Chronic Obstructive Pulmonary Disease

OR...

“Airflow obstruction that is not fully reversible: Post-bronchodilator FEV1/FVC <0.70 and FEV1 <80% Predicted”
Background/Context

- 7.5% of Australians aged >40 years have COPD
- 50% not diagnosed
- 2nd most common cause of ‘avoidable’ hospital admissions

- **Southern Tasmania:**
  - 475 admissions
  - Average stay 3.8 days
  - 20% re-admission rate
  - 10% require acute NIV
  - Inpatient mortality 7%

- 5th leading cause of death in Australia (2012)- 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 FEV1/FVC < 0.7

• If FEV1 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 production\(^4\) SR ME
  - all smokers/ex-smokers > 35 years of age\(^4\) SR ME
- Document smoking history, current smoking status, and work history including occupational exposure in all patients with suspected COPD. SR LE
Rationale for early diagnosis of COPD

• COPD progresses for decades before symptoms develop.
• The majority of cases are currently diagnosed in the severe stage.
• Spirometry can easily detect COPD in the mild stage.
• Office spirometers are inexpensive, easy-to-use, and safe.
Arguments *against* early diagnosis

• Everyone should be helped to stop smoking regardless of spirometry results.

• *GPs don’t obtain adequate quality tests.*

• *Inhaled medications in those with mild COPD don’t affect morbidity or mortality.*
Spirometry detects COPD before other tests

Enright 1987
Spirometry and confirmation

**Recommendation**

- Spirometry should be performed using techniques that meet published standards. (SR LE)
- Perform pre- and post-bronchodilator spirometry to confirm COPD, which is characterised by airflow limitation that is not fully reversible (post-bronchodilator FEV₁/FVC ratio < 0.7 and FEV₁ < 80% predicted). (SR 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. (SR ME)
- In patients with borderline spirometry, consider alternative diagnoses and investigate appropriately. (SR ME)
Asthma:
Variable course,
Younger,
Atopy,
<15 pack year history,
Reversible airflow limitation
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.
### COPD Severity

<table>
<thead>
<tr>
<th>COPD SEVERITY</th>
<th>FEV₁ (% predicted)</th>
<th>Symptoms</th>
<th>History of exacerbations</th>
<th>Comorbid conditions*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>60-80</td>
<td>- Breathlessness on moderate exertion&lt;br&gt;- Recurrent chest infections&lt;br&gt;- Little or no effect on daily activities</td>
<td>Frequency may increase with severity</td>
<td>Present across all severity groups²</td>
</tr>
<tr>
<td>Moderate</td>
<td>40-59</td>
<td>- Increasing dyspnoea&lt;br&gt;- Breathlessness walking on level ground&lt;br&gt;- Increasing limitation of daily activities&lt;br&gt;- Cough and sputum production&lt;br&gt;- Exacerbations requiring corticosteroids and/or antibiotics</td>
<td>Frequency may increase with severity</td>
<td>Present across all severity groups²</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 40</td>
<td>- Dyspnoea on minimal exertion&lt;br&gt;- Daily activities severely curtailed&lt;br&gt;- Experiencing regular sputum production&lt;br&gt;- Chronic cough</td>
<td>Frequency may increase with severity</td>
<td>Present across all severity groups²</td>
</tr>
</tbody>
</table>

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

• Randomised trial of smoking cessation (and inhaled BD) in smokers aged 35-60 with mild/asymptomatic COPD

• Usual care vs smoking intervention

• Followed up to 14 years

Mild COPD-Mortality benefit

All-cause 14.5-year survival

5yr survival 97%

Mortality 12.4%

Smoking cessation-pharmacological

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum</td>
<td>8%</td>
</tr>
<tr>
<td>Nicotine transdermal patch</td>
<td>6%</td>
</tr>
<tr>
<td>Bupropion (Zyban 300 mg)</td>
<td>9%</td>
</tr>
<tr>
<td>Varenicline (Champix 1mg bd)</td>
<td>13%</td>
</tr>
<tr>
<td>Intensive behavioural support plus NRT or</td>
<td></td>
</tr>
<tr>
<td>Bupropion (eg smoking cessation clinic)</td>
<td>13-19%</td>
</tr>
</tbody>
</table>

In clinical practice: counselling plus NRT or pharmacotherapy 10%

(Katz JNatlCancerInstitute 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 intervieweing, 1 home visit, 7 weeks phone follow-up, unsupervised exercise

- **Tele-rehabilitation**
  REACH trial recruiting, exercise bikes/live sessions
Over 5 years choice for maintenance:
4 → 13 inhalers
“OLD”

**LABA**

- Onbrez: Indacterol 150 or 300 mcg

**LAMA**

- Spirvia: Tiotropium 18 mcg

**ICS/LABA**

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

**LABA**
- Striverdi: Olodaterol

**LAMA**
- Spirva: Tiotropium Respimat 5 mcg 2 inhalations daily
- Seebri: Glycopyrronium 50 mcg 1 inhalation daily
- Bretaris: Aclidinium 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: Glycopyronnium/Inadacterol 50/110mcg 1 inhalation daily
- Brimica: Aclidinium/Eformoterol 340/12 1 mcg inhalation BD

**ICS/LABA**
- Breo: Fluticasone furoate/vilanterol 92/25 mcg 1 inhalation daily
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% \(NNT \ 37 \ for \ 3 \ years \ (p=0.052)\)
Optimise pharmacotherapy using a stepwise approach

Recommendations (see Figure 1)

For all symptomatic patients with COPD:
- Follow a stepwise approach to pharmacological treatment until adequate control of breathlessness, functional capacity, and exacerbation frequency is achieved.
- Use short-acting inhaled bronchodilator therapy for short-term relief of breathlessness.

For patients receiving short-acting bronchodilators who have persistent troublesome dyspnoea, add a long-acting beta$_2$-agonist or long-acting muscarinic antagonist (or both in combination if monotherapy is not adequate) for regular use.

LAMA/LABA fixed dose combinations in a single inhaler (glycopyrronium/indacaterol, umeclidinium/vilanterol, tiotropium/olodaterol, aclidinium/eformoterol) are available for patients who remain symptomatic despite monotherapy with either alone.

For patients with FEV$_1$ < 50% predicted and ≥ 2 exacerbations in 12 months:
- Initiate an inhaled corticosteroid + long-acting beta$_2$-agonist fixed dose combination and discontinue long-acting beta$_2$-agonist monotherapy.
- For patients with moderate-to-severe COPD with frequent exacerbations who are not receiving a long-acting muscarinic antagonist, consider addition of a long-acting muscarinic antagonist to the inhaled corticosteroid + long-acting beta$_2$-agonist.
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
<table>
<thead>
<tr>
<th></th>
<th>SABA</th>
<th>SAMA</th>
<th>LAMA</th>
<th>LABA</th>
<th>LABA/LAMA</th>
<th>ICS/LABA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SABA</strong></td>
<td>salbutamol (Ventolin™, Airomin™, Asmol™)</td>
<td>terbutaline (Bricanyl™)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>SAMA</strong></td>
<td>ipratropium (Atrovent™)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>LAMA</strong></td>
<td>tiotropium (Spiriva™)</td>
<td>glycopyrronium (Seebri™)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>LABA</strong></td>
<td>salmeterol (Serevent™)</td>
<td>eformoterol (Oxis™, Foradil™)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>LABA/LAMA</strong></td>
<td>indacaterol/glycopyrronium (Ultibro™)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>ICS/LABA</strong></td>
<td>fluticasone propionate/salmeterol (Seretide™)</td>
<td>fluticasone furoate/vilanterol (Breo™)</td>
<td></td>
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</tbody>
</table>

Green tick indicates therapies that can be used together.

Red indicates combinations not recommended.
ICS and Pneumonia

- ICS equivalence
  - 500 mcg Fluticasone =
  - 800 mcg budesonide =
  - 92 mcg fluticasone furoate

- 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*
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, SpO\textsuperscript{2} <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
Lung Volume Reduction Procedures

- Lung Volume Reduction Surgery for upper zone predominant emphysema
- Endobronchial LVR for advanced emphysema with severe hyperinflation – eg coils, valve
Figure 1. Computed tomography showing an incomplete major fissure on the right and a complete interlobar fissure on the left.

Notes: (A) No reduction in flow F(mL/min): orange lines visualize indicating presence of collateral ventilation and incomplete fissure in the right upper lobe. The blue lines show the changes in intrathoracic 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
- Pt has undergone pulmonary rehab within the last 2 yrs

#### Risks/benefits

- 18% Pneumothorax
- 74 metre increase 6MWD

MoU with Alfred Hospital
Prevent deterioration

• Smoking cessation is the most important intervention to prevent worsening of COPD
• Preventing exacerbations has a key role in preventing deterioration.
• *Immunisation reduces the risks associated with influenza and pneumococcal infection.
• *Long-term oxygen therapy has survival benefits for COPD patients with hypoxaemia.
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)
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, Spo$_2$ $\geq 80\%$ for $\geq 5$ minutes and $< 90\%$ for $\geq 10$ seconds.

• No significant difference in any outcomes at all!!

• Likely change to prescribing criteria 2017
Lung transplant for COPD

- **Timing of referral for lung transplant:** COPD-disease specific

- FEV1 <20%, hypercapnia, homogeneous emphysema with TLCO <20%, α1-AT, (pulmonary hypertension)
  
  (Glanville et al ERJ 2003)

- Single lung transplant → improve FEV1 to 60% + QoL, exercise performance
Lung Transplantation in Tasmania 2016

- n=107 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%
Develop a plan of care

• Good chronic disease care anticipates the wide range of needs in patients with COPD.

• Patients *may benefit* from self-management support.

• *Accurate assessment of approaching end of life is difficult.*
Self-Management

- **Action plan alone** - not enough  
  Walters Cochrane 2014

- Comprehensive Self Mx plan *may lead to 30-40% decrease in admissions*  
  Cochrane 2014

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
COPD Survival

• 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%
Manage eXacerbations

• A COPD exacerbation is characterised by a change in the patient’s baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication or hospital admission.

• Early diagnosis and treatment of exacerbations may prevent hospital admission and delay COPD progression.

• *Indications for hospitalisation of patients with COPD.

• Inhaled bronchodilators are effective for initial treatment of acute exacerbations.

• *Systemic corticosteroids reduce the severity of, and shorten recovery from exacerbations.

• *Exacerbations with clinical features of infection (increased volume and change in colour of sputum and/or fever) benefit from antibiotic therapy.
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%
Treatment

• Oral corticosteroids - prednisolone 30-50 mg or equivalent, taken in the morning for 5 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
COPD Bacteriology

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

McDonald, Harkness Respirology 2002