = Total lung capacity (5700 ml)

Predicted normal values vary with age, height, gender,..

Values are average for a healthy young adult male; values for females are somewhat lower.

Examples of typical spirograms for obstructive lung diseases – asthma and COPD



Adapted from Miller MR et al. 2005[2]

- Whilst the above flow-volume loops depict examples of asthma and COPD, in general spirometry confirms chronic airflow limitations, but will be of limited value in distinguishing between asthma with fixed airflow obstruction, **COPD and Asthma-COPD Overlap Syndrome (ACOS)[2]**

- COPD = chronic obstructive pulmonary disease

References: [1]Miller MR *et al. Eur Respir J* 2005;26:319–338. 2 Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2015.

Diagnostic features of ACOS (asthma-COPD overlap syndrome)

- **Global Initiatives for Chronic Obstructive Lung Disease:**[1]

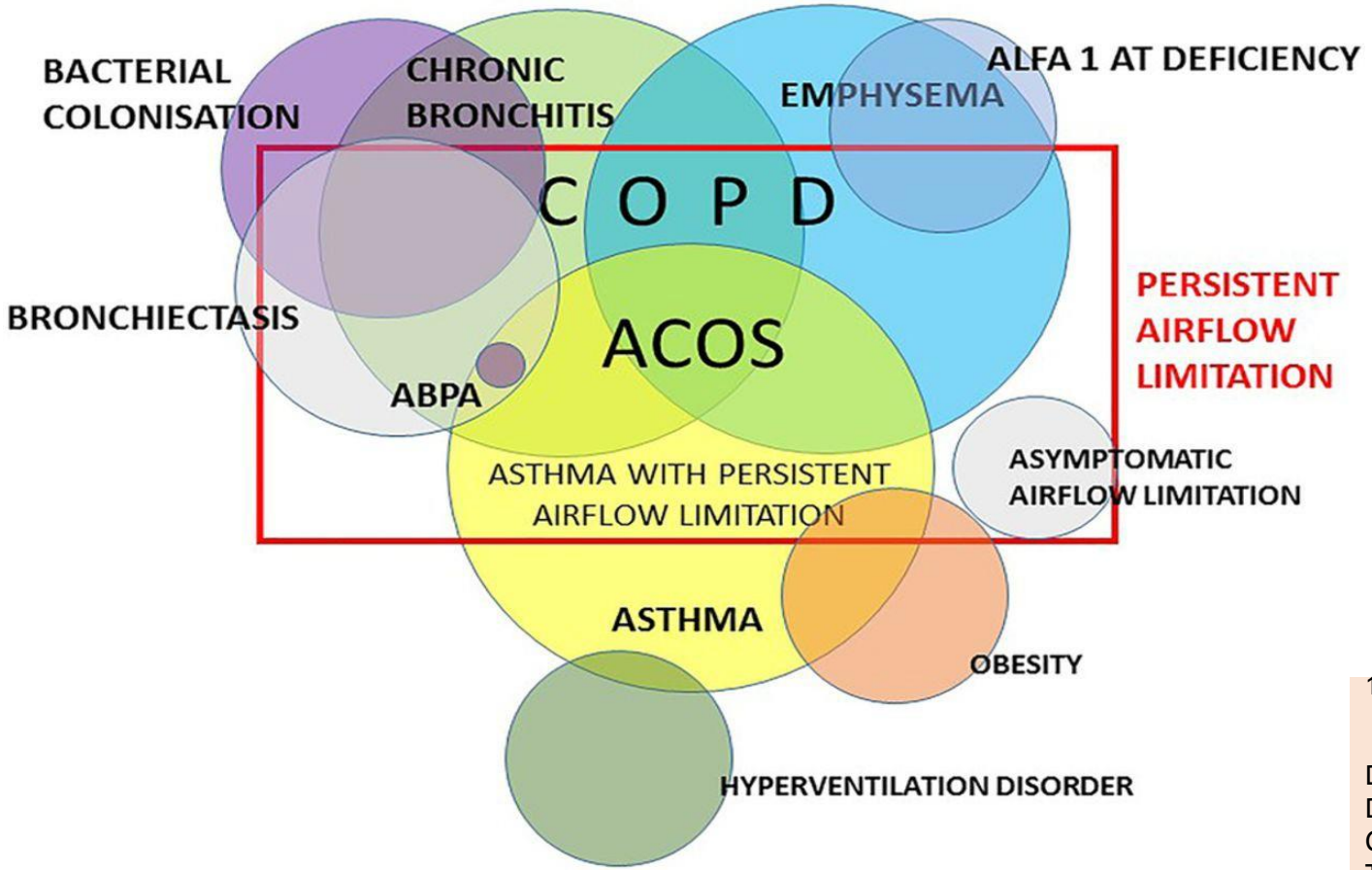
1. Post-BD FEV_1/FVC < lower limit of normal + self-reported history of asthma or positive BD test (increase in FEV_1 >15% and >400 mls) OR

2. Post-BD FEV_1/FVC < lower limit of normal + positive BD test (increase in FEV_1 >12% and >200 mls) + self-reported history of atopy + history of wheezing

Note:

- **Post-BD FEV_1/FVC < lower limit of normal** = COPD
- **Positive BD test (increase in FEV_1 >12% and >200 mls) + self-reported history of atopy + history of wheezing** = Asthma

Reference:
[1] Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2017 Global Strategy for Prevention, Diagnosis and Management of COPD, http://goldcopd.org.



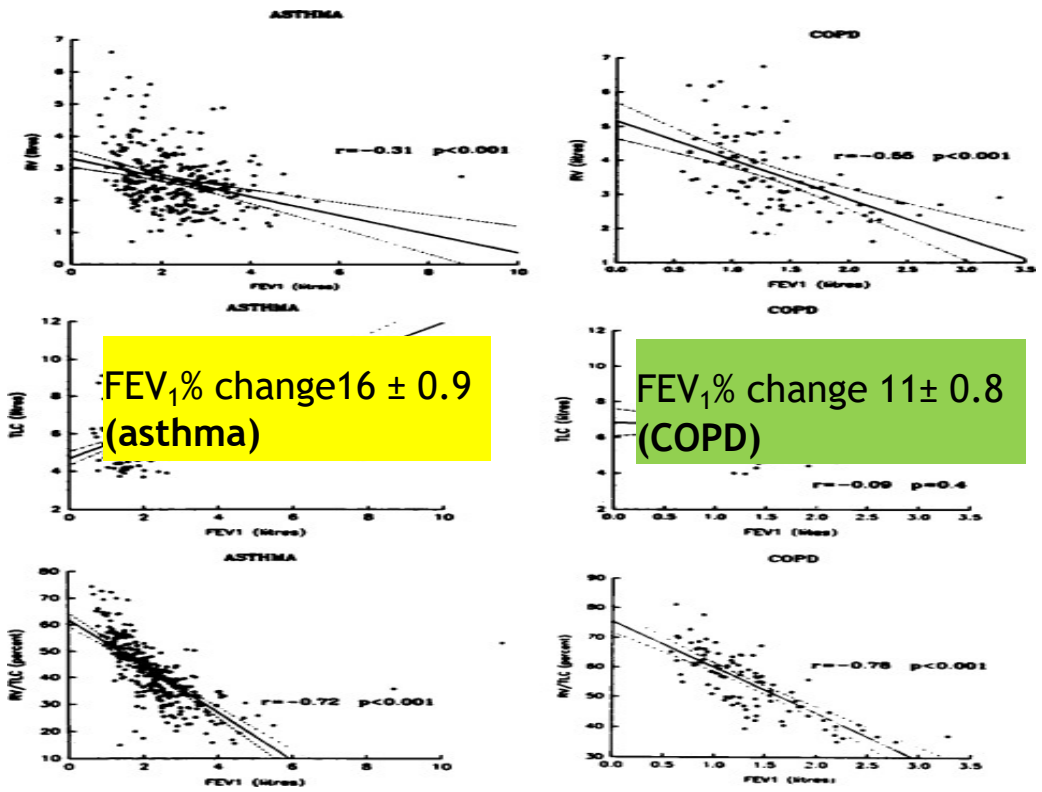
[1] Courtesy of Lowie Vanfleteren,

Department of Research and Development, Centre of Expertise for Chronic Organ Failure, Hornerheide, The Netherlands

Reference:
[1]Vanfleteren LE, 'Asymptomatic COPD, until you take it to exertion' [Editorial], 71 (2016) Thorax 781

Poor diagnostic response to beta-agonist (bronchodilator) challenge:

N=450 screened with confirmed diagnosis of 395 (87%) COPD or asthma[1]



FEV_1% change16 ± 0.9 **(asthma)**

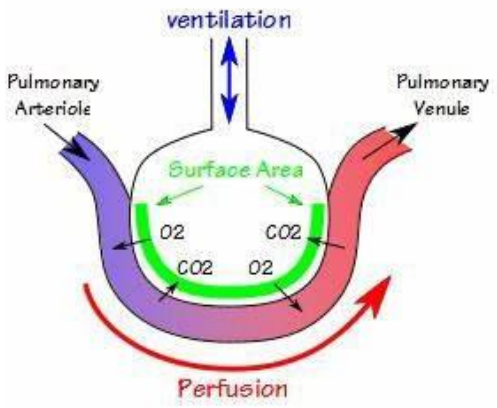
FEV_1% change 11± 0.8 **(COPD)**

Acute responses to BD in FEV_1 or FVC are <u>unreliable</u> for diagnosis

Even HRCT chest lacks sensitivity according to lung function

Reference:

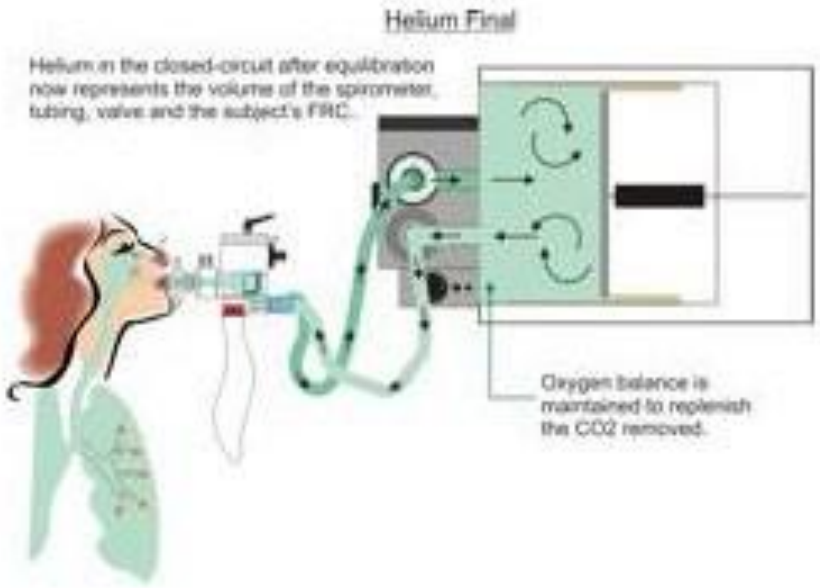
[1]Kesten S, Rebuck AS, 'Is the Short-term Response to Inhaled β-adrenergic agonist sensitive of specific for Distinguishing between Asthma and COPD?', 105 (1994) *Chest* 1042

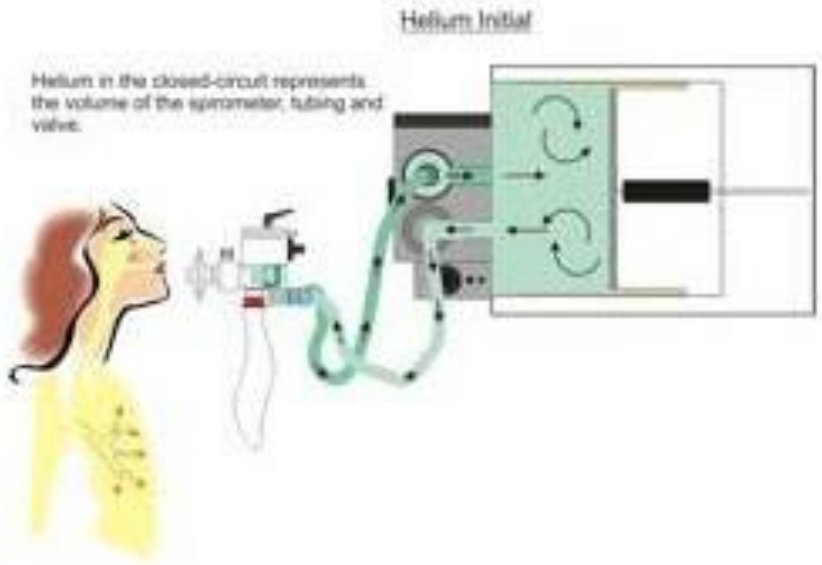


Gas transfer (TLCO)[1]

TLCO = **VA x KCO** where **VA** = alveolar volume, **KCO** = transfer coefficient

Application of Fick's Law,[2] i.e. $V_{gas} = A \times \Delta(P1-P2)/t$
where t = breath-holding time (usually 8-10 seconds) using CO-He marker gas[3]





Reference:
[1]Enright PL, Studnicka M, Zielinski J, '*Spirometry to detect and manage chronic obstructive pulmonary disease and asthma in the primary care setting*' in Gosselink R, Stam H (eds.) Lung Function Testing (2005) vol. 10. Monograph 31, European Respiratory Society Journals Ltd, The Charlesworth Group, Wakefield, UK; 2Krogh M, 'The diffusion of gases through the lungs of man' (1014) 49 J Physiology 271;
[3]Blakemore WS et al, 'A standardised breath holding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide' (1957) 36 *J Clinical Investigation* 1.

Performing gas transfer

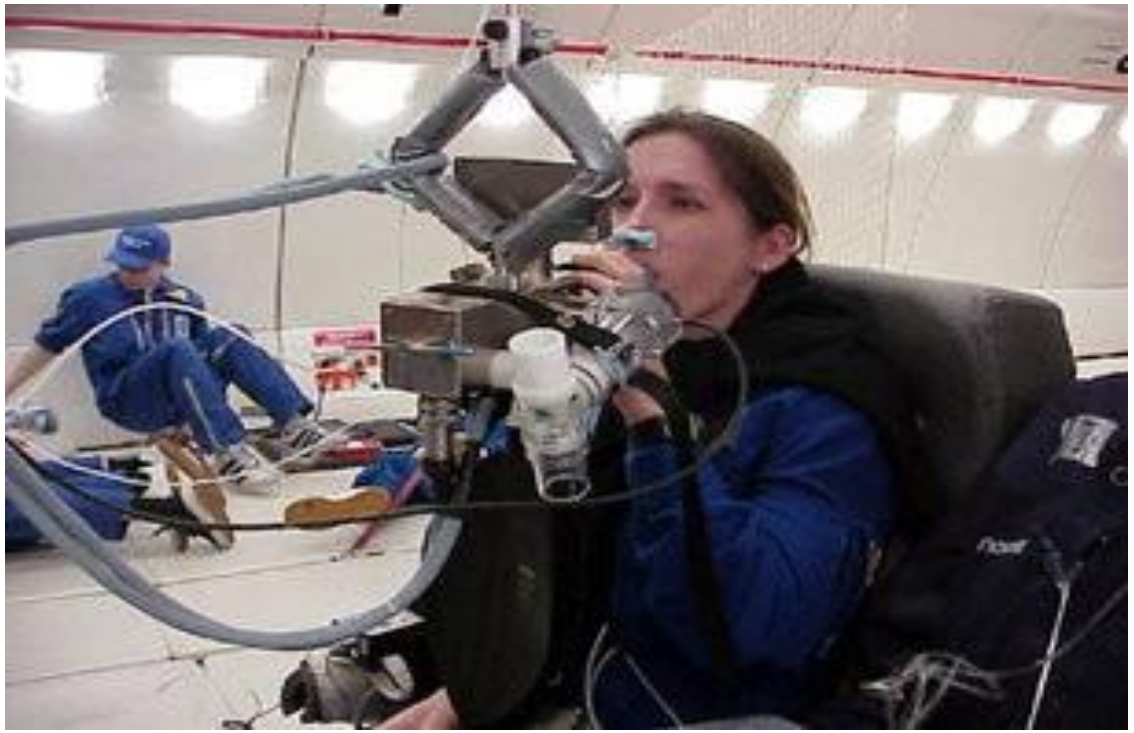
Lung Volumes and Capacities

	Description	Average Value
Tidal volume (TV)	Volume of air entering or leaving lungs during a single breath	500 ml
Inspiratory reserve volume (IRV)	Extra volume of air that can be maximally inspired over and above the typical resting tidal volume	3000 ml
Inspiratory capacity (IC)	Maximum volume of air that can be inspired at the end of a normal quiet expiration (IC =IRV + TV)	3500 ml
Expiratory reserve volume (ERV)	Extra volume of air that can be actively expired by maximal contraction beyond the normal volume of air after a resting tidal volume	1000 ml
Residual volume (RV)	Minimum volume of air remaining in the lungs even after a maximal expiration	1200 ml

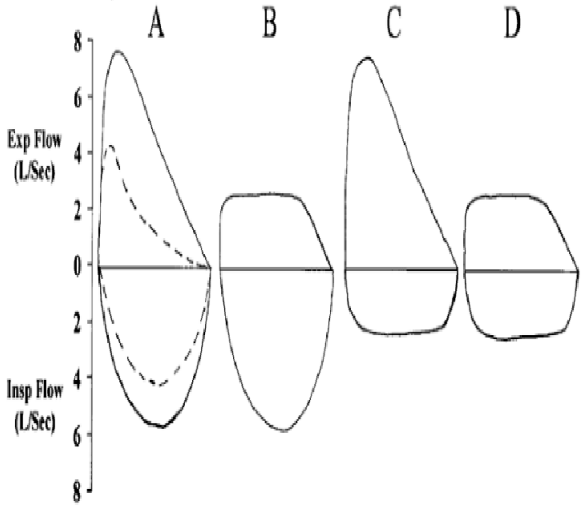
Lung Volumes and Capacities

	Description	Average Value
Functional residual capacity (FRC)	Volume of air in lungs at end of normal passive expiration (FRC = ERV + RV)	2200 ml
Vital capacity (VC)	**Maximum volume of air that can be moved out during a single breath following a maximal inspiration (VC = IRV + TV + ERV)**	4500 ml
Total lung capacity (TLC)	Maximum volume of air that the lungs can hold (TLC = VC + RV)	5700 ml
Forced expiratory volume in one second (FEV_1): Dynamic volume	Volume of air that can be expired during the first second of expiration in an FVC (Forced Vital Capacity) determination	FEV_1% = FEV_1/FVC ratio Normal >75%

Lung function report analysis



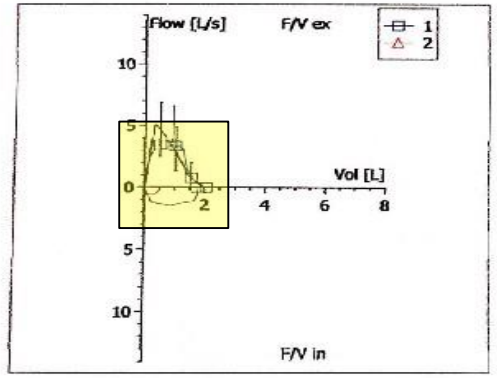
Case 1

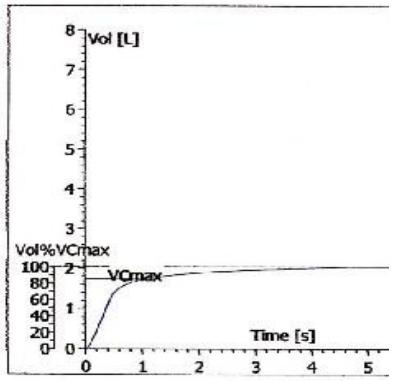


Large airway obstruction can be detected by flow-volume loop: characterised by **truncation on inspiratory or expiratory loop**

Complex Pulmonary Function Report

Hemoglobin:	[redacted]	Ref. Physician:	–
BMI:	35.46		
Diagnosis:	[redacted]		
Last Name:			
First Name:			
Date of Birth:	02/11/1943	Age:	74 Years
Sex:	female	Weight:	83 kg
		Height:	153 cm





Dynamic spirometry

		Pred	Pre	Post	%Pre	%(Pre/Post)
FVC	[L]	1.96	2.05		104	
FEV 1	[L]	1.59	1.74		109	
FEV 1 % VC MAX	[%]	75.04	84.96		113	
MMEF 75/25	[L/s]	2.32	2.30		99	
PEF	[L/s]	5.09	3.44		68	
FIV1	[L]		1.40	0.46		32
PIF	[L/s]		1.44	0.61		42
FEV 1*30	[L/min]	73.42	52.15		71	

Static lung volumes

Pred

[redacted]

References:

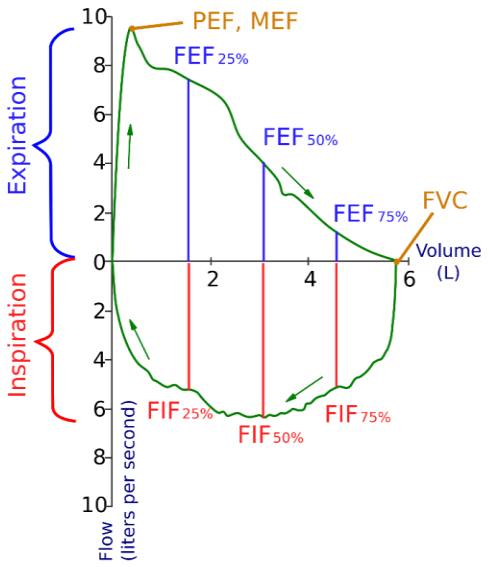
Dynamic FEV_1, FVC: **+/- 20%**

Static lung volumes **+/- 20%**

Gas transfer **+/- 20%**

Reversibility:
FEV_1 +12%
MMFR +40%

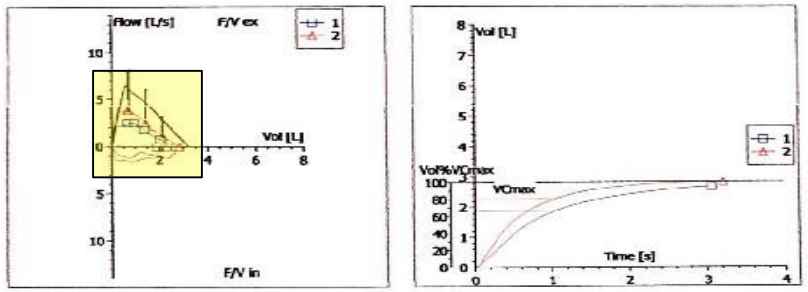
Case 2



Small to medium sized airway obstruction can be detected by flow-volume loop, and **reversibility study** on **beta-agonist challenge testing**

Complex Pulmonary Function Report

Hemoglobin:	[redacted]	Ref. Physician:	–
BMI:	23.37		
Diagnosis:	[redacted]		
Last Name:			
First Name:			
Date of Birth:	13/04/1995	Age:	22 Years
Sex:	female	Weight:	54 kg
		Height:	152 cm



Dynamic spirometry

		Pred	Pre	Post	%Pre	%(Pre/Post)
FVC	[L]	3.19	2.69	2.82	84	105
FEV 1	[L]	2.78	1.89	2.27	68	120
FEV 1 % VC MAX	[%]	84.35	70.13	80.43	83	115
MMEF 75/25	[L/s]	3.97	1.47	2.18	37	147
PEF	[L/s]	6.50	2.52	3.83	39	152
FIV1	[L]		1.15	1.55		135
PIF	[L/s]		1.13	1.54		137
FEV 1*30	[L/min]	107.51	56.61	68.07	53	120

Static lung volumes

		Pred	Post
TLC-SB	[L]	4.24	4.29
VIN	[L]	3.20	2.42
FRC-SB	[L]	2.43	2.30
ERV	[L]	1.31	0.43
RV-SB	[L]	1.15	1.87
RV%TLC-SB	[%]	27.46	43.54

Gas transfer

	Pred	Post
DLCO SB [mmol/min/kPa]	8.47	6.62
DLCO/VA[mmol/min/kPa/L]	2.00	1.59

Signature: .....

Report summary to follow on Page 2

[redacted]

References:

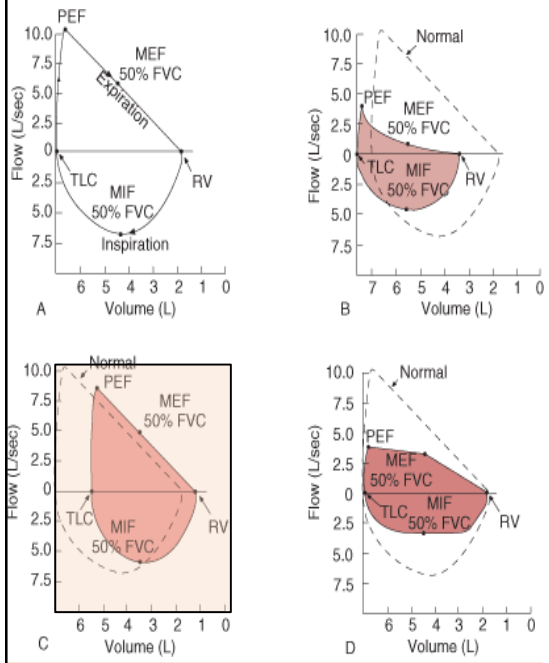
Dynamic FEV_1, FVC: **+/- 20%**

Static lung volumes **+/- 20%**

Gas transfer **+/- 20%**

Reversibility:
FEV_1 +12%
MMFR +40%

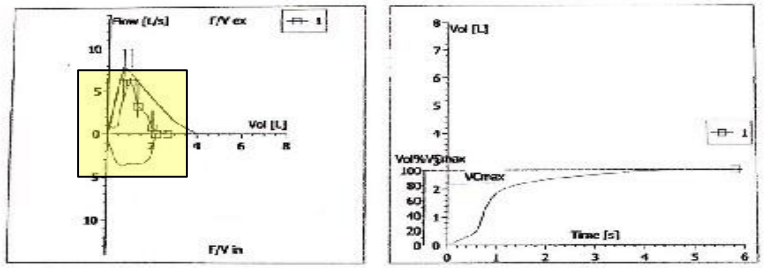
Case 3



Restrictive lung diseases can be differentiated from FVC, TLC and gas transfers

Complex Pulmonary Function Report

Hemoglobin:	[redacted]	Ref. Physician:	–
BMI:	26.79		
Diagnosis:	[redacted]		
Last Name:			
First Name:			
Date of Birth:	09/10/1948	Age:	69 Years
Sex:	male	Weight:	83 kg
		Height:	176 cm



Dynamic spirometry

		Pred	Pre	%Pre
FVC	[L]	3.98	2.68	67
FEV 1	[L]	3.05	2.20	72
FEV 1 % VC MAX	[%]	74.61	82.12	110
MMEF 75/25	[L/s]	3.10	2.44	79
PEF	[L/s]	7.95	5.98	75
FIV1	[L]		2.09	
PIF	[L/s]		3.67	
FEV 1*30	[L/min]	114.95	65.98	57

Static lung volumes

		Pred	Pre	%Pred
TLC-SB	[L]	6.98	3.67	53
VIN	[L]	4.13	2.58	63
FRC-SB	[L]	3.66	1.95	53
ERV	[L]	1.94	0.86	89
RV-SB	[L]	2.62	1.09	42
RV%TLC-SB	[%]	41.26	29.73	72

Gas transfer

	Pred	Pre	%Pred
DLCO SB [mmol/min/kPa]	8.90	2.17	24
DLCO/VA[mmol/min/kPa/L]	1.28	0.62	49

Signature:.....

Report summary to follow on Page 2

[redacted]

References:

Dynamic FEV_1, FVC: **+/- 20%**

Static lung volumes **+/- 20%**

Gas transfer **+/- 20%**

Reversibility:
FEV_1 +12%
MMFR +40%

Case 4

If unsure of asthma diagnosis, request for **Mannitol-based Bronchial provocation testing**

PD15 = minimal threshold dose for **FEV_1 decline >15%**

RDR = **Response Dose Ratio** (final % FEV_1 fall divided by cumulative dose of Mannitol)

MANNITOL PROVOCATION REPORT

Name: [redacted]

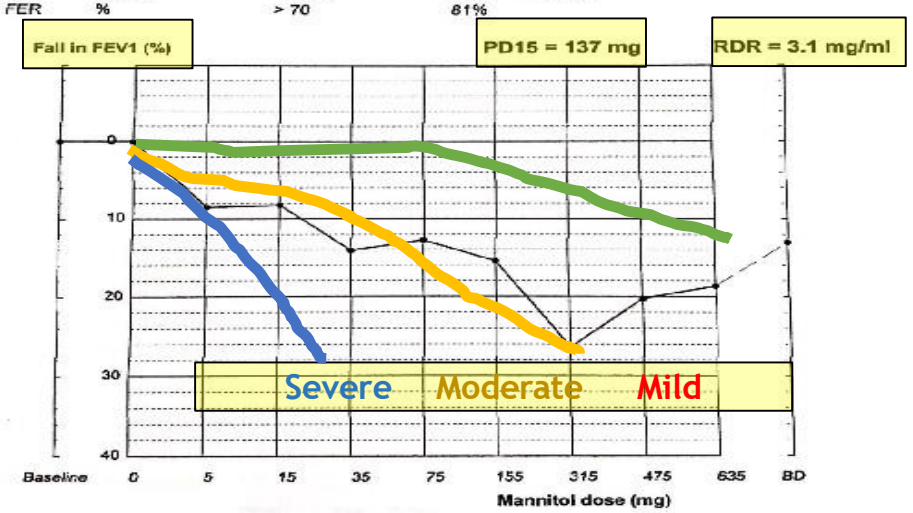
ID: 19071979
Gender: Male
Birthdate: 19/07/1979 (39)

Referred From: Dr Samuel Kim FRACP [redacted] FRACGP

Height (cm): 170
Weight (kg): 69
BMI (kg/m/m): 23.9

Test Date: 24/07/2018

		Normal range*	Baseline	% of predicted*
FEV_1	L BTPS	> 3.14	3.75	(97%)
FVC	L BTPS	> 3.96	4.65	(97%)
FER	%	> 70	81%	



Technical comment: Moderately-severe asthma and BHR confirmed on Mannitol challenge - not for diving for six months until asthma stabilised on treatment.

Dr. Sam Kim FRACP

[redacted]

References:

Dynamic FEV_1, FVC: **+/- 20%**

Static lung volumes **+/- 20%**

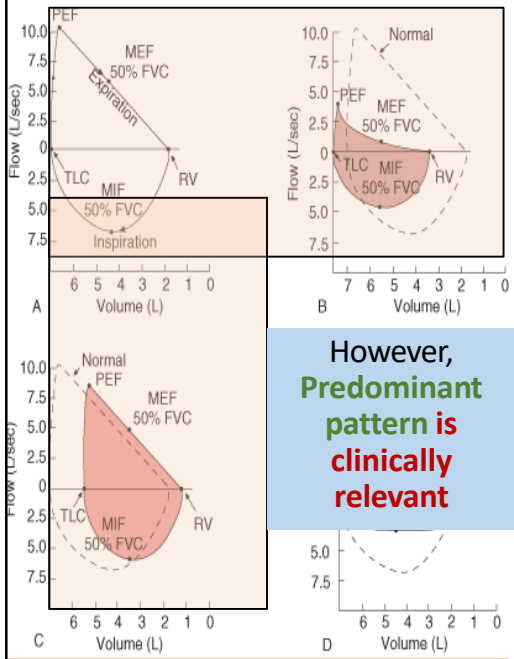
Gas transfer **+/- 20%**

Reversibility:
FEV_1 +12%
MMFR +40%

Case 5

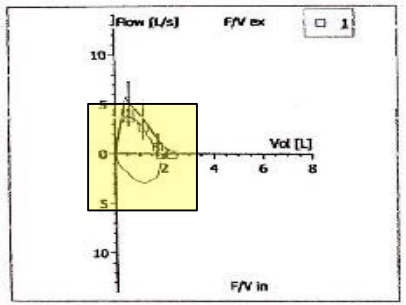
Complex Pulmonary Function Report

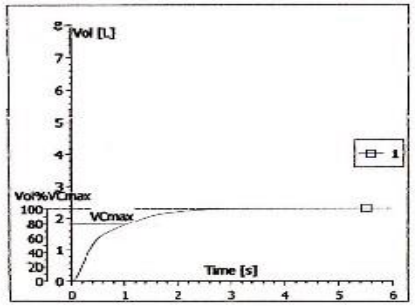
Hemoglobin:	[redacted]	Ref. Physician:	–
BMI:	20.8		
Diagnosis:	[redacted]		
Last Name:			
First Name:			
Date of Birth:	13/10/1940	Age:	73 Years
Sex:	female	Weight:	58 kg
		Height:	167 cm



However, **Predominant pattern is clinically relevant**

Most population subjects have **mixed ventilatory limitations** (i.e. effects of weight, body habitus, disease in evolution etc)





Dynamic spirometry

		Pred	Pre	%Pre
FVC	[L]	2.48	2.29	92
FEV 1	[L]	2.05	1.83	90
FEV 1 % VC MAX	[%]	74.28	80.09	108
MMEF 75/25	[L/s]	2.36	1.73	74
PEF	[L/s]	5.74	4.03	70
FIV1	[L]		1.87	
PIF	[L/s]		2.91	
FEV 1*30	[L/min]	82.48	55.02	67

Static lung volumes

		Pred	Pre	%Pred
TLC-SB	[L]	5.23	4.47	86
VIN	[L]	2.63	2.20	84
FRC-SB	[L]	2.82	3.26	116
ERV	[L]	0.55	0.99	181
RV-SB	[L]	2.27	2.27	100
RV%TLC-SB	[%]	45.48	50.77	112

Gas transfer

	Pred	Pre	%Pred
DLCO SB [mmol/min/kPa]	7.10	5.16	73
DLCO/VA[mmol/min/kPa/L]	1.36	1.19	88

Signature:.....

Report summary to follow on Page 2

[redacted]

References:

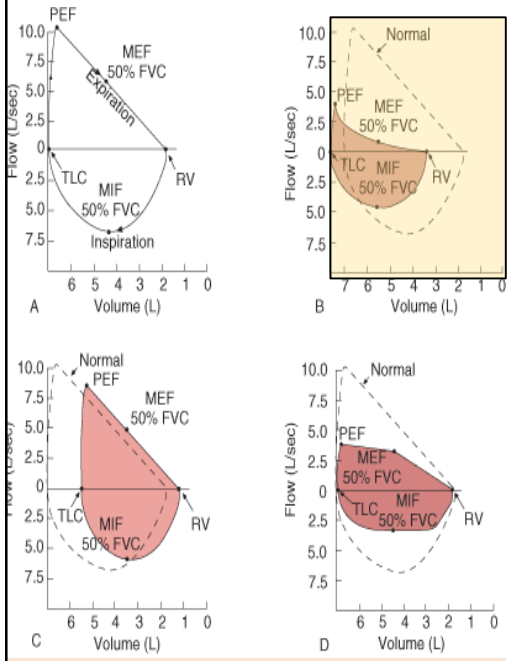
Dynamic FEV_1, FVC: **+/- 20%**

Static lung volumes **+/- 20%**

Gas transfer **+/- 20%**

Reversibility:
FEV_1 +12%
MMFR +40%

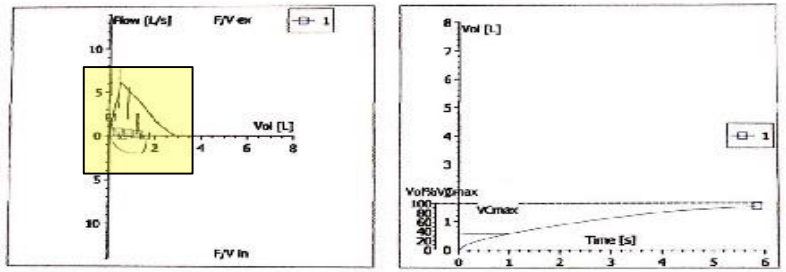
Case 6



However, severe COPD is very obvious due to **hyperinflation, gas trapping** and characteristic flow-volume loop pattern

Complex Pulmonary Function Report

Hemoglobin: [redacted] Ref. Physician: --
BMI:
Diagnosis:
Last Name:
First Name:
Date of Birth: 13/05/1960 Age: 58 Years
Sex: female Weight: 75 kg
Height: 163 cm



Dynamic spirometry

		Pred	Pre	%Pre
FVC	[L]	2.82	1.57	55
FEV 1	[L]	2.39	0.57	24
FEV 1 % VC MAX	[%]	78.08	35.09	45
MMFF 75/25	[L/s]	2.99	0.28	9
PEF	[L/s]	6.11	2.15	35
FIV1	[L]		1.52	
PIF	[L/s]		2.04	
FEV 1*30	[L/min]	92.81	17.18	19

Static lung volumes

		Pred	Pre	%Pred
TLC-SB	[L]	4.97	3.89	78
VIN	[L]	2.92	1.54	53
ERV	[L]	0.83	*	*
RV-SB	[L]	1.88	2.35	125
RV%TLC-SB	[%]	38.68	60.47	156

Gas transfer

	Pred	Pre	%Pred
DLCO SB [mmol/min/kPa]	7.75	1.57	20
DLCO/VA [mmol/min/kPa/L]	1.56	0.42	27

Signature:.....

Report summary to follow on Page 2

However,
Hyperinflation can be reduced by effects of body habitus

References:

Dynamic FEV_1, FVC: **+/- 20%**

Static lung volumes **+/- 20%**

Gas transfer **+/- 20%**

Reversibility:
FEV_1 +12%
MMFR +40%

[redacted]

Summary

- What's new? What's True?
  - Prepare the less anxious patient ("**it is not an exam or a trial**")
  - Be aware of misclassification (= delayed diagnosis)
  - Be aware of ACOS, and consider at least 1 baseline complex lung function testing
- What's old?
  - The best out of 3 is **unhelpful** (i.e. look at the overall pattern, see the numbers and apply pattern recognition
- What's Gold? (gold nugget/take home message)
  - Take time and go through systematically
  - Use gas transfers…. They are "**gold nuggets**"