INTERVENTIONAL
Pulmonology Clinic

GP Education Series: COPD

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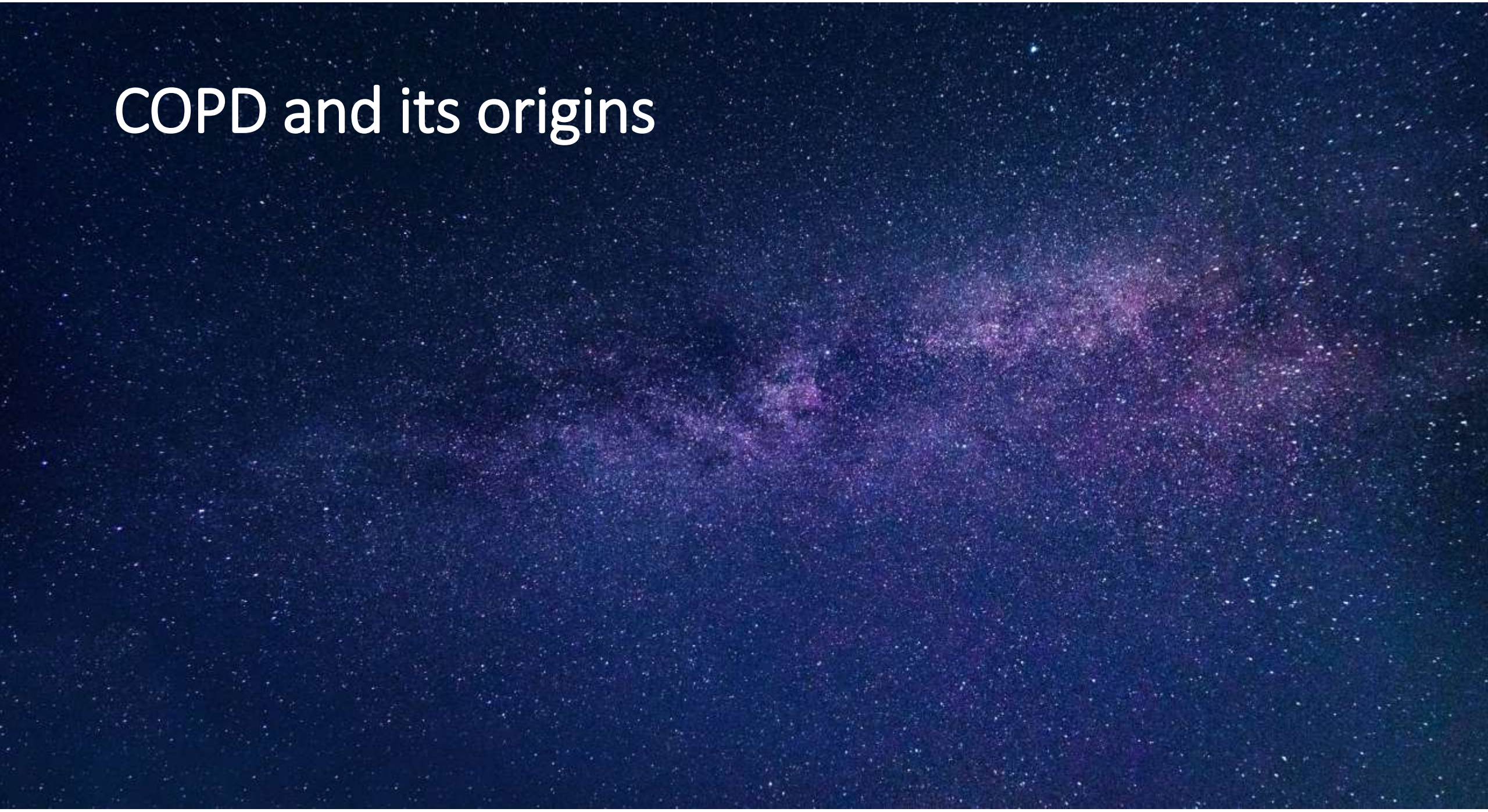
Respiratory (Interventional Pulmonologist) and General Physician

2021

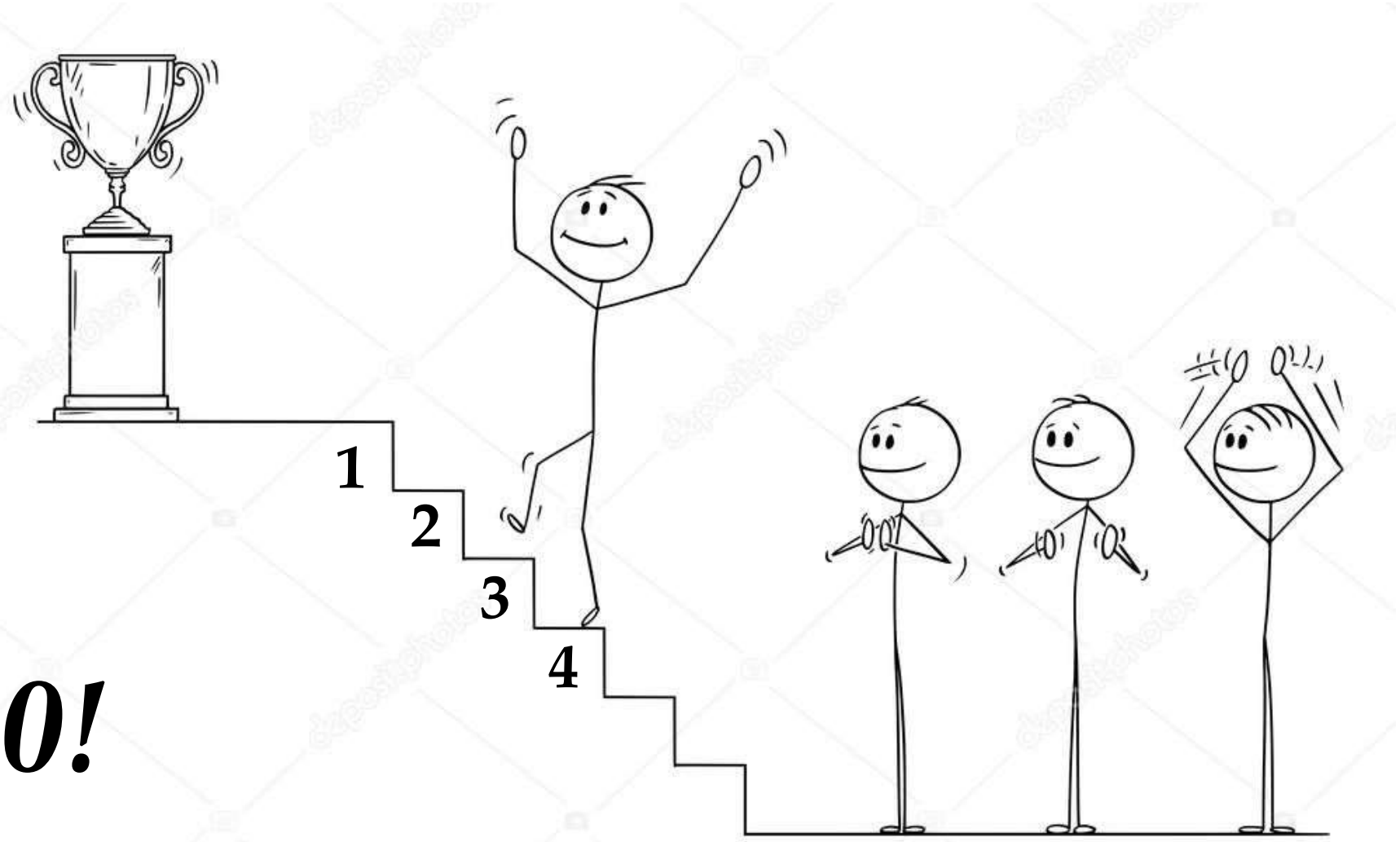
COPD

- Introduction
- Act 1: COPD and its origins
- Act 2: Spirometry and lung function
- Act 3: COPD treatment: Approach to Inhaler devices
- Conclusion

COPD and its origins



Chronic Obstructive Pulmonary Disease



2030!

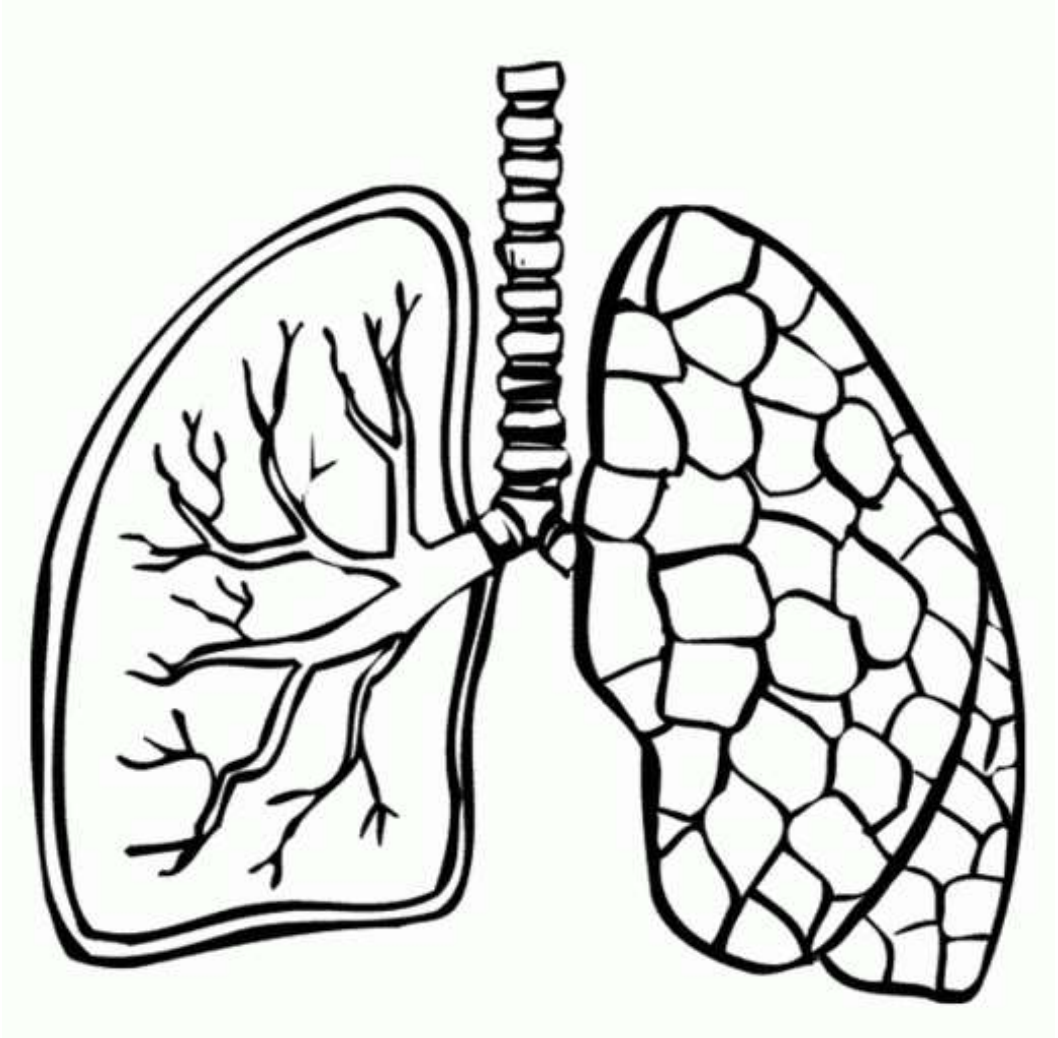
Gold 2020, ERS Handbook of Respiratory medicine 2019

Chronic Obstructive pulmonary disease

- Defined as per GOLD:
  - Common, preventable and treatable
  - Persistent respiratory symptoms
  - Airflow limitation that is due to airway and/or alveolar abnormalities
  - Usually caused by significant exposure to noxious particles or gases

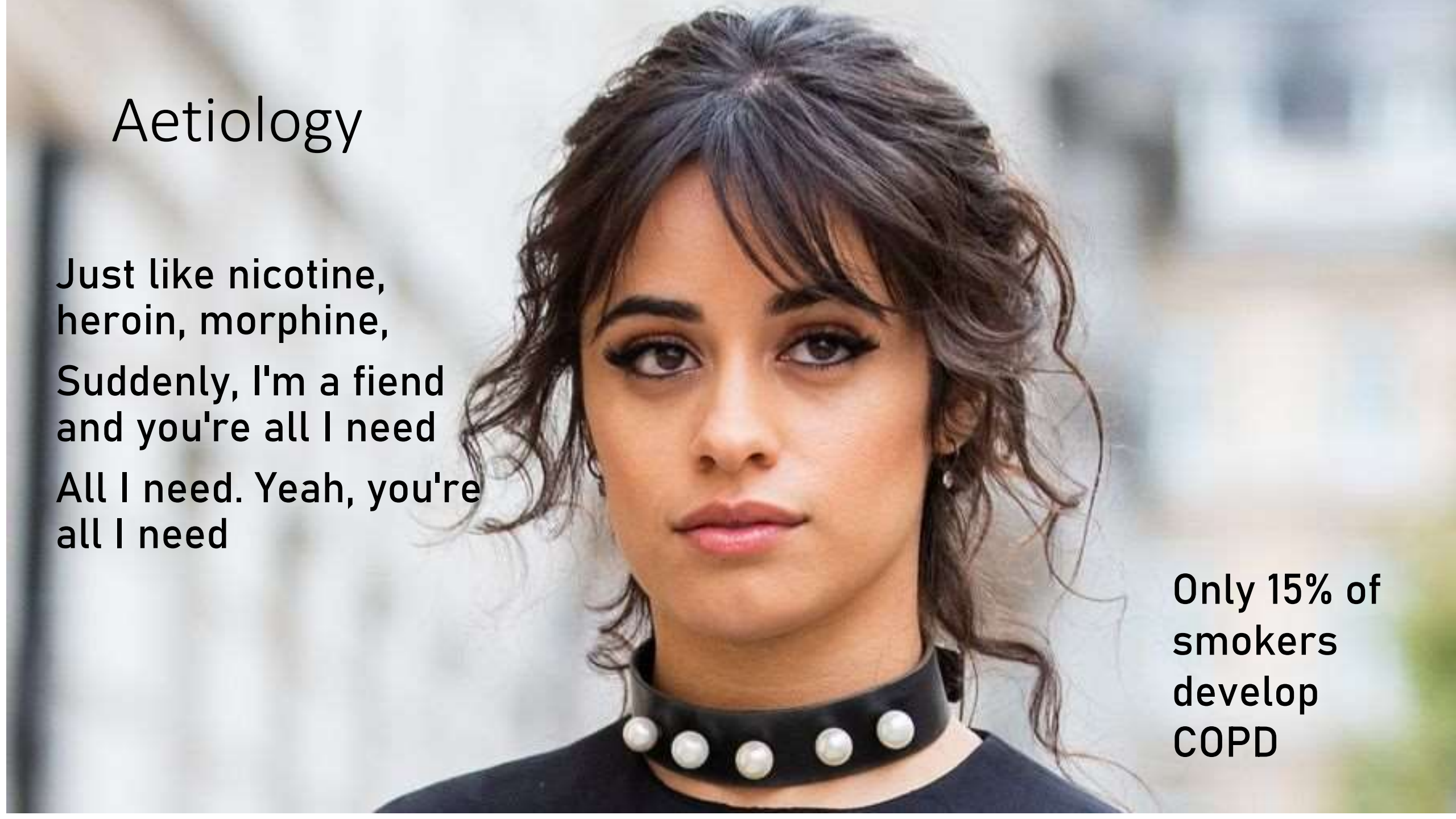
Gold 2020, ERS Handbook of Respiratory medicine 2019

Chronic bronchitis - Cough productive of sputum on most days of the week >3m/yr x 2 consecutive years (clinical diagnosis)



Emphysema - permanent destruction of alveoli resulting in larger airspaces, leading to impaired gas transfer (anatomical diagnosis)

Aetiology



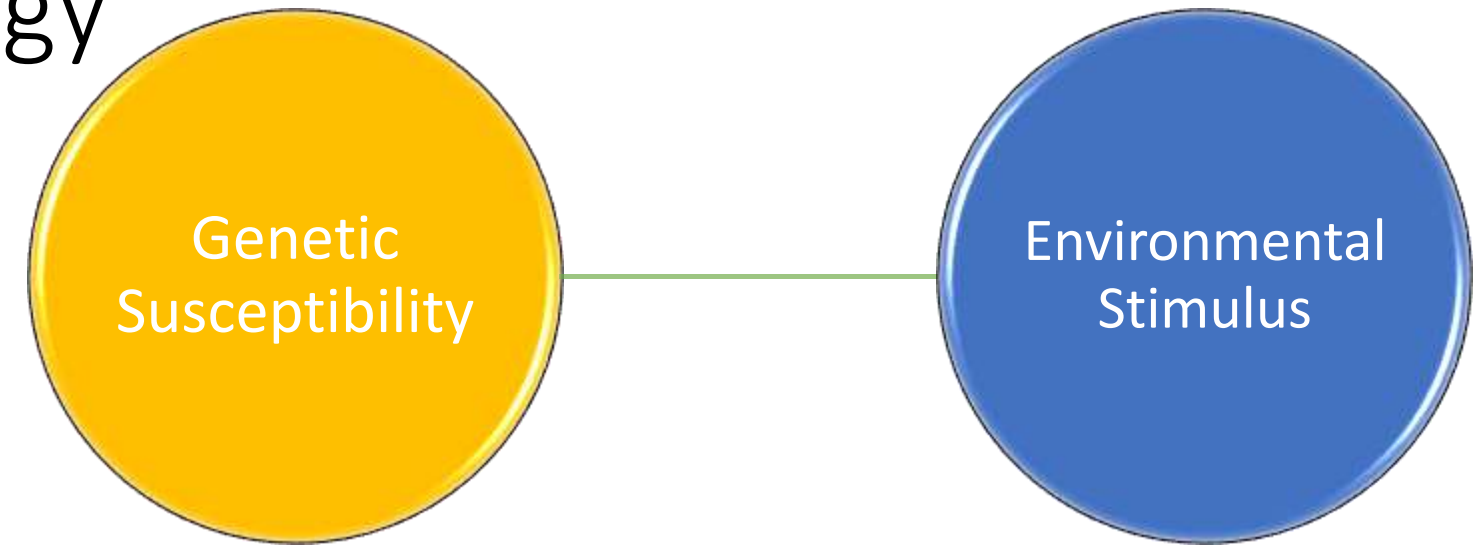
Just like nicotine,
heroin, morphine,

Suddenly, I'm a fiend
and you're all I need

All I need. Yeah, you're
all I need

Only 15% of smokers develop COPD

Aetiology



Susceptibility	Environmental Stimulus
Polygenic, Monogenic (A1AT) Low BW Failure to attain max lung function Early lung insults Accelerated decline	Tobacco smoke Air Pollution Vapes, ecigarettes, Shisha – unknown Marijuana - unknown

Early lung insults

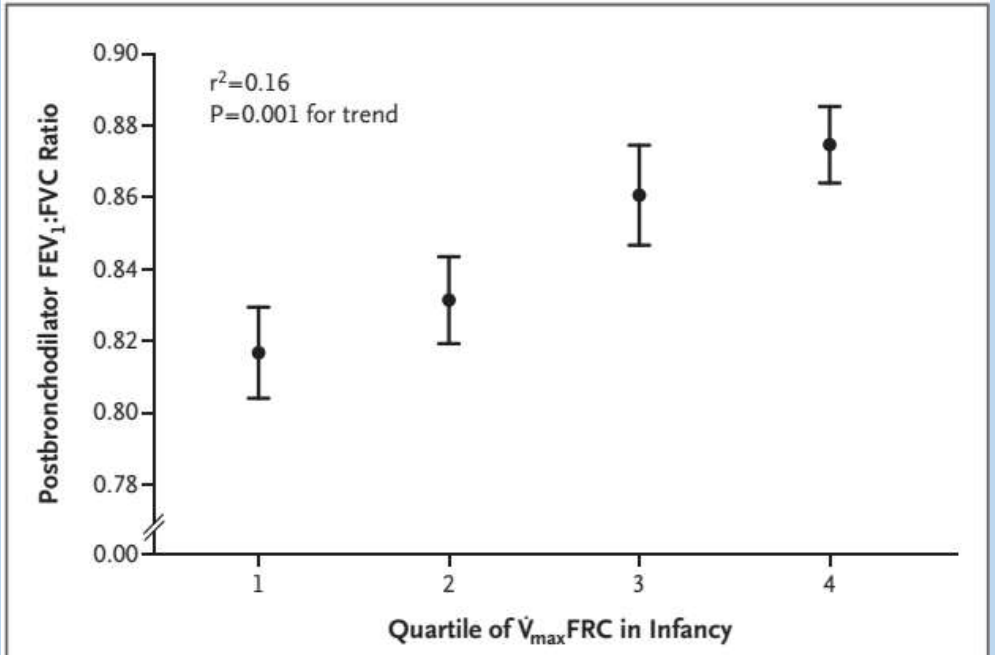
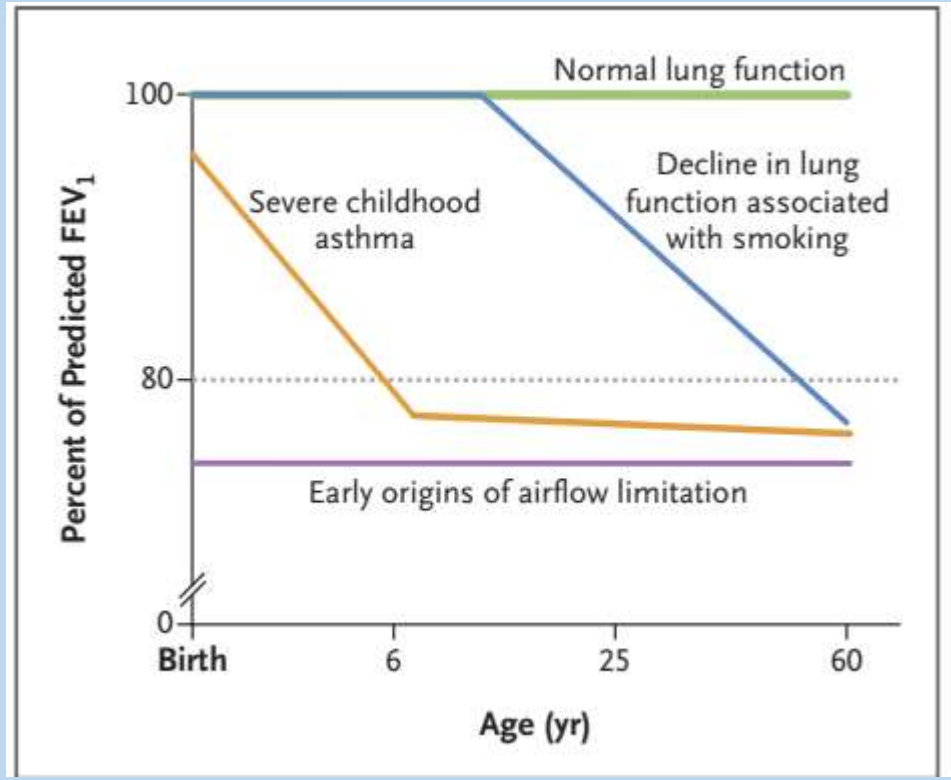


Figure 2. Relationship between the Quartile of Lung Function in Early Life and the FEV_1:FVC Ratio at 26 to 32 Years of Age.



Early origins of COPD Martinez et al nejm 375;9 September 1, 2016

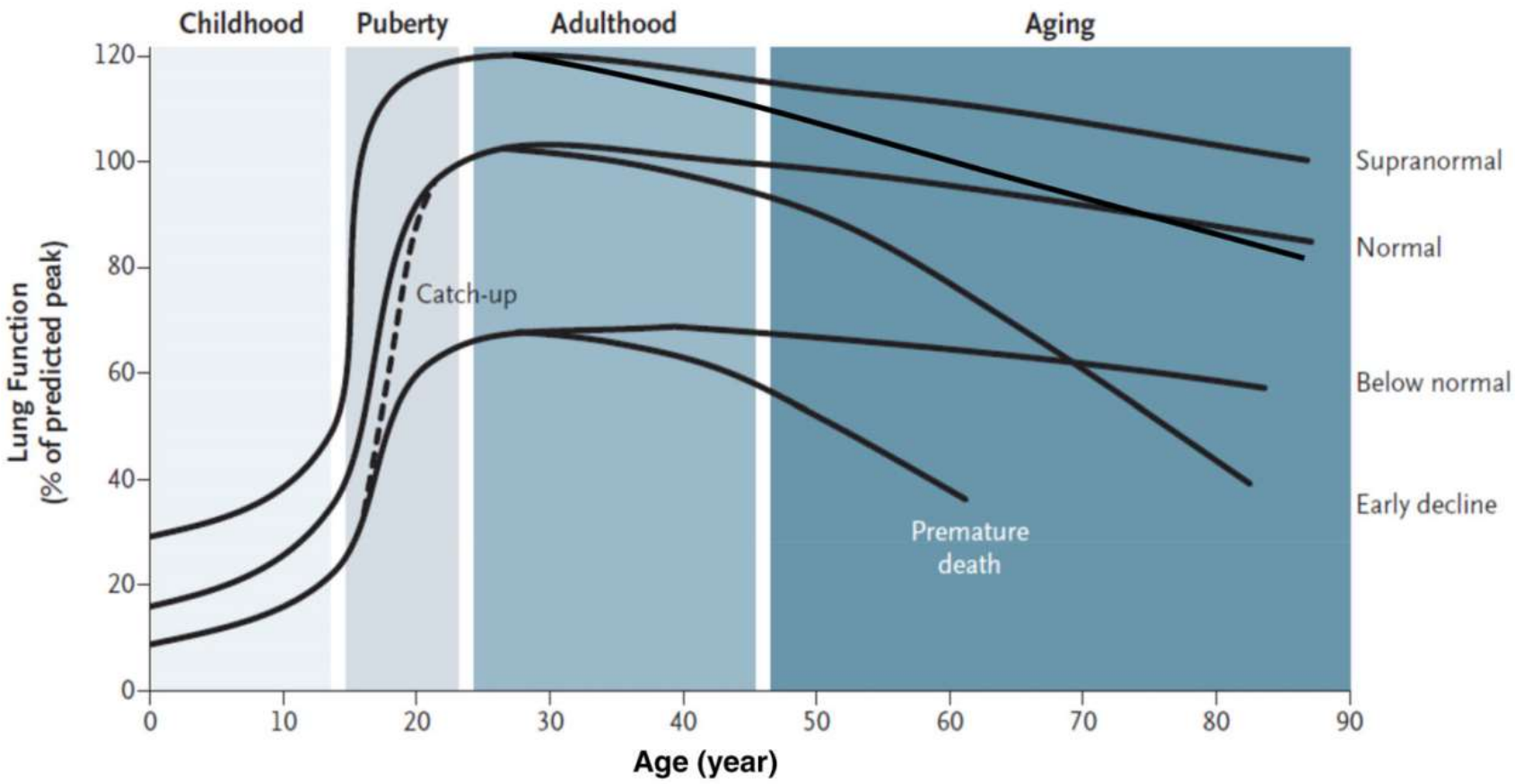
Early lung insults

Early insults impairing maximum lung development

- Maternal smoking (~1.5% decrease in FEV1)
- Preterm birth (<27wks, need O2 for >28days)
- Maternal and childhood malnutrition
- Early respiratory tract infections (pneumonia <3yrs ago)
- Air pollution exposure
- Childhood asthma
- Adolescence smoking

Early origins of COPD Martinez et al nejm 375;9 September 1, 2016

Lung development and trajectories



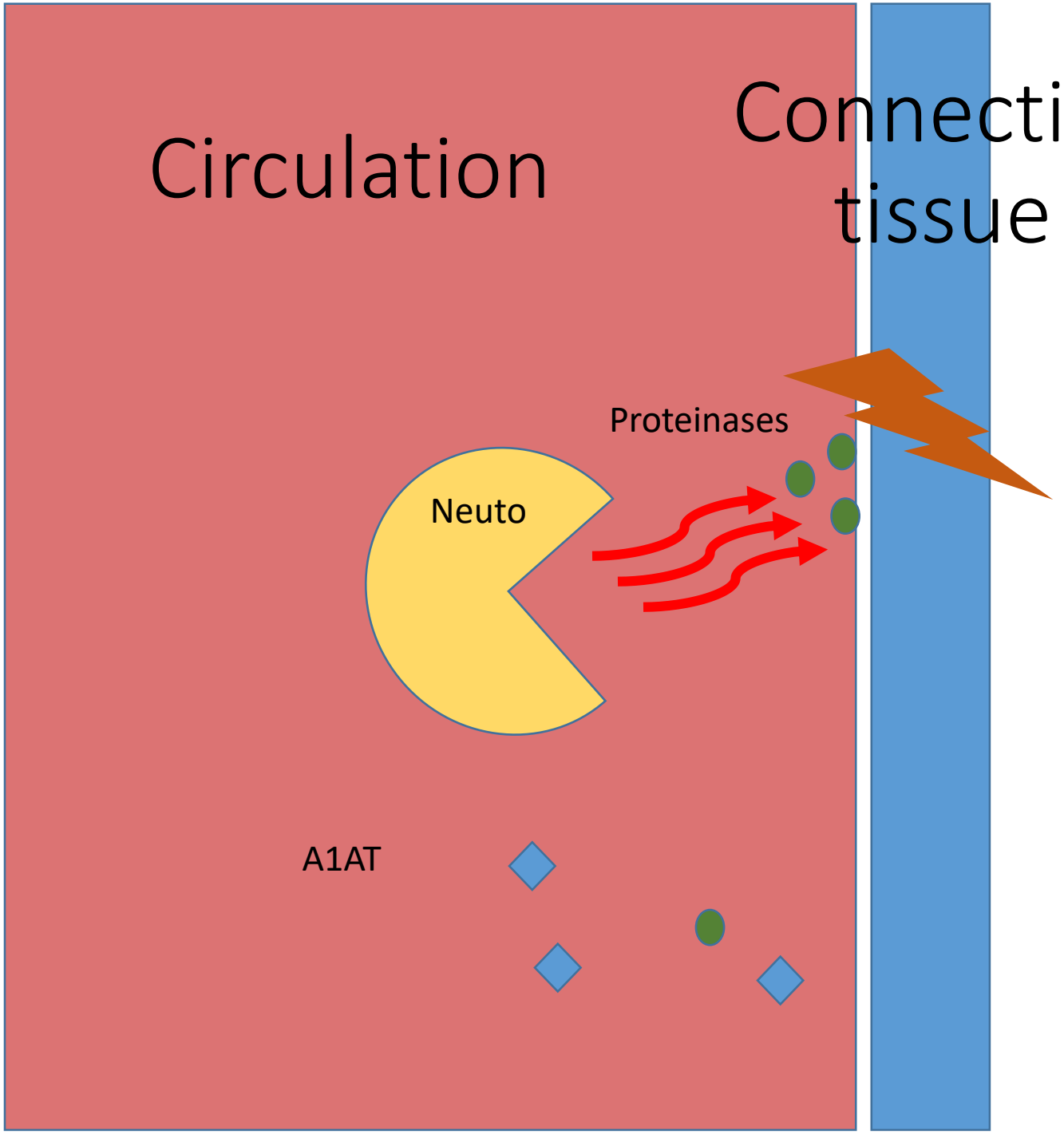
Natural history and mechanism of COPD, Lange et al Respirology 2021

Genetic: A1 Antitrypsin deficiency (A1ATD)

- Associated with the development of emphysema in smokers and never-smokers

- >500 genetic variants - Most have fully functional protein
  - Several - Reduced plasma concentrations
  - Few – Critically low deficiency state (Homozygous ZZ)
  - Null variants - Incomplete protein production and secretion failures ie no protein secretion

ERS Handbook of Respiratory medicine 2019



AAT controls the serine proteinases at point of release (contains the damage)

Features

- Early development of emphysema, especially in smokers
- Lung function
  - Reduction in gas transfer, airflow, air trapping, bronchial reactivity (confused with adult onset asthma)
- CT - panlobular emphysema in the lower zones, LZ>UZ
- Extrapulmonary: Liver cirrhosis, panniculitis, systemic vasculitis, ulcerative colitis
- Test: AAT level and genotype (normal is M)
  - Critically low A1AT <20% (Z homozygosity and Z null heterozygotes)

ERS Handbook of Respiratory medicine 2019

Pathology of COPD

- Small airway
  - Inflammation → airflow obstruction
  - Airway remodelling
- Large airway
  - Hypertrophy of mucous glands

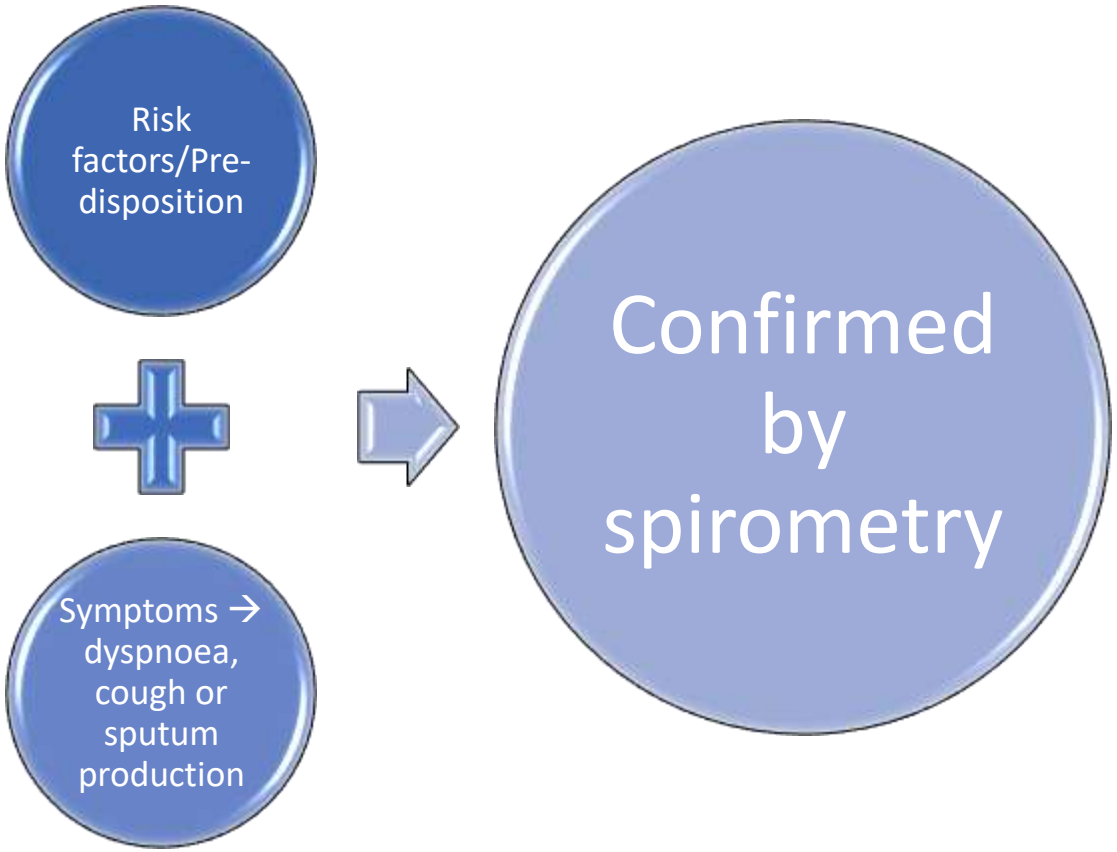
ERS Handbook of Respiratory medicine 2019

Symptoms

- Dyspnoea - is complex
  - Pulmonary/Extrapulmonary function
  - Demand
  - Perception
- Cough +/- sputum
- Wheezing
- Exacerbations

Gold 2020, ERS Handbook of Respiratory medicine 2019

Diagnosis



Post-bronchodilator airflow obstruction (FEV1/VC ratio (<0.70), or <LLN)

*Over-diagnose obstruction in the elderly and under-diagnose obstruction in young

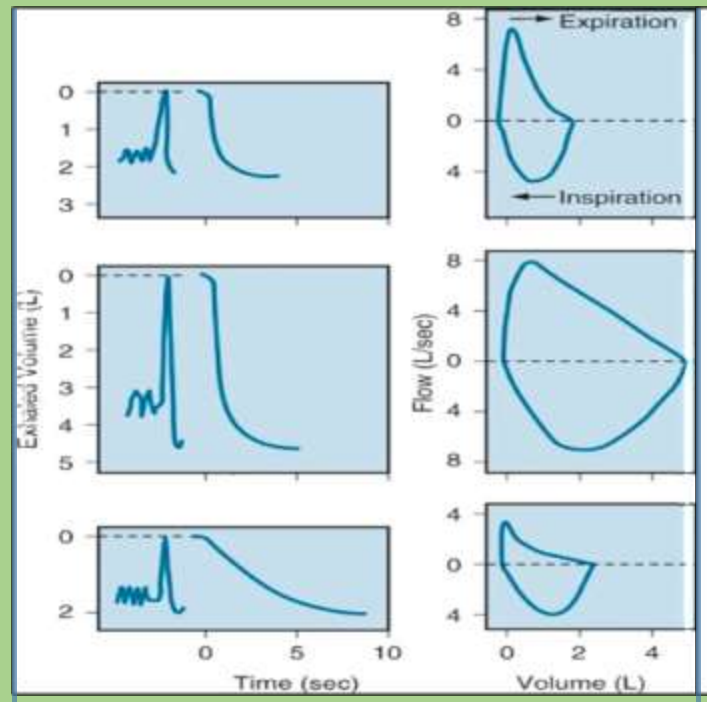
*LLN requires knowledge of normal values

Gold 2020

Act 2: Spirometry and Lung function

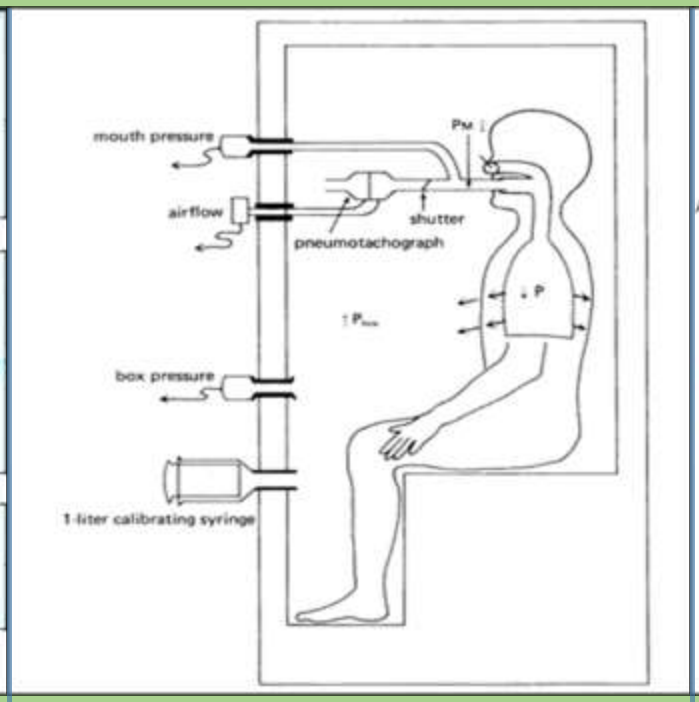
- Spirometry does not equal lung function
- Lung function tests = Spirometry, lung volumes, gas exchange
- Lung function test does not equal lung function*

*Not lung function alone – lungs, muscles, diaphragm, heart, anaemia, cognition, coordination etc



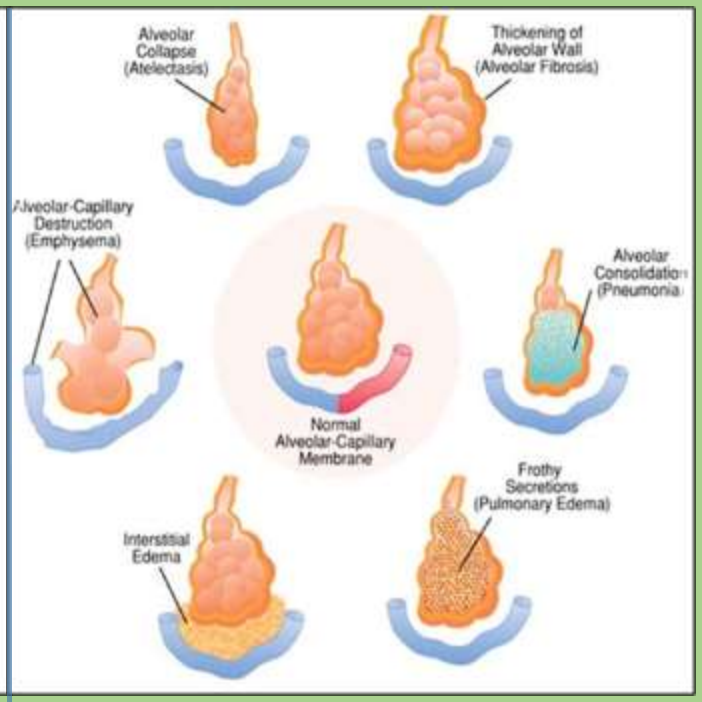
Spirometry

- Dynamic flow volumes
- Measures airflow to assess for airflow obstruction.
- Low risk, effort dependent
- Sensitive and specific for the accurate diagnosis of obstructive respiratory disease and bronchodilator response
- <u>May only suggest restrictive lung disease</u>



Lung Volumes

- Measures static lung volumes
- Measured by body plethysmography or gas dilution
- Diagnosis of restrictive disorders (Restriction – Reduction in TLC)
- Lung volumes and capacities provide information of air trapping and hyper-expansion



Gas Exchange

- Primary function of the lungs
- Ficks law and diffusivity
- Influenced by ventilation, perfusion, surface membrane and gas mixing
- Interpretations takes into account KCO, VA, Hb and DLCO.
- <u>Relationship between DLCO and lung volume is not linear</u>

Murray and Nadel Text book of respiratory medicine

Pulmonary function assessment

- ABG
- Imaging – CXR, CT chest
- VQ scans
- LFT
- 6MWT
- CPET
- Echo
- Research tools

Indications

Diagnosis
- To evaluate symptoms, signs, or abnormal laboratory test results
- To measure the physiologic effect of disease or disorder
- To screen individuals at risk of having pulmonary disease
- To assess preoperative risk
- To assess prognosis

Monitoring
- To assess response to therapeutic intervention
- To monitor disease progression
- To monitor patients for exacerbations of disease and recovery from exacerbations
- To monitor people for adverse effects of exposure to injurious agents
- To watch for adverse reactions to drugs with known pulmonary toxicity

Disability/impairment evaluations
- To assess patients as part of a rehabilitation program
- To assess risks as part of an insurance evaluation
- To assess individuals for legal reasons

Other
- Research and clinical trials
- Epidemiological surveys
- Derivation of reference equations
- Preemployment and lung health monitoring for at-risk occupations
- To assess health status before beginning at-risk physical activities

Standardization of Spirometry 2019 Update AJRCCM Vol 200, Iss 8, pp e70–e88, Oct 15, 2019

Contra - indications

Due to increases in myocardial demand or changes in blood pressure
- Acute myocardial infarction within 1 wk
- Systemic hypotension or severe hypertension
- Significant atrial/ventricular arrhythmia
- Noncompensated heart failure
- Uncontrolled pulmonary hypertension
- Acute cor pulmonale
- Clinically unstable pulmonary embolism
- History of syncope related to forced expiration/cough

Due to increases in intracranial/intraocular pressure
- Cerebral aneurysm
- Brain surgery within 4 wk
- Recent concussion with continuing symptoms
- Eye surgery within 1 wk

Due to increases in sinus and middle ear pressures
- Sinus surgery or middle ear surgery or infection within 1 wk

Due to increases in intrathoracic and intraabdominal pressure
- Presence of pneumothorax
- Thoracic surgery within 4 wk
- Abdominal surgery within 4 wk
- Late-term pregnancy

Infection control issues
- Active or suspected transmissible respiratory or systemic infection, including tuberculosis
- Physical conditions predisposing to transmission of infections, such as hemoptysis, significant secretions, or oral lesions or oral bleeding

Standardization of Spirometry 2019 Update AJRCCM Vol 200, Iss 8, pp e70–e88, Oct 15, 2019

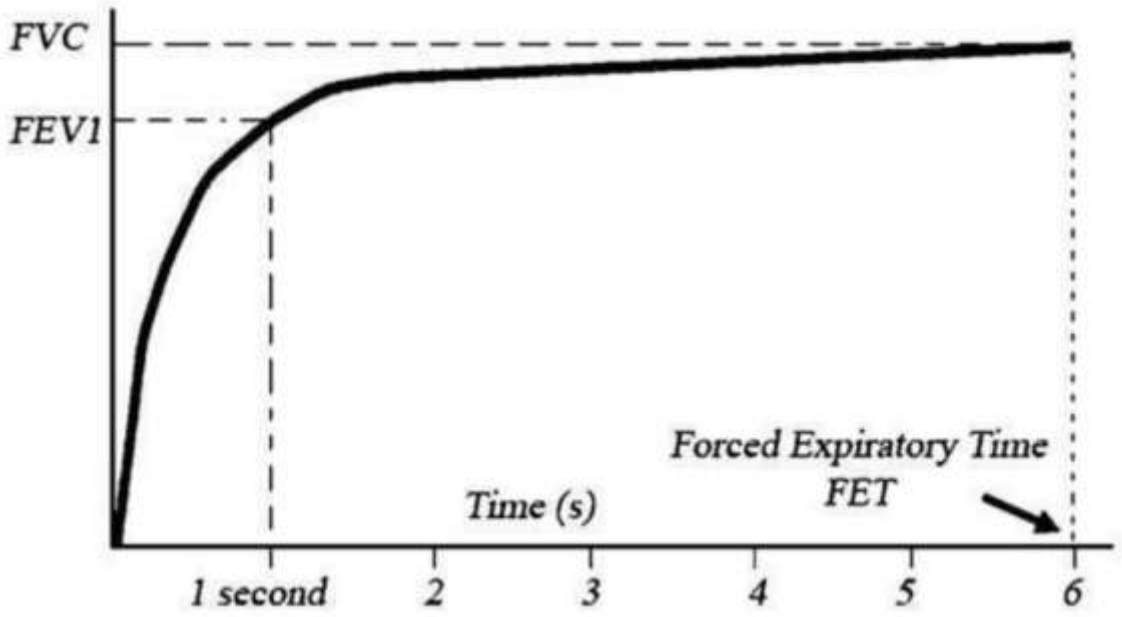
Spirometry - How to do it

- Patient should sit straight, with head erect, nose clip in place
- Hold the mouthpiece tightly between the lips
- Normal, quiet tidal breathing initially (Recording TV)
- When ready, maximal inhalation followed by forced fast explosive exhalation till “completely empty” (Recording FEV1, FVC) and inhale normally to maximum (Records IVC)

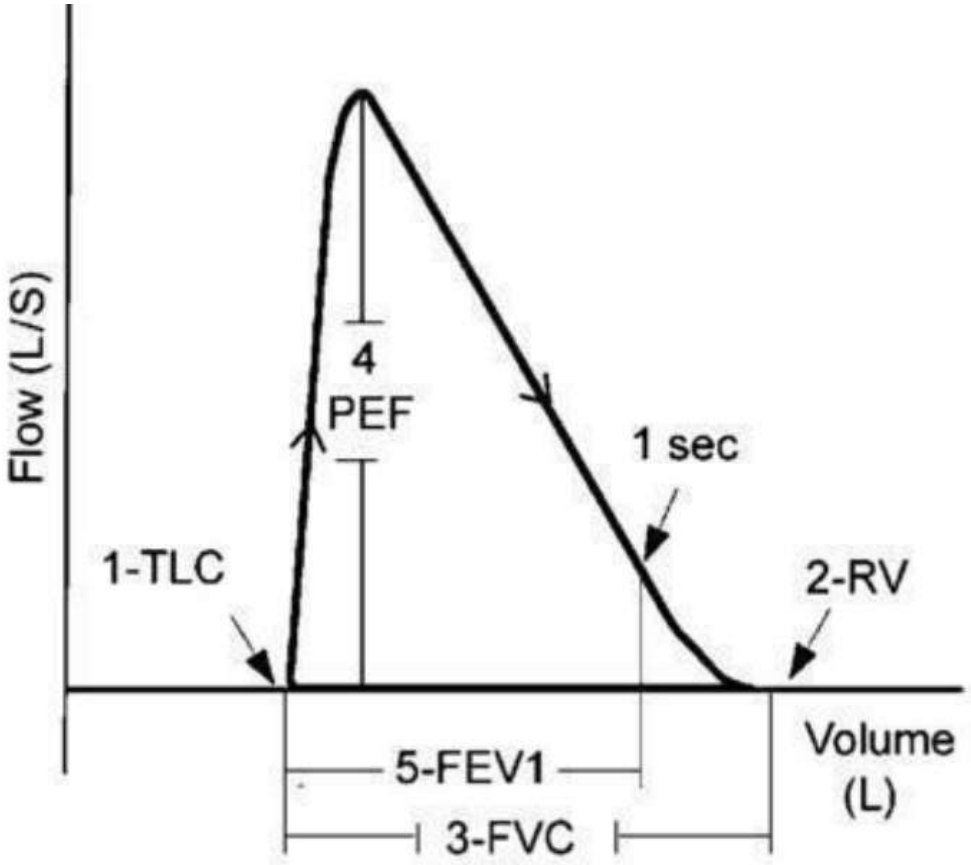
Spirometry - Tips

- Calibrate daily
- Stable patients
- PB4VGO
- Accurate demographic inputs
- Specific, consistent instructions
- Walk through
- Coach through
- Look for quality markers

Flow time curve

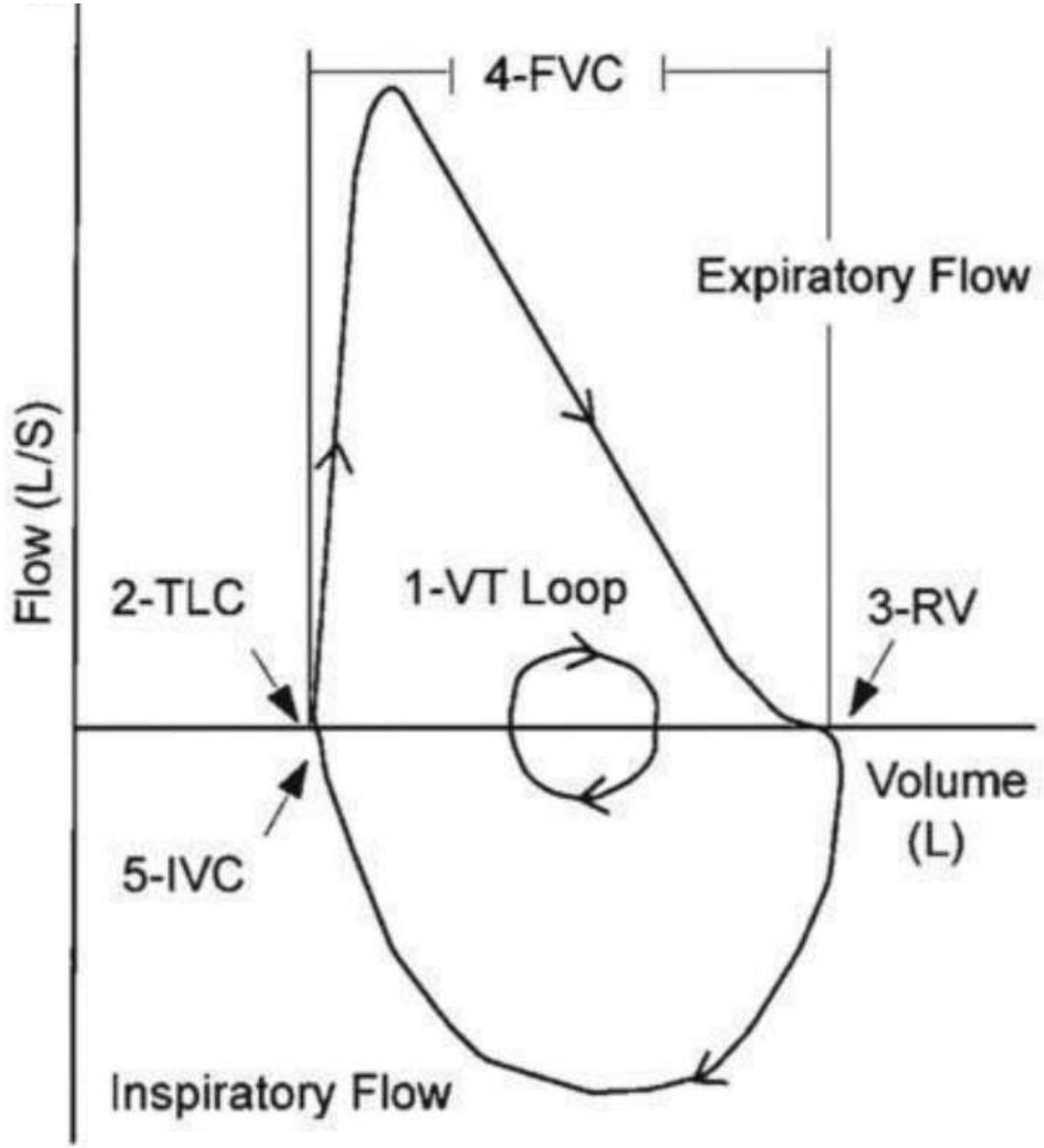


Expiratory Flow volume



Altalag et al Pulmonary function testing in clinical practice

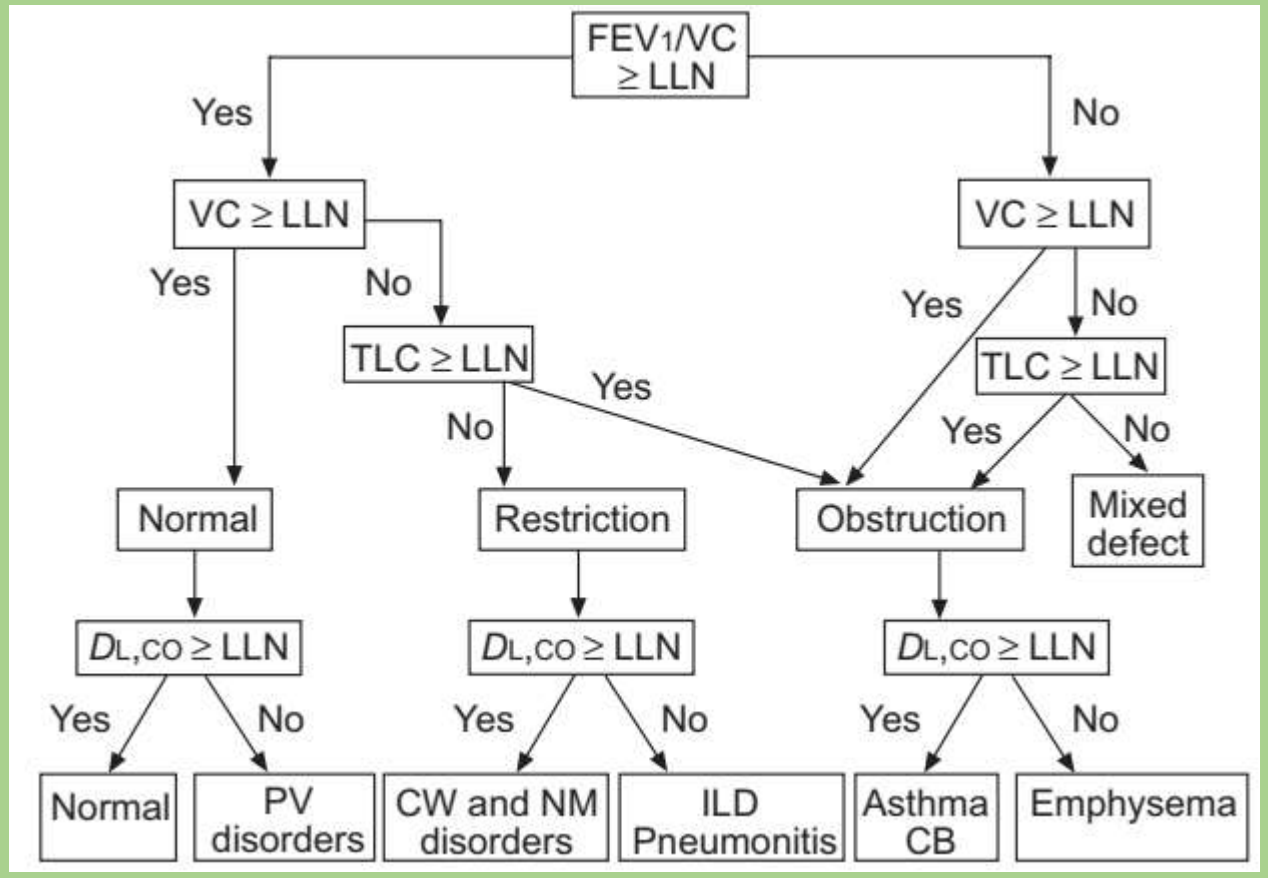
Flow volume loop



Altalag et al Pulmonary function testing in clinical practice

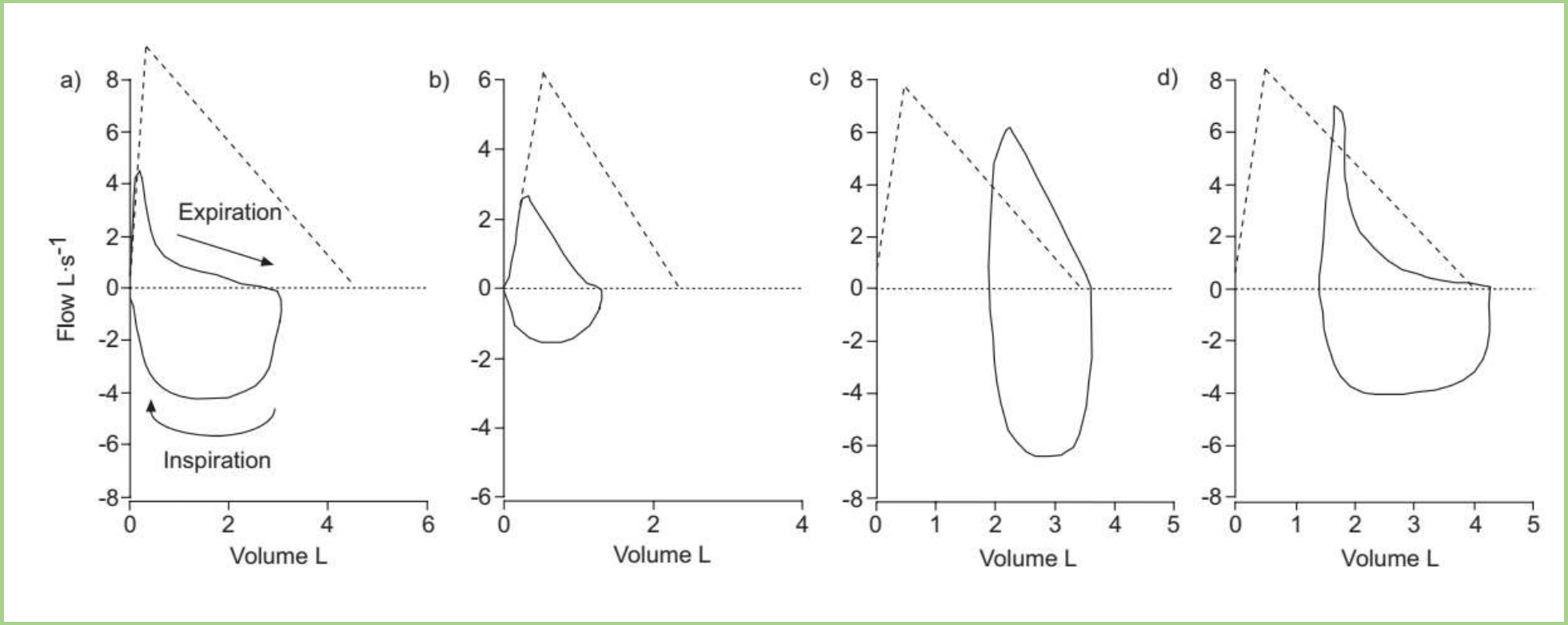
Establishing a diagnosis

Normal
Obstructive pattern
Restrictive pattern



Interpretative strategies for lung function tests, Pellergrino et al, ERJ 2005; 26: 948–968

Common patterns of pathology



Obstructive | Obstructive | Restrictive | Mixed

Interpretative strategies for lung function tests, Pellergrino et al, ERJ 2005; 26: 948–968

Severity

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.

TABLE 14 Degree of severity of decrease in diffusing capacity for carbon monoxide ($D_{L,CO}$)

Degree of severity	$D_{L,CO}$ % pred
Mild	>60% and <LLN
Moderate	40–60%
Severe	<40

% pred: % predicted; LLN: lower limits of normal.

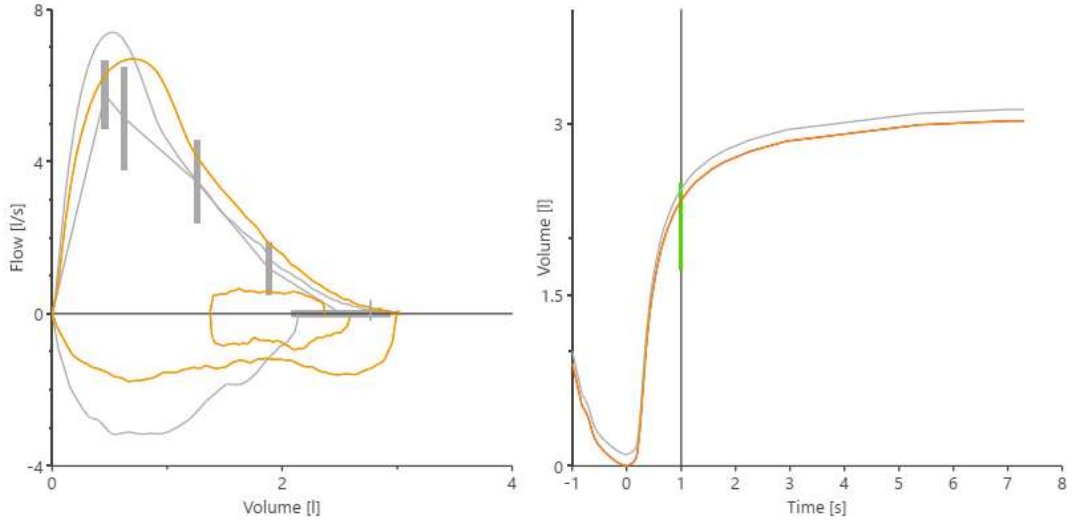
Interpretative strategies for lung function tests, Pellergrino et al, ERJ 2005; 26: 948–968

Anatomy of lung function test report

Pulmonary Function Test

4/06/2020 2:56 PM

Height	159.5 cm	Physician	
Weight	63.6 kg	Smoker	Current
BMI	25.0	Pack years	4.00
Age	64 years	Technician	AS
Gender	female		



		Pred	Pre	Pre % Pred	Post	% Pred	% Change
TLC	**[L]**	4.74	5.22	110 %			
VC MAX	**[L]**	2.62	3.11	119 %			
RV	**[L]**	1.91	2.11	110 %			
FEV 1	**[L]**	2.10	2.34	111 %	2.45	117 %	5 %
FVC	**[L]**	2.51	2.88	115 %	3.02	120 %	5 %
FEV1%VCmax	**[%]**	76.94	84.98	110 %	81.00	105 %	-5 %
PEF	**[L/s]**	5.74	7.39	129 %	6.69	116 %	-10 %
DLCO	**[ml/min/mmHg]**	21.41			18.92	88 %	
VA	**[L]**	4.59			4.47	98 %	
KCO	**[ml/min/mmHg/L]**	4.52			4.23	94 %	
DLCOc	**[ml/min/mmHg]**	21.41			18.92	88 %	

Clinical: smoker, pulmonary nodules, chronic cough

Demographics

Flow volume and Volume time graphs

Lung volumes

Spirometry

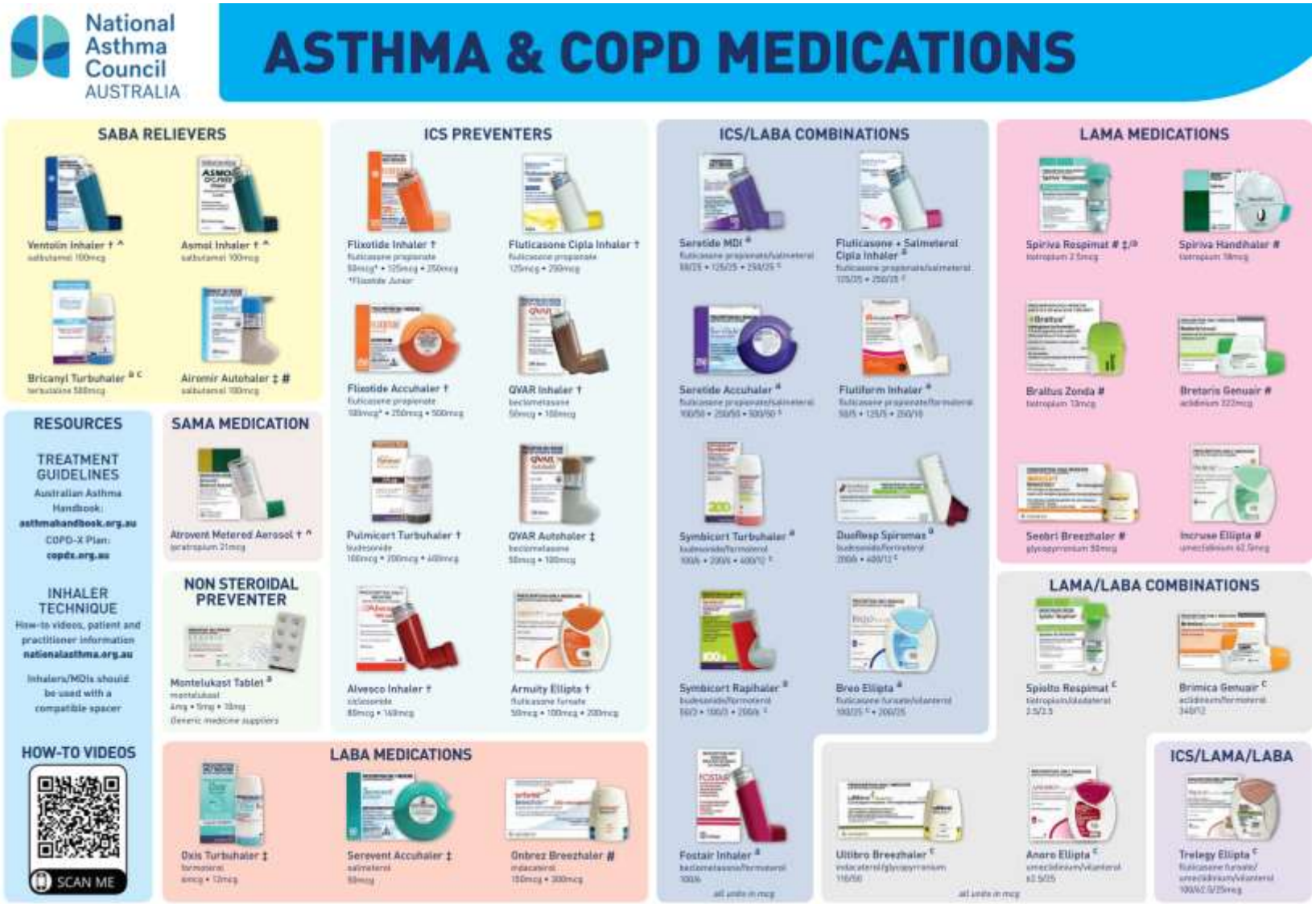
Gas exchange

Scientist comments

Further reading

- Pulmonary function testing, Crapo et al NEJM 1994
- Interpretative strategies for lung function tests, Pellergrino et al, ERJ 2005; 26: 948–968
- Standardization of Spirometry 2019 Update AJRCCM Vol 200, Iss 8, pp e70–e88, Oct 15, 2019
- Stepwise interpretation of pulmonary function tests, American family physician Volume 89, Number 5, March 1, 2014

Act 3: COPD treatment: Approach to Inhalers



COPD: Assessment

Severity based on spirometry - FEV1 – GOLD or ERS

MMRC score or COPD assessment test

Exacerbation history

BODE index – Better predictor of death from resp causes than FEV1

Table 2. Variables and Point Values Used for the Computation of the Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity (BODE) Index.*

Variable	Points on BODE Index			
	0	1	2	3
FEV_1 (% of predicted)†	≥65	50–64	36–49	≤35
Distance walked in 6 min (m)	≥350	250–349	150–249	≤149
MMRC dyspnea scale‡	0–1	2	3	4
Body-mass index§	>21	≤21		

Grade of dyspnea	Symptoms
Grade 0	Not troubled by breathlessness except on strenuous exercise
Grade 1	Short of breath when hurrying or walking up a slight hill
Grade 2	Walks slower than contemporaries on the level because of breathlessness or has to stop for breath when walking at own pace
Grade 3	Stops for breath after walking 100 m or after a few minutes on the level
Grade 4	Too breathless to leave the house or breathless when dressing or undressing

GOLD – symptoms, exacerbations, comorbidities

- Group A - low symptom burden + low exacerbation risk (<2 ex/last yr)
- Group B - higher symptom burden + low exacerbation risk.
- Group C - low symptom burden + high risk
- Group D – high symptoms + high risk

Management Goals

A. Reduce symptoms,
B. Reduce exacerbations
C. Maximise functional capacity.

Non-pharmacological intervention

Reduction of environmental exposure

- Smoking cessation
  - Only intervention shown to reduce the rate of lung function decline
  - ASK/ADVISE/ACT
- Vaccinations against influenza and pneumococcus are generally recommended for those living with COPD.

Pulmonary rehabilitation - reduces symptoms and exacerbation risk, and improves quality of life and/or exercise performance in most participants.

Pharmacotherapy

ASSESSMENT	INITIAL	INSUFFICIENT SYMPTOM CONTROL	INSUFFICIENT EXACERBATION CONTROL	COMMON
A	SABA PRN	LAMA/LABA	LAMA/ICS(e)	Assess comorbidities Assess triggers Assess inhaler technique and usage
B	LAMA or LABA	LAMA+LABA	+ICS(e)	
C	LAMA	LAMA+LABA	LABA/+ICS(e)	
D	LAMA, LAMA-LABA*	LAMA+LABA +ICS	+ICS(e)	

Inhaler devices - Challenges

- Recent flood in market
- No head to head evidence
- Brand names for preparation
- Brand names for devices
- Need for patient education
- Unable to monitor usage

Types of preparation

- Dry powder
- Inhalant
- Fine mist

Devices

Pressurized Metered Dose Inhaler	Breath actuated Metered Dose Inhaler	Dry powder	Soft Mist
• CFC Free • Need coordination • Need hand articulation • Spacer	• Breath initiates flow • Less Coordination	• Maximum evidence • Multiple devices • Deposition in throat and mouth • Need high flow rates • Cough	• Newer • Increased deposition to lower airways • Need less flow

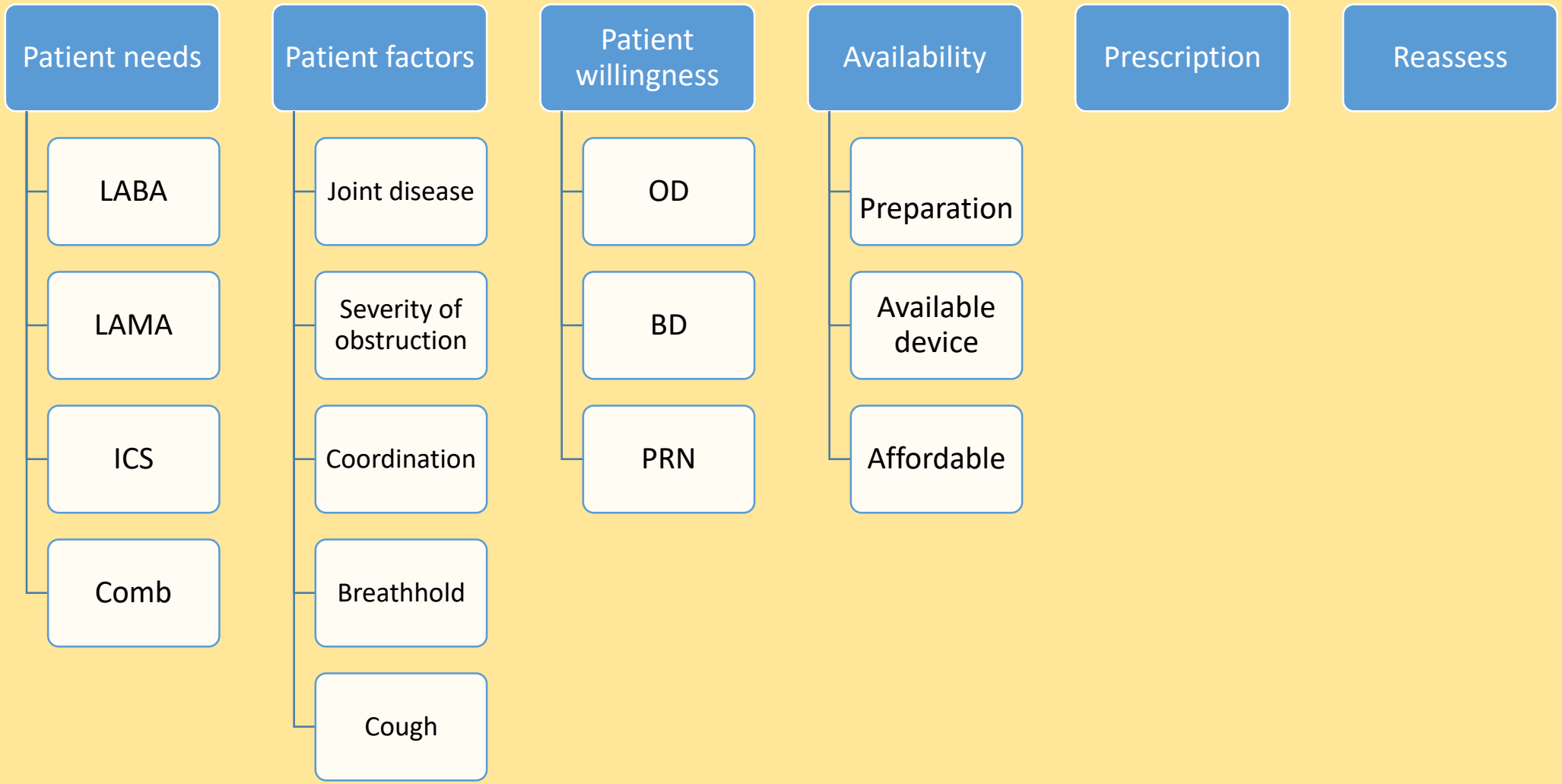
Types

Reliever	Preventer
SABA, SAMA	ICS LABA LAMA LABA/LAMA ICS/LABA ICS/LABA/LAMA

Devices

DEVICE	TYPE
Inhaler	MDI
Accuhaler	Dry powder
Autohaler	Breath actuated MDI
Turbohaler	Dry powder
Ellipta	Dry powder
Breezhaler	Dry powder
Genuair	Dry powder
Handihaler	Dry powder
Zonda	Dry powder
Respimat	Fine mist

Inhaler Device Selection



Notes

- No inhaler has shown to slow FEV1 decline or reduce mortality
- ICS use should be targeted
- Long-term oral steroids are not recommended in COPD.
- Macrolide antibiotics reduce exacerbations in COPD. Risks include toxicity and resistance
- Limited evidence for theophylline
- Long-term O2 therapy (> 15h/ 24h period) improves survival in patients with COPD and respiratory failure
- For patients with hypercapnic (type 2) respiratory failure who have been admitted to hospital and required ventilatory support, home NIV reduces the risk of readmission and death

Extra-pulmonary COPD

- Smoking
- Cardiovascular diseases,
- Lung cancer,
- Osteoporosis
- Depression/Anxiety
- Urinary incontinence
- Loss of independence
- Malnutrition

Complications

- Cor pulmonale
- Hypoxic respiratory failure
- Hypercarbia
- Lung cancers
- Pneumothorax

Case: History revisited: Key points

- Term birth. No childhood respiratory insults. Excelled at sport
- Experimented with cigarettes aged 17, Extensive 2nd hand smoke exposure (both parents). No cannabis, E cigarettes or Vapes.
- Sister- asthma. Mother - COPD
- Many pets; 3 cats, 2 dogs and 2 snakes. Remotely - Pet birds
- Worked at a mushroom farm from the age of 28 to 36 years
- Minimal dust, fumes, chemical and asbestos exposure
- 18m exertional dyspnoea. MMRC Grade 2
- Adherent to Breo and only uses Ventolin once-a-day.
- GORD +. Hayfever +, OSA +, Obesity +
- Exam – Soft wheeze. No RHF

Case: Lung function

- FEV1/VC ratio 34.96. FEV1 0.87 L (39%), FVC 2.20 L (83%). Post bronchodilator FEV1 is 1.04 L (46%). This is an increase of 170 ml or 20%. It does not quite meet criteria for significance.
- TLC is 6.13 L (136%), RV 3.66 L (219%).
- DLCO 16.28 (73%), KCO 4.21 L (85%).

→This is consistent with severe obstruction with evidence of hyperexpansion and severe gas trapping with preserved gas exchange.

Case: Other Inx

Transthoracic echocardiogram

- Normal LV size, systolic function (EF70%) and diastolic function
- Normal RV size and systolic function.
- Biatrial size is normal. Normal valvular function.
- Unable to measure RVSP.

Exercise stress echocardiogram

- Negative for inducible ischaemia and patient had satisfactory exercise capacity (Exercise time was only 4 minutes and 59 seconds!)

Case: CT chest

- Bilateral centrilobular and paraseptal emphysema.
- Bilateral bronchial wall thickening with mild bronchiectasis. No evidence of groundglass changes, reticular thickening or pulmonary fibrosis. Central Airways appear normal. There is no thoracic adenopathy.

Case Impression and Plan

PFT and CT fit with COPD but there is minimal smoking history. History does not fit with long standing asthma.

Plan:

1) Blood tests including alpha 1 antitrypsin
2) Lung protection
   - ❑Annual vaccination against flu and infection prevention strategy
   - ❑Recommend early access to oral antibiotics
3) Continue Breo Ellipta, add Ciclesonide inhaled
4) Referral to asthma WA for education
5) Encourage weight loss
6) Recommended Sleep study - Does not have a hospital cover

Case Follow up - Undetectable levels of A1AT (ZZ genotype).

Abnormal LFT - USG liver (PRC 17/11/2020) shows Steatosis, No cirrhosis.

Plan:

1. Provided information regarding A1AT Clinical trial and link to the website
2. Information to support website (www.alpha1.org) and Lung foundation brochure.
3. Continue Trelegy. Use Ventolin PRN
4. Encourage exercise
5. Referral to pulmonary rehabilitation
6. Dietitian review to assist with weight loss
7. Recommend testing of relatives

Treatment of A1AT deficiency Emphysema

- Treat as COPD
- Specific augmentation
  - involves weekly intravenous infusions of AAT restoring close to normal or ‘protective’ levels of the protein.
  - Slows the progression of the lung destruction causing emphysema
- Lung volume reduction - Surgical or Bronchoscopic in suitable patients.
- Lung transplantation
  - May not improve overall survival, but improves symptoms and QOL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THANK YOU
STAY 6 FEET AWAY

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