

Chronic Obstructive Pulmonary Disease -Clinical Update 2021

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Background/Context

- 7.5% of Australians aged >40 years have COPD
- 50% not diagnosed
- 2nd most common cause of '*avoidable*' hospital admissions
- **Southern Tasmania:**
 - 500 admissions
 - Average stay 4 days
 - 20% re-admission rate
 - 10% require acute NIV
 - Inpatient mortality 7%
- 5th leading cause of death in Australia 4.0% of all deaths
- **Direct Health costs:**
 - >\$900 million/year, \$473 million Hospital costs, Oxygen >\$20 million

COPD-X

- C: Case finding and confirm diagnosis
- O: Optimise function
- P: Prevent deterioration
- D: Develop a plan of care
- X: Manage eXacerbations







Case finding and confirm diagnosis

- Smoking is the most important risk factor in COPD development.
- A thorough history and examination is the first step in COPD diagnosis.
- COPD is confirmed by the presence of persistent airflow limitation
 - post-bronchodilator $FEV_1/FVC < 0.7$
- If FEV_1 increases > 400 mL following bronchodilator, consider asthma or asthma / COPD overlap

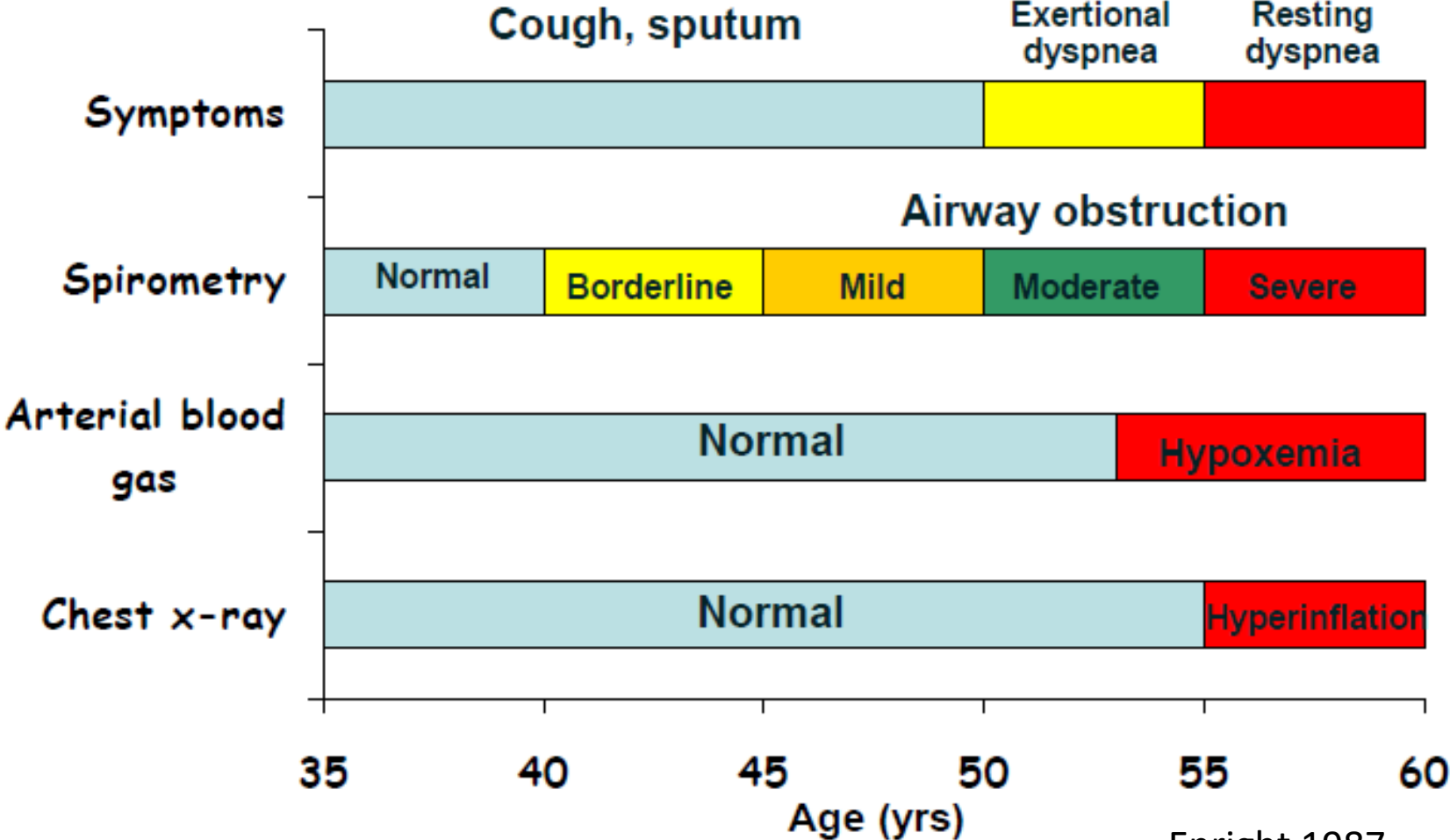
C: Case finding and confirm diagnosis



Recommendation

- Consider COPD in:
 - patients > 35 years of age with symptoms such as breathlessness, cough, and / or sputum production⁴  
 - all smokers / ex-smokers > 35 years of age.⁴  
- Document smoking history, current smoking status, and work history including occupational exposure in all patients with suspected COPD.  

Spirometry detects COPD before other tests



Enright 1987

Spirometry and confirmation



Recommendation





- Spirometry should be performed using techniques that meet published standards. **EB** **LE**
- Perform pre- and post-bronchodilator spirometry to confirm COPD, which is characterised by airflow limitation that is not fully reversible (post-bronchodilator FEV_1/FVC ratio < 0.7 and $FEV_1 < 80\%$ predicted). **EB** **HE**
- Interpret borderline spirometry results with caution, particularly in older (> 65 years of age) and younger patients (< 45 years of age), or those without a history of smoking or exposure to occupational / environmental pollutants or dust. **EB** **HE**
- In patients with borderline spirometry, consider alternative diagnoses and investigate appropriately. **EB** **ME**

?COPD, Asthma, Asthma/COPD Overlap



Recommendation

If the FEV₁ response to bronchodilator is:

- > 400 mL, strongly consider asthma or asthma / COPD overlap.  
- < 400 mL (but \geq 200 mL and \geq 12%), consider asthma / COPD overlap or an asthma component depending on history and pattern of symptoms.  

Asthma:

Variable course,

Younger,

Atopy,

<15 pack year history,

Reversible airflow limitation

COPDX Severity



Recommendation

- To guide ongoing management, assess COPD severity based on lung function and a careful assessment of symptoms and signs, and review the history of exacerbations at least annually. **SR ME**

Table 1. Guide to the severity of COPD.⁵

		FEV ₁ (% predicted)	Symptoms	History of exacerbations	Comorbid conditions*
COPD SEVERITY	Mild	60-80	<ul style="list-style-type: none"> Breathlessness on moderate exertion Recurrent chest infections Little or no effect on daily activities 	Frequency may increase with severity	Present across all severity groups [§]
	Moderate	40-59	<ul style="list-style-type: none"> Increasing dyspnoea Breathlessness walking on level ground Increasing limitation of daily activities Cough and sputum production Exacerbations requiring corticosteroids and/or antibiotics 		
	Severe	< 40	<ul style="list-style-type: none"> Dyspnoea on minimal exertion Daily activities severely curtailed Experiencing regular sputum production Chronic cough 		

*common comorbid conditions include cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, anxiety or depression, lung cancer, peripheral vascular disease and sleep apnoea.

Optimise function

- Assessment is the first step to optimising function
- Non-pharmacological strategies such as pulmonary rehabilitation, smoking cessation and regular exercise should be provided to all patients with COPD.
- Optimise pharmacotherapy using a stepwise approach.
- Adherence and inhaler technique need to be checked on a regular basis.
- Comorbid conditions are common in patients with COPD.
- Referral to specialist respiratory services may be required.

Smoking Cessation

“Offer brief smoking cessation counselling and details for Quitline (13 78 48) as a minimum intervention at every visit to all smokers.”

- 12% decrease in mortality Lung Health Study 1
- Reduces the decline in lung function by 50%
ECLIPSE NEJM 2011
- Reduces exacerbations in mild COPD
Lung Health Study 2 Thorax 2007

Smoking cessation-pharmacological

Difference between >6 month abstinence rates between intervention and control/placebo

Nicotine gum	8%
Nicotine transdermal patch	6%
Bupropion (Zyban 300 mg)	9%
Varenicline (Champix 1mg bd)	13%
Intensive behavioural support plus NRT or Bupropion (eg smoking cessation clinic)	13-19%

In clinical practice: counselling plus NRT or pharmacotherapy
10%

(Katz J Natl Cancer Institute 2004)

Pulmonary Rehabilitation

- Exercise training - Aerobic, upper limbs exercise, improved cardio-respiratory function
- Nutritional advice, Counselling/Education
- **Results:** ↑ QoL, ↓ use of health care
 - ↑ peak workload 18%
 - ↑ peak oxygen consumption 11%
 - ↑ endurance time 87% of baseline
 - ↑ 49 metre 6MWT

Pulmonary rehabilitation

“Refer for pulmonary rehabilitation for *all* patients with exertional dyspnoea. Re-assess and consider re-referral to pulmonary rehabilitation for patients who have stopped being active”

21st Century Challenge: Access and capacity

- Only 42% of patients referred complete PR

BTS PR Clinical Audit 2016

- Only 10% of COPD patients access and complete pulmonary rehabilitation

2010 NSW Agency for Clinical Innovation

Pulmonary Rehabilitation-Southern Tasmania

Uptake of PR in 2016 RHH

- n= 300 referrals
- Enrolment n=66 patients, 60% full completion
- Both RHH and CICC (Clarence Integrated Care Centre) programs over 10 months (RHH re-development/gym)
- Similar to 2016 UK Survey ie, only completed in 10%

New models for PR

- **Home based pulmonary rehab**

Holland Thorax 2016 RCT n=166

Demonstrated non-inferiority for: 6MWD, Dyspnoea

Costs: Hospital vs Home per patient \$312 vs \$298

- Experienced physiotherapist trained in motivational interviewing, 1 home visit, 7 weeks phone follow-up, unsupervised exercise

- **Tele- rehabilitation**

REACH trial recruiting at RHH; exercise bikes/live sessions

Vaccinations

- **Pneumococcal**

- 1) Absence of evidence in COPD group but still indicated
(Cochrane review, TSANZ 2005)

- **Annual influenza vaccination**

- 1) General mortality reduction of 15% (28% during epidemics)

- 2) 302 vaccinations to prevent one death

Voordouw et al JAMA 2004

- 3) In COPD – mortality reduction of 40-55%

ie NNT=3 (during epidemic)

Self-Management

- **Action plan alone** - not enough Walters Cochrane 2014
- Comprehensive Self Mx plan *may lead to 30-40% decrease in admissions*
Cochrane2014

But...

- RCT– *?excess mortality* - early termination of trial /No QoL benefit
AnnalsIntMed 2012
- May have a role in the highly motivated patient
- **Tele-monitoring**
Excess mortality, No QoL, not cost effective
Possible role in very remote??

Pinnock, Henderson BMJ 2013

2012-2017 choice for maintenance:
 4 → 13 inhalers

Relievers		Maintenance											
SABA		LAMA		LAMA/LABA		ICS/LABA		ICS (For patients with COPD and Asthma)					
 Ventolin® MDI	 Asma® MDI	 Spinira® HandiHaler®	 Spinira® Respimat®	 Ultibro® Breezhaler®	 Spiolto® Respimat®	 Symbicort® Turbuhaler®	 Symbicort® Respimat®	 *Flixotide® MDI	 *Flixotide® Accuhaler®				
 #Airomir® MDI	 Airomir® Autohaler®	 Seobri® Breezhaler®	 Bretaris® Genuair®	 Anoro® Elipta®	 Brimicor® Genuair®	 Seretide® Accuhaler®	 Seretide® MDI	 *QVAR® MDI	 *Fulvicort® Turbuhaler®				
SAMA		LABA		LABA		LABA		LABA		LABA		LABA	
 Bricanyl® Turbuhaler®	 Atrovent® MDI	 Incruse® Elipta®	 Onbrez® Breezhaler®	 *Foradil® Aerofor®	 *Oxis® Turbuhaler®	 *Seravent® Accuhaler®	 Breo® Elipta®	 *Airesco® MDI	 *Flutiform® MDI				

“OLD”

LAMA

- Spiriva: Tiotropium 18 mcg

ICS/LABA

- Seretide: Fluticasone 500/Salmeterol 50 mcg
- Symbicort: Budesonide 400/Eformoterol 8 mcg

ASTHMA & COPD MEDICATIONS

SABA RELIEVERS



Ventolin Inhaler †^A
salbutamol 100mcg



Asmot Inhaler †^A
salbutamol 100mcg



Bricanyl Turbuhaler †^A †^C
terbutaline 500mcg



Airomir Autohaler † †[#]
salbutamol 100mcg

RESOURCES

TREATMENT GUIDELINES

Australian Asthma Handbook:
asthmahandbook.org.au

COPD-X Plan:
copdx.org.au

INHALER TECHNIQUE

How-to videos, patient and practitioner information
nationalasthma.org.au

Inhalers/MDIs should be used with a compatible spacer

HOW-TO VIDEOS



SAMA MEDICATION



Atrovent Metered Aerosol †^A †[#]
ipratropium 21mcg

NON STEROIDAL PREVENTER



Montelukast Tablet †^A
montelukast
4mg • 5mg • 10mg
Generic medicine suppliers

ICS PREVENTERS



Flixotide Inhaler †
fluticasone propionate
50mcg* • 125mcg • 250mcg
*Flixotide Junior



Flixotide Accuhaler †
fluticasone propionate
100mcg* • 250mcg • 500mcg



Pulmicort Turbuhaler †
budesonide
100mcg • 200mcg • 400mcg



Atvesco Inhaler †
ciclesonide
80mcg • 160mcg



Fluticasone Cipla Inhaler †
fluticasone propionate
125mcg • 250mcg



QVAR Inhaler †
bectometasone
50mcg • 100mcg



QVAR Autohaler †
bectometasone
50mcg • 100mcg



Arnully Ellipta †
fluticasone furoate
50mcg • 100mcg • 200mcg

LABA MEDICATIONS



Serevent Accuhaler †
salmeterol
50mcg



Onbrez Breezhaler †[#]
indacaterol
150mcg • 300mcg

ICS/LABA COMBINATIONS



Seretide MDI †^A
fluticasone propionate/salmeterol
50/25 • 125/25 • 250/25 †^C



Seretide Accuhaler †^A
fluticasone propionate/salmeterol
100/50 • 250/50 • 500/50 †^C



Symbicort Turbuhaler †^A
budesonide/formoterol
100/6 • 200/6 • 400/12 †^C



Symbicort Rapihaler †^A
budesonide/formoterol
50/3 • 100/3 • 200/6 †^C



Fostair Inhaler †^A
bectometasone/formoterol
100/6

all units in mcg



Fluticasone + Salmeterol Cipla Inhaler †^A
fluticasone propionate/salmeterol
125/25 • 250/25 †^C



Flutiform Inhaler †^A
fluticasone propionate/formoterol
50/5 • 125/5 • 250/10



DuoResp Spiromax †^A
budesonide/formoterol
200/6 • 400/12 †^C



Breo Ellipta †^A
fluticasone furoate/vilanterol
100/25 †^C • 200/25



Ultibro Breezhaler †^C
indacaterol/glycopyrronium
110/50

all units in mcg

LAMA MEDICATIONS



Spiriva Respimat † †^A
tiotropium 2.5mcg



Bratus Zonda †
tiotropium 13mcg



Seebri Breezhaler †
glycopyrronium 50mcg



Spiolto Respimat †^C
tiotropium/olodaterol
2.5/2.5



Spiriva Handihaler †
tiotropium 18mcg



Bretaris Genuair †
acridinium 322mcg



Incruse Ellipta †
umeclidinium 62.5mcg



Brimica Genuair †^C
acridinium/formoterol
340/12



Anoro Ellipta †^C
umeclidinium/vilanterol
62.5/25



Trellego Ellipta †^C
fluticasone furoate/
umeclidinium/vilanterol
100/62.5/25mcg

ICS/LAMA/LABA

“New”

LABA

Striverdi: Olodaterol
Onbrez: Indacaterol 150 or 300 mcg

LAMA

- Spiriva: Tiotropium Respimat 5 mcg 2 inhalations daily
- Seebri: Glycopyrronium 50 mcg 1 inhalation daily
- Bretaris: Acclidinium 322 mcg 1 inhalation BD
- Incruse: Umeclidinium 62.5 mcg 1 inhalation daily

LAMA/LABA

- Spiolto: Tiotropium /Olodaterol 5/5 mcg 2 inhalations daily
- Anoro: Umeclidinium/Vilanterol 62.5/25mcg 1 inhalation daily
- Ultibro: Glycopyrronium/Inadacaterol 50/110mcg 1 inhalation daily
- Brimica: Acclidinium/Eformoterol 340/12 1 mcg inhalation BD

ICS/LABA

- Breo: Fluticasone furoate/vilanterol 92/25 mcg 1 inhalation daily

ICS/LAMALABA

- Trelagy Fluticasone furoate/ Umeclidinium /vilanterol 100/62.5/25 mcg 1 inhalation daily

Therapeutic pyramid

- Mild/moderate – prn SABA+LAMA
- Still symptomatic-change to LAMA/LABA
- Exacerbations? – change to ICS/LABA + LAMA
- *Don't use SAMAs, prefer older LAMA safety data, don't double up with LABAs
- Very frequent exacerbations/hospitalisations-*Respiratory review-
Azithromycin in very frequent exacerbators 38% decrease in
exacerbations NNT 2.8 NEJM 2011

Optimise pharmacotherapy using a stepwise approach

- **Treatment goals in stable COPD:**

Relieve symptoms,

Prevent disease progression,

Prevent exacerbations,

Reduce mortality

- Avoid theophylline, prednisolone in stable COPD
- Keep it simple with inhaled therapies
- Don't overlap drug classes
- Risks with ICS-Pneumonia
- Mucolytics (NAC) and roflumilast (PDE4 inhibitor) not PBS listed in Australia plus minimal benefits as add on therapy

Drugs: evidence and effect

- **Relieve symptoms:** SABA, SAMA, LAMA, LABA, LAMA/LABA
- **Prevent disease progression:** Borderline for: LAMA, ICS
- **Prevent exacerbations:** LAMA, LABA, LAMA/LABA, ICS/LABA

-ICS/LABA in severe COPD with exacerbations:

25% absolute reduction in exacerbations (NNT 4)
17% in Exacerbation/hospitalisation (NNT 32)

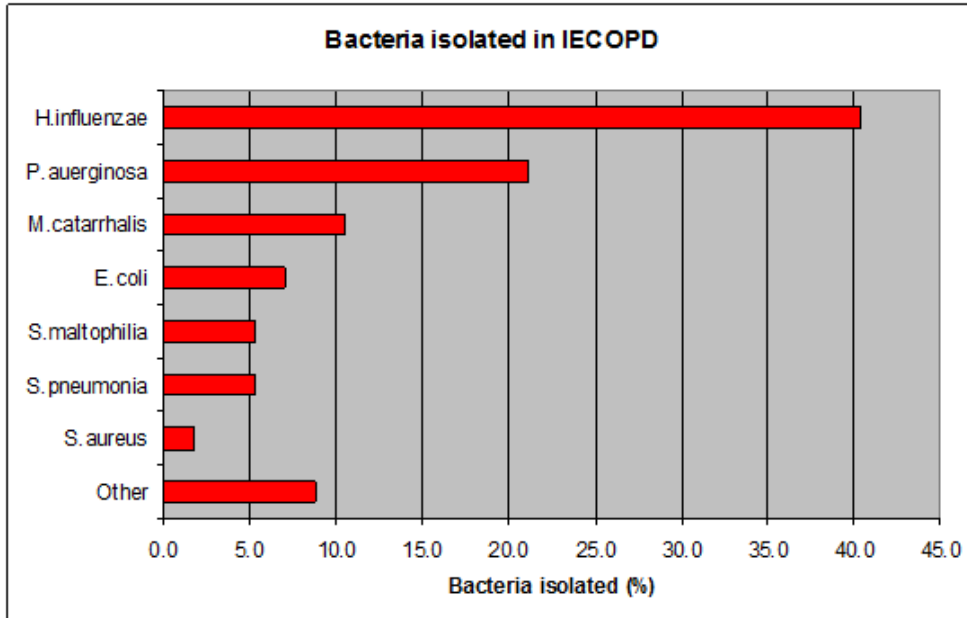
- **Reduce mortality:**

-Smoking cessation: 12.4% NNT 8
-Oxygen Therapy: 20% NNT 5 for 5 years
-??Seretide 500/50: 2.65% *NNT 37 for 3 years (p=0.052)*

ICS and Pneumonia

- ICS equivalence
 - 500 mcg Fluticasone =
 - 800 mcg budesonide =
 - 92 mcg fluticasone furoate
- COPD dosing: Seretide 1000/d > Symbicort 800/d; Breo 92/d
- NNT for 1 extra pneumonia 47 (ie 2.1%)
- Fluticasone>budesonide (Pathos BMJ 2013)
- WISDOM trial-NEJM 2014-can safely stop ICS
- ***Reserve ICS for exacerbators**

COPD Exacerbation Bacteriology-RHH



- Infection 80% exacerbations
- Bacteria 50-70%
- Sputum + 40%
- *H.influenzae* amoxycillin resistance 30%

McDonald, Harkness Respiriology 2002

Manage eXacerbations

- Oral corticosteroids - prednisolone 37.5-50 mg or equivalent, taken in the morning for 5-7 days and then cease; tapering not necessary
- Clinical features of infection; oral amoxicillin 500mg tds or doxycycline 200mg orally 1st dose dose, then 100mg daily for 5 days
- If the patient is not improving and the sputum culture grows a resistant organism a change in antibiotics should be considered

Indications for hospitalisation

- Inadequate response to appropriate community-based management
- Inability to walk between rooms when previously mobile
- Inability to eat or sleep because of dyspnoea
- Cannot manage at home even with homecare resources
- High-risk comorbid condition (pulmonary or non-pulmonary)
- Altered mental status suggestive of hypercapnia
- Worsening hypoxaemia or cor pulmonale
- Newly occurring arrhythmia
- SpO₂ < 92%

Respiratory Specialist Referral

- Diagnostic uncertainty and exclusion of asthma
- Unusual symptoms such as haemoptysis
- Frequent chest infections (i.e. more than 2/year) - rule out co-existing bronchiectasis, optimise treatment
- Oxygen saturation, SpO₂ <92% when stable for long-term oxygen therapy
- Bullous lung disease on CXR or CT
- COPD < 40 years of age - alpha1-antitrypsin deficiency
- Persistent dyspnoea, marked hyperinflation, severe airflow limitation - assessment for lung transplantation or lung volume reduction procedure
- Daytime sleepiness, complaints by partner of heavy snoring - assess for sleep disordered breathing and refer for sleep studies if needed

COPD Survival and Respiratory Failure

Hypoxaemic respiratory failure

3 year survival 40%.

Admission to hospital with an infective exacerbation of COPD complicated by hypercapnic respiratory failure ie $\text{PaCO}_2 > 50$

2 year survival 51%

Chronic carbon dioxide retention (25% of admitted with hypercapnic exacerbations)

5-year survival 11%

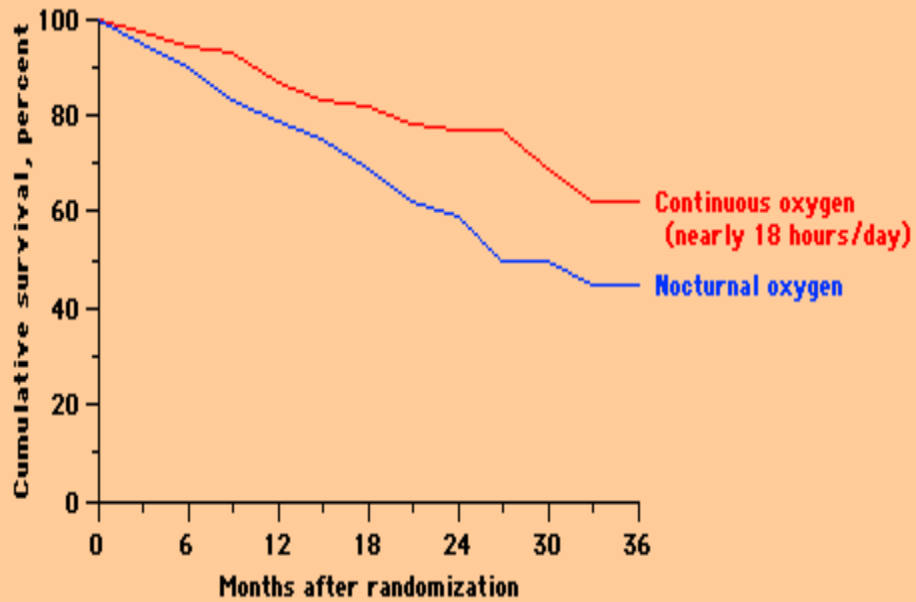
Oxygen Therapy

- **Indications:**

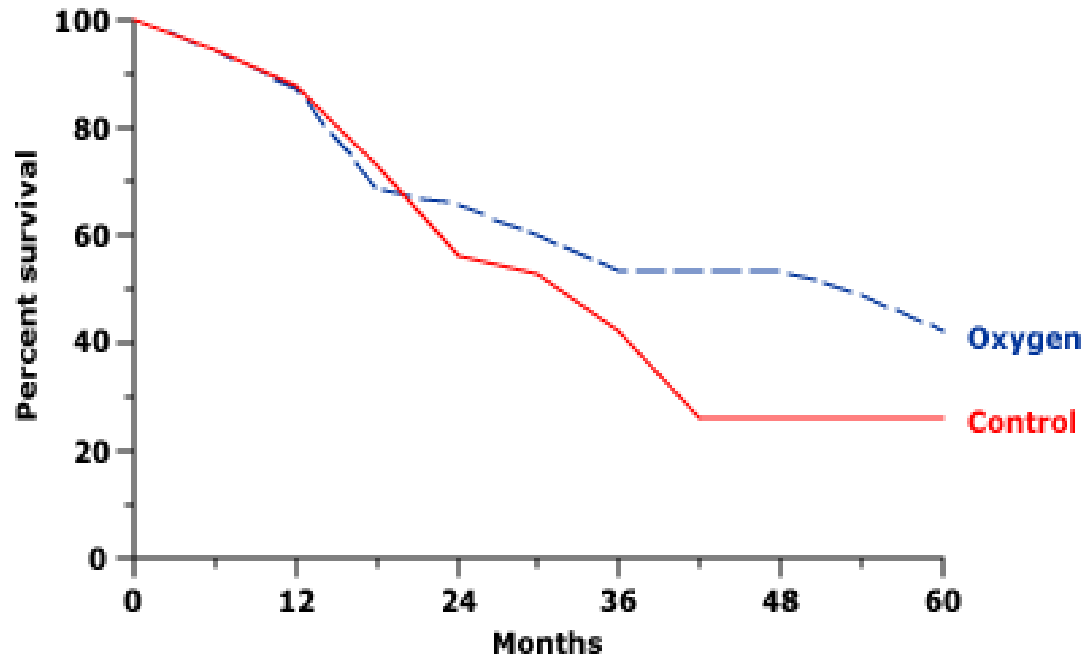
Long term oxygen therapy (more than 15 hrs/day) reduces mortality in hypoxemic COPD patients with resting PaO₂ < 55 mmHg

Resting PaO₂ 55-60 mmHg with polycythemia, clinical evidence of pulmonary hypertension or cor pulmonale

NNT to prevent one death over 5 years = 5



NOTT 1980



MRC 1981

Exertional Oxygen in COPD

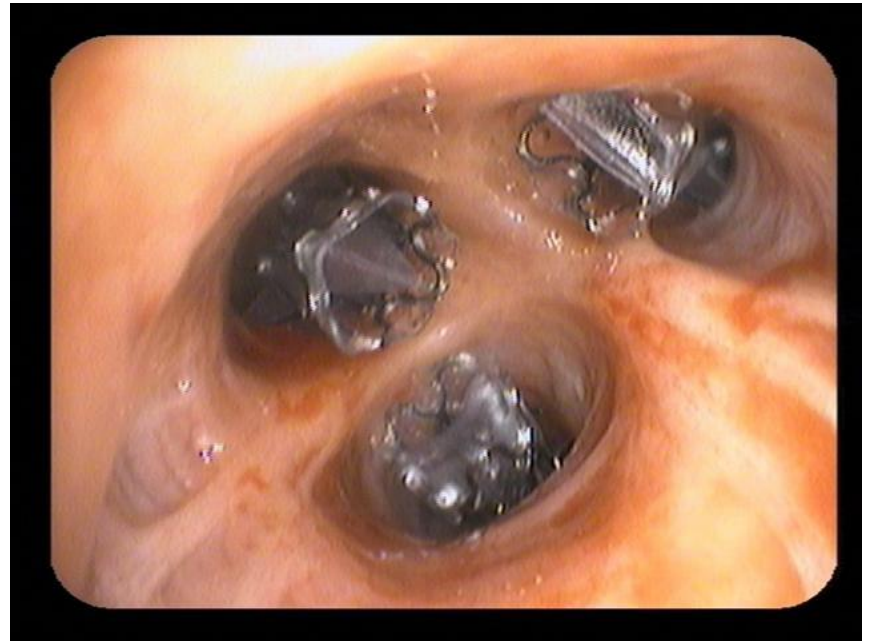
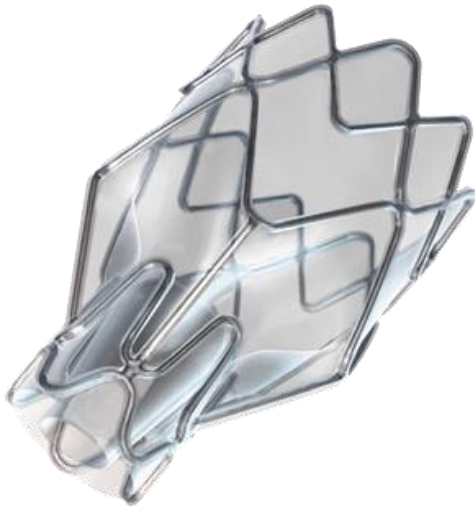
- Long-Term Oxygen Treatment Trial (LOTT)

Lancet 2016

- Stable COPD with SpO_2 89-93% or moderate exercise-induced desaturation-during the 6-minute walk test, $\text{SpO}_2 \geq 80\%$ for ≥ 5 minutes and $< 90\%$ for ≥ 10 seconds.
- No significant difference in any outcomes at all!!

Lung Volume Reduction Procedures

- Lung Volume Reduction Surgery for upper zone predominant emphysema
- Endobronchial LVR for advanced emphysema with severe hyperinflation
 - eg coils, valve



Collateral Ventilation

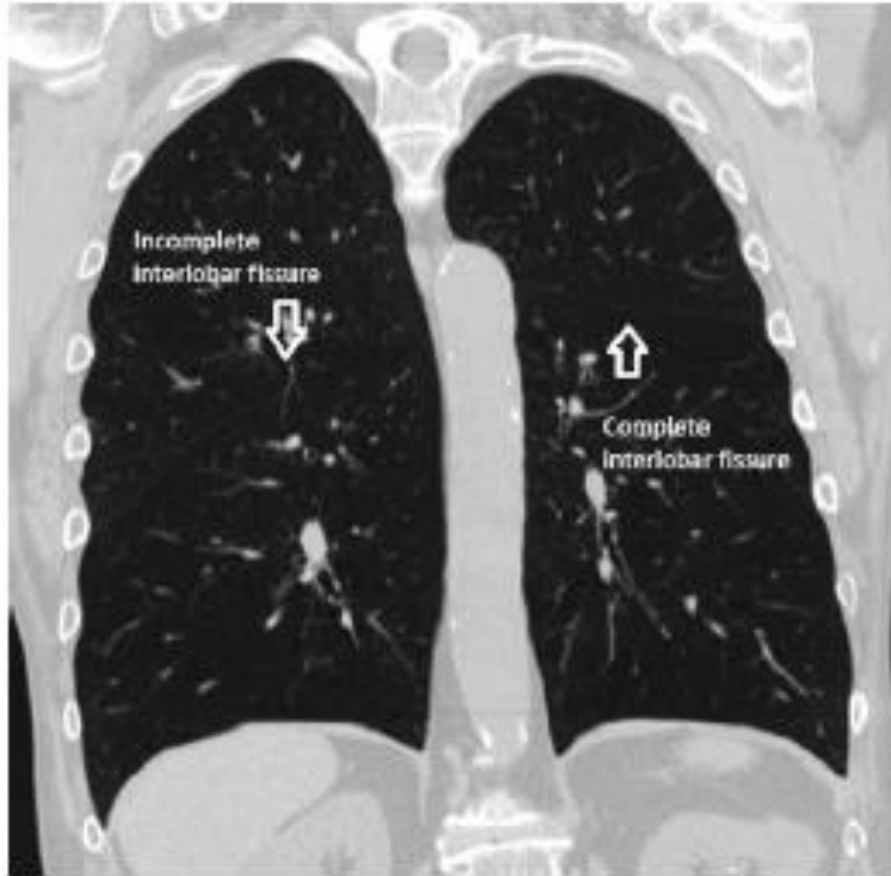


Figure 1. Computed tomography showing an incomplete major fissure on the right and a complete interlobar fissure on the left.

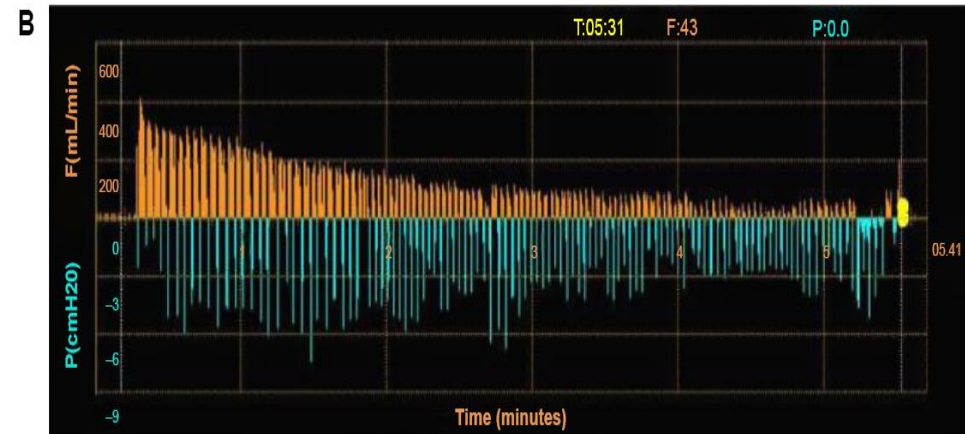
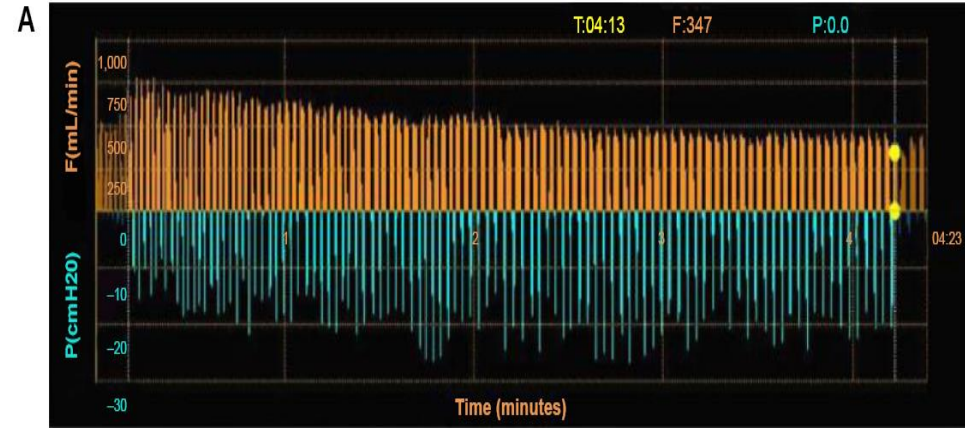


Figure 5 Assessment of collateral ventilation using Chartis system (Pulmonx Corp., Redwood City, CA, USA).

Notes: (A) No reduction in flow (mL/min); orange lines visualized indicating presence of collateral ventilation and incomplete fissure in the right upper lobe. The blue lines show the changes in intralobar pressure P(cmH2O) during spontaneous respiration. (B) A reduction in flow (orange lines) can be seen in the left upper lobe over a time period of more than 5 minutes, while the breathing effort (blue lines) does not change. This indicates no collateral ventilation and complete fissure in the left lung making valve placement possible.

Abbreviations: P, pressure; F, flow.

Difficult Selection/High Risk

Inclusion Criteria

- COPD/Emphysema
- FEV1 15-45%
- TLC > 120%
- RV > 150%
- DLCO > 20%
- PaCO₂ < 55mmHg
- PaO₂ > 45mmHg
- PAP on Echo < 50mmHg
- 120m on preliminary 6MWT
- No collateral ventilation
- Completed pulmonary rehab

Risks/benefits

- 18% Pneumothorax
- 74 metre increase 6MWD

Recent trials-endoscopic LVR

- 6 month multi-centre RCT - TRANSFORM (heterogeneous):
 - Average increase FEV1: 29.3%
 - Average increase 6MWT: 78.7m
 - Average increase SGRQ: 6.5 points
- 6 month prospective RCT - IMPACT (homogeneous):
 - Average increase FEV1: 16.3%
 - Average increase 6MWT: 28.3m
 - Average improvement SGRQ: 7.5 points
- Additional published clinical data demonstrates sustained benefits out to 5 years suggesting survival benefit at 5 and 10 years post treatment.

COPD

Timing of referral:

- Disease is progressive, despite maximal medication, pulmonary rehabilitation, and oxygen therapy
- **Patient is not a candidate for endoscopic or surgical LVRS**
- BODE index of 5 to 6
- PaCO₂ >50 mm Hg or 6.6 kPa and/or PaO₂ < 60 mm Hg or 8 kPa
- **FEV1 <25% predicted**

Timing of listing (presence of one criterion is sufficient):

- BODE index >7
- **FEV1 <15% to 20% predicted**
- Three or more severe exacerbations during the preceding year
- One severe exacerbation with acute hypercapnic respiratory failure
- Moderate to severe pulmonary hypertension

Lung Transplantation in Tasmania 2020

- n=127 over last 15 years
- 49% for COPD
- 5 year survival 53%
- 10 year survival 31%
- Cause of death:

Acute rejection	3%
Infection	11%
Chronic rejection (BOS)	47%