Modern Management of COPD.

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Disclosures: Dr Robert Young

Never received funding from the tobacco industry

Associate Professor in Medicine and Molecular Genetics, University of Auckland, NZ

Received travel grant and honorarium for talks on COPD and smoking cessation from GSK

Chief Scientific Officer of Synergenz BioScience who helped fund development of a lung cancer risk score (Respiragene)
COPD Management - Confused

Breathlessness and exercise limitation

Short acting beta agonist or short acting muscarinic antagonist as required*

Forced expiratory volume in 1 second ≥50%

Exacerbations or persistent breathlessness

Long acting beta agonist

Forced expiratory volume in 1 second <50%

Long acting muscarinic antagonist
Discontinue SAMA

Long acting beta agonist plus inhaled corticosteroid in a combination inhaler

Long acting muscarinic antagonist
Offer LAMA in preference to regular SAMA four times a day

Consider LABA plus LAMA if ICS declined or not tolerated

Consider LABA plus LAMA if ICS declined or not tolerated

Long acting muscarinic antagonist
Discontinue SAMA

Offer LAMA in preference to regular SAMA four times a day

Persistent exacerbations or breathlessness

Long acting beta agonist plus inhaled corticosteroid in a combination inhaler

Consider LABA plus LAMA if ICS is declined or not tolerated

Long acting muscarinic antagonist plus long acting beta agonist plus inhaled corticosteroid in a combination inhaler

Abbreviations: SAMA = short acting muscarinic antagonist, LAMA = long acting muscarinic antagonist, LABA = long acting beta agonist, ICS = inhaled corticosteroid

* Short acting beta agonist (as required) may continue at all stages

Offer therapy (strong evidence)  Consider therapy (less strong evidence)
## COPD Management - ?confused

### Patient-centred management of stable COPD in primary care

**For all patients:**
- provide smoking cessation advice
- provide patient education/self management
- assess co-morbidity
- give dietary advice if BMI > 25 kg/m²
- promote exercise
- offer pneumococcal vaccination
- offer annual influenza vaccination
- refer to a dietary specialist if BMI < 20 kg/m²

<table>
<thead>
<tr>
<th>SYMPTOMS?</th>
<th>FUNCTIONAL LIMITATION?</th>
<th>EXACERBATIONS</th>
<th>HYPOXIA?</th>
<th>HOLISTIC CARE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BREATHELESSNESS</strong></td>
<td>MRC score ≥ 3</td>
<td>(Oral steroids/ antibiotics/hospital admissions)</td>
<td>Oxygen saturation ≤ 92% at rest in air</td>
<td>Check social support (e.g. carers and benefits)</td>
</tr>
<tr>
<td>Prescribe short-acting bronchodilators (beta₂ agonist/ antimuscarinic) for relief of symptoms</td>
<td>Optimise pharmacotherapy See NICE pharmacotherapy algorithm</td>
<td>Optimise pharmacological therapy</td>
<td>FEV₁ &lt; 30% predicted</td>
<td>Treat co-morbidities</td>
</tr>
<tr>
<td><strong>PERSISTENT SYMPTOMS</strong></td>
<td></td>
<td></td>
<td>Discus action plans including use of standby oral steroids and antibiotics</td>
<td>Refer for oxygen assessment</td>
</tr>
<tr>
<td>Offer pharmacotherapy in line with NICE guideline</td>
<td>Offer pulmonary rehabilitation</td>
<td></td>
<td></td>
<td>Refer to specialist palliative care teams for end-of-life care</td>
</tr>
<tr>
<td><strong>PRODUCTIVE COUGH</strong></td>
<td>Screen for anxiety/depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider use of mucolytics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
COPD - simplified

TREATMENT OPTIONS FOR COPD

Self-Management Education and Smoking Cessation
Bronchodilators
Inhaled Corticosteroids
Pulmonary Rehabilitation
Oxygen
Surgery

But how do you define severity?
Topics

1. What is COPD and why diagnose it
2. Treatment options in COPD – a symptom based approach
3. Treatment options in COPD – when to add the inhaled steroids
4. Treatment options – beyond the airways
5. Management options in the future
1. What is COPD and why diagnose it
What is COPD and why diagnose it

- Affects 8% of adult population (1 in 12)
- Affects 20% of adult smokers (1 in 5)
- Affects 30% of adult general medical admissions
- Affects 50% of pneumonia over 65 yrs old

COPD and asthma are very different diseases
COPD health status in New Zealand

• Prevalence COPD
  – 6.6% equivalent to 96,100 adults (formal diagnosis)

• COPD hospitalisation rates
  – 2,021 per 100,000 – Maori
  – 484 per 100,000 – non-Maori

• COPD Mortality rates
  – 129 per 100,000 – Maori
  – 46 per 100,000 – Non-Maori

MOH. A Portrait of Health – Key Results of the 2006/07 NZ Health Survey. Wellington. 2008
MOH. Tatau Kajukura:Maori Health Chart Book 2010. 2nd Ed. Wellington 2010
“COPD is highly prevalent, underdiagnosed, undertreated and underpercieved”

Bart Celli 2008
“COPD is highly prevalent, underdiagnosed, undertreated and underpercieved”

Bart Celli 2008

50-80% of COPD is undiagnosed
Diagnosis and management of COPD

• Diagnose - assess airflow limitation (spirometry, PEFR)
• Assess symptoms (CAT and mMRC score)
• Assess exacerbation risk (PHx of exacerbation, FEV₁%pred)
• Assess COPD comorbidities (anxiety/depression, muscle wasting/fatigue)
• Assess COPD-related comorbidities (CHD/CHF, lung cancer, osteoporosis)
• Manage – reduce risk and reduce symptoms
Diagnosis and management of COPD

- Diagnose - assess airflow limitation (spirometry, PEFR)
- Assess symptoms (CAT and MRC score)
- Assess risk of exacerbations (PHx of exacerbation)
- Assess COPD comorbidities (anxiety/depression, muscle wasting/fatigue)
- Assess COPD-related comorbidities (CHD/CHF, lung cancer, osteoporosis)

- Manage – reduce risk and reduce symptoms
Diagnosis
Spirometry and lung age
(diagnosis, engage and risk)
Lung Health Clinic (Auckland)

Contact us: Ph 0800 789999 or 09 630 9967 or Fax 09 623 6456 or email: lunghealthclinic@adhb.govt.nz

For assessment of patients with breathlessness or suspected of asthma or COPD (especially those exposed to smoking or aero-pollutants).

For lung function testing, medication review, smoking cessation, inhaler technique, COPD unresponsive to treatment and lung cancer screening.

Refer your patient for a personal consultation with Raewyn Hopkins (BN, MPH) or Associate Professor Robert Young, Consultant Physician (FRACP, PhD)
Decline of Lung Function: variable susceptibility

- Not Susceptible to Smoke (60%)
- Intermediate Smokers (20%)
- Susceptible Smokers (COPD) (20%)

Onset of symptoms
Severe disability
Death

FEV1 (% of value at age 25 years)

Age (years)

25 50 60yr old 75
Decline in lung function with COPD severity

Nonsmoker decline is 20-30 mL/yr
Decline in lung function with COPD severity

- Diagnosed with screening spirometry of smokers/ex-smokers
- Diagnosed with SOB/cough/sputum and wheeze (AECOPD)
Decline of Lung Function: variable susceptibility

↓FEV1: other morbidities apart from COPD
- 5x ↑Lung cancer
-5x ↑ heart attack
- 2-3x ↑ stroke (Young et al. ERJ 2007)
What is COPD and why diagnose it

- Results from genetic susceptibility and aero-pollutant (smoking) exposure
- Neutrophilic airway inflammation
- Presents with
  - exertional breathlessness and LRTI (cough, sputum, wheeze and SOB)
  - Fatigue and poor exercise tolerance
- Systemic inflammation and co-morbidities
- Precursor illness to 70-80% of all lung cancer
Genetic susceptibility
Combined effects of susceptibility and protective genetic effects

Cigarette smoke
Biomass particles and particulates

Anti-oxidants
Lung inflammation
Anti-proteases

Oxidative stress
Proteinases
COPD pathology

Host factors and amplifying mechanisms
Repair mechanisms

Proposed Pathogenesis of COPD

Small Airway Lumen
- Cigarette Smoke
- Nicotine
- Oxidants (ROS)
- Heavy Metals
- LPS
- Goblet Cell Hyperplasia
  - Mucus

Airway Wall
- PMN Influx
- MØ Influx
- MPO
- Oxidant Load
  - Exogenous
  - Endogenous
- Acquired Antiprotease Deficiency
- TMPS
- αAT
- TGFB1
- Fibronectin
- Smooth Muscle Proliferation
- VEGF
- Apoptosis
- Fibroblast
- Airways Narrowing
- Emphysema
- Lymphocytes
- Collagen

Pulmonary Circulation
- Cytokines
  - IL-8
  - IL-6
  - TNFα
- PMN
- MØ
- Oxidants
- MMP 1, 2, 9, 12, 15

Systemic Circulation
- Arteries
- ↑ Atherosclerosis
- ↑ Plaque rupture
- Muscle
- - Wasting
- - Fatigue
- Liver
- ↑ CRP
- αAT
- IL-6
- Bone
- Osteoporosis

Alveolar Wall
- Young RP, et al. (European Respir Review 2009)
Systemic manifestations and comorbidities of COPD

PJ Barnes and BR Celli
2. A symptom based approach (Assess)
# Management of COPD – the aims

<table>
<thead>
<tr>
<th>Reduce symptoms</th>
<th>Relieve symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Improve exercise tolerance</td>
</tr>
<tr>
<td></td>
<td>Improve health status</td>
</tr>
<tr>
<td>Reduce risk</td>
<td>Prevent disease progression</td>
</tr>
<tr>
<td></td>
<td>Prevent and treat exacerbations</td>
</tr>
<tr>
<td></td>
<td>Reduce mortality</td>
</tr>
</tbody>
</table>

GOLD Strategy Document 2011 (http://www.goldcopd.org/)
Development and progression of COPD – FEV$_1$ vs symptoms

Smoke from tobacco and biomass fuel contains ROS, toxins, and particulate matter

Viral and bacterial infections

FEV$_1$(% of predicted) vs Age (years)

Stage I
Stage II
Stage III
Stage IV

Signs and symptoms

Asymptomatic
Progressive dyspnoea
Systemic disease Comorbidities
Respiratory failure Death
Treatment options in COPD – a symptom based approach

• Spirometry – document severity of airways obstruction (confirm diagnosis, end organ damage)

• Establish – symptom profile (CAT), tendency to LRTI, AECOPD, hospitalisation for acute exacerbations (direct inhaler treatment).

• Consider COPD a CVS risk factor

• Consider COPD a precursor to lung cancer
Standards for the Diagnosis and Management of Patients with COPD

Clinical Presentation
- At Risk
- Symptomatic
- Exacerbations
- Respiratory Failure

Interventions
- Smoking Cessation
- Disease Management
- Pulmonary Rehabilitation
- Other Options

Disease Progression
- FEV₁
- Symptoms

Other Options
SABA/SAMA prn
then LABA/LAMA bd
then LABA + ICS bd
then LABA /ICS + LAMA

Plus

• Oral AB/Prednisone
• Pulmonary rehab
• LTOT and surgery/valves
A symptom based approach

HEED study

- Lung function alone is a poor predictor of symptoms
- Symptoms of COPD should be assessed regularly in patients with COPD (self administered CAT questionnaire, www.catestonline.co.uk)
- Reduced exercise tolerance was seen in 70% with mild disease (%predFEV1 > 80%) and 74% with moderate disease (%predFEV1 50-80%).

The CAT questionnaire (download from - www.catestonline.co.uk)

<table>
<thead>
<tr>
<th>Cough</th>
<th>I never cough</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>I cough all the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phlegm</td>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>My chest is full of phlegm (mucus)</td>
</tr>
<tr>
<td>Tight</td>
<td>My chest does not feel tight at all</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>My chest feels very tight</td>
</tr>
<tr>
<td>SOB</td>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
</tr>
<tr>
<td>Activity</td>
<td>I am not limited doing any activities at home</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>I am very limited doing activities at home</td>
</tr>
<tr>
<td>Confidence</td>
<td>I am confident leaving my home despite my lung condition</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>I am not at all confident leaving my home because of my lung condition</td>
</tr>
<tr>
<td>Sleep</td>
<td>I sleep soundly</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>I don't sleep soundly because of my lung condition</td>
</tr>
<tr>
<td>Energy</td>
<td>I have lots of energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>I have no energy at all</td>
</tr>
</tbody>
</table>

**A symptom based approach – CAT**

COPD Self Assessment Test

Score/40
- mild 0-10
- mod 10-15
- severe 15-25
- very severe 25-40

Basis on which to establish
- overall disability
- specific disabilities and
- response to treatments
The CAT questionnaire (download from - www.catestonline.co.uk)

**A symptom based approach – CAT**

**COPD Self Assessment Test**

**Score/40**
- mild 0-10
- mod 10-15
- severe 15-25
- very severe 25-40

Basis on which to establish
- overall disability
- specific disabilities and
- response to treatments
## CAT Score – patient data

<table>
<thead>
<tr>
<th>CAT Score Description</th>
<th>CAT Score Points</th>
<th>Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td>0 2 3 4 5</td>
<td>1</td>
</tr>
<tr>
<td>I cough all the time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>0 2 3 4 5</td>
<td>1</td>
</tr>
<tr>
<td>My chest is completely full of phlegm (mucus)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td>0 1 3 4 5</td>
<td>2</td>
</tr>
<tr>
<td>My chest feels very tight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>0 1 2 3 5</td>
<td>4</td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td>0 1 2 4 5</td>
<td>3</td>
</tr>
<tr>
<td>I am very limited doing activities at home</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am confident leaving my home despite my lung condition</td>
<td>0 1 2 3 5</td>
<td>4</td>
</tr>
<tr>
<td>I am not at all confident leaving my home because of my lung condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I sleep soundly</td>
<td>0 1 3 4 5</td>
<td>2</td>
</tr>
<tr>
<td>I don’t sleep soundly because of my lung condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have lots of energy</td>
<td>0 1 2 3 4</td>
<td>5</td>
</tr>
<tr>
<td>I have no energy at all</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Severe**

Scoring range 0-40

<table>
<thead>
<tr>
<th>Total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
</tr>
</tbody>
</table>
# Modified MRC Breathlessness Score

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description of Breathlessness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise.</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on level ground or walking up a slight hill.</td>
</tr>
<tr>
<td>2</td>
<td>On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace.</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 yards or after a few minutes on level ground.</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing.</td>
</tr>
</tbody>
</table>
No correlation between QOL and FEV$_1$ severity

FEV$_1$ (% predicted) vs. SGRQ score (CAT)

- Stage 4
- Stage 3
- Stage 2

Breathless walking on level ground

Upper limit of normal

$r=-0.23$
P$<0.0001$
ECLIPSE showed weak correlation between disease outcome parameters & FEV$_1$

- **mMRC score**
  - Rho = -0.36
  - p < 0.001

- **SGRQ-C Total score**
  - Rho = -0.38
  - p < 0.001

- **6MWD (Metres)**
  - Rho = -0.34
  - p < 0.001

- **Number of exacerbations**
  - Rho = -0.21
  - p < 0.001

Agusti et al. Resp Res 2010
3. When to start long acting bronchodilators and when to add steroids

(Manage)
COPD Management – adding inhalers

GOLD Therapy at Each Stage of COPD

I: Mild
- FEV₁/FVC <0.70
- FEV₁ ≥80% predicted

Active reduction of risk factor(s):
- influenza vaccination
- Add short-acting bronchodilator (when needed)

II: Moderate
- FEV₁/FVC <0.70
- 50% ≤FEV₁ <80% predicted

Add regular treatment with one or more long-acting bronchodilators (when needed):
- Add pulmonary rehabilitation

III: Severe
- FEV₁/FVC <0.70
- 30% ≤FEV₁ <50% predicted

Add inhaled glucocorticosteroids if repeated exacerbations

IV: Very Severe
- FEV₁/FVC <0.70
- FEV₁ <30% predicted or FEV₁ <50% predicted plus chronic respiratory failure

Add long-term oxygen if chronic respiratory failure
Consider surgical treatments
A symptom based approach

Eclipse study

• “Frequent exacerbator*” is a specific type of COPD that requires aggressive treatment with combination therapy (preferably fixed dose ICS and LABA)

• “Frequent exacerbators” may be found in those with moderate COPD (22%) and not just severe disease (30-50%).

* 2+ exacerbations per year

The ‘frequent exacerbator phenotype’: Frequency/severity by GOLD Category (1)

ECLIPSE 1 year data

Frequent exacerbators represent stable COPD phenotype - independent of severity

- Proportion of subjects experiencing ≥2 exacerbations/year increases year-on-year
- Stable population provides potential to understand the cause(s) of the phenotype

ECLIPSE 3 year data

New GOLD patient groups

(GOLD Classification of Airflow Limitation)

RISK*

Exacerbation history

2 or more

Less than 2

mMRC 0-1

(C)

(D)

(A)

(B)

mMRC ≥ 2

CAT <10

CAT ≥10

SYMPTOMS†

(mMRC or CAT score)
New GOLD patient groups

GOLD Classification of Airflow Limitation:

- **RISK*:**
  - 1: mMRC 0-1
  - 2: mMRC > 2

- **RISK** (Exacerbation history):
  - Less than 2
  - 2 or more

**Symptoms and Risk**
- FEV₁
- Symptom score
- Exacerbation Hx

**SYMPTOMS†**
(mMRC or CAT score)
New GOLD-defined patient groups

**RISK** (GOLD Classification of Airflow Limitation)

- **4 (C)** or **2 or more**
- **3** or **2**
- **1** or **less than 2**

**SYMPTOMS†** (mMRC or CAT score)

- **mMRC 0-1** or **mMRC ≥ 2**

**RISK** (Exacerbation history)

- **Poor spirometry (FEV%pred≤50%) or 2+ exacerbations/yr (AB/pred/yr)**
- **ET≥ SOB up slight hills Poor QOL CAT≥10**

**Reduced spirometry (FEV%pred>50%) or 0-1 exacerbation/yr (AB/pred/yr)**

- **ET= manages hills ok Good QOL CAT<10**

**Poor spirometry (FEV%pred≤50%) or 2+ exacerbations/yr (AB/pred/yr)**

- **ET= manages hills ok Good QOL CAT<10**

**Reduced spirometry (FEV%pred>50%) or 0-1 exacerbation/yr (AB/pred/yr) and ET≥ SOB up slight hills Poor QOL CAT≥10**
New GOLD-defined patient groups

- **Poor spirometry (FEV%pred≤50%)** or 2+ exacerbations/yr (AB/pred/yr) but ET = manages hills ok Good QOL CAT<10

- **Mild (early)**
  - mMRC 0-1
  - CAT <10

- **“Exacerbator”**
  - mMRC ≥ 2
  - CAT ≥10

- **“Symptomatic”**
  - Reduced spirometry (FEV%pred>50%) or 0-1 exacerbation/yr (AB/pred/yr) but ET = manages hills ok Good QOL CAT>10

- **Severe (both)**
  - Poor spirometry (FEV%pred≤50%) or 2+ exacerbations/yr (AB/pred/yr) and ET ≥ SOB up slight hills Poor QOL CAT≥10

**RISK* (GOLD Classification of Airflow Limitation)**

- 1
  - mMRC 0-1
  - CAT <10

- 2
  - mMRC ≥ 2
  - CAT ≥10

- 3
  - Reduced spirometry (FEV%pred>50%) or 0-1 exacerbation/yr (AB/pred/yr) but ET = manages hills ok Good QOL CAT>10

**Exacerbation history**

- Less than 2
- 2 or more

**SYMPTOMS† (mMRC or CAT score)**

- Poor spirometry (FEV%pred≤50%) or 2+ exacerbations/yr (AB/pred/yr) and ET ≥ SOB up slight hills Poor QOL CAT≥10

- Reduced spirometry (FEV%pred>50%) or 0-1 exacerbation/yr (AB/pred/yr) and ET = manages hills ok Good QOL CAT<10
New GOLD-defined patient groups

**RISK**

(GOLD Classification of Airflow Limitation)

- **1**
  - Reduced spirometry (FEV%pred>50%)
    - or
    - 0-1 exacerbation/yr (AB/pred/yr)
      - but
      - ET=manages hills ok
      - Good QOL CAT<10
  
- **2**
  - mMRC 0-1
    - CAT <10
  
- **3**
  - mMRC ≥ 2
    - CAT ≥10

**SYMPTOMS†**

(mMRC or CAT score)

**ICS/LABA or LAMA**

- Poor spirometry (FEV%pred≤50%)
  - or
  - 2+ exacerbations/yr (AB/pred/yr)
  
**LABA or LAMA**

- Reduced spirometry (FEV%pred>50%)
  - or
  - 0-1 exacerbation/yr (AB/pred/yr)
  
**“Exacerbator”** (wet and wheezy)

- ET≥ SOB up slight hills
- Poor QOL CAT≥10

**Severe (combined-www)**

**“Symptomatic”** (weak and wheezy)

- ET≥ SOB up slight hills
- Poor QOL CAT≥10

**Mild (early)**

- ET= manages hills ok
- Good QOL CAT<10
New GOLD-defined patient groups

RISK

- **Poor spirometry (FEV%pred≤50%)**
  - or
  - 2+ exacerbations/yr (AB/pred/yr)
  - but
  - ET= manages hills ok
    - Good QOL CAT<10

- Reduced spirometry (FEV%pred>50%)
  - or
  - 0-1 exacerbation/yr (AB/pred/yr)
  - but
  - ET=manages hills ok
    - Good QOL CAT<10

RISK*

- **Exacerbation history**
  - 2 or more
  - Less than 2

SYMPTOMS†

- **mMRC 0-1**
  - CAT <10
  - SABA or SAMA prn

- **mMRC ≥ 2**
  - CAT ≥10
  - LABA or LAMA

- **Exacerbator**
  - (wet and wheezy)

- **Symptomatic**
  - (weak and wheezy)

Severe (combined)

- **Poor spirometry (FEV%pred≤50%)**
  - or
  - 2+ exacerbations/yr (AB/pred/yr)
  - and
  - ET≥ SOB up slight hills
    - Poor QOL CAT≥10

Reduced spirometry (FEV%pred>50%)
  - or
  - 0-1 exacerbation/yr (AB/pred/yr)
  - and
  - ET≥SOB up slight hills
    - Poor QOL CAT≥10
## CAT Score – patient data

<table>
<thead>
<tr>
<th>Item</th>
<th>Score Range</th>
<th>Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td>0-5</td>
<td>1</td>
</tr>
<tr>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>0-5</td>
<td>1</td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td>0-5</td>
<td>2</td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>0-5</td>
<td>4</td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td>0-5</td>
<td>3</td>
</tr>
<tr>
<td>I am confident leaving my home despite my lung condition</td>
<td>0-5</td>
<td>4</td>
</tr>
<tr>
<td>I sleep soundly</td>
<td>0-5</td>
<td>2</td>
</tr>
<tr>
<td>I have lots of energy</td>
<td>0-5</td>
<td>5</td>
</tr>
</tbody>
</table>

- **WHEEZY**
- **WEAK**

### Scoring range 0-40

- **Severe** 25-40
- **Very Severe** 25-40
- **Severe** 15-25
- **Moderate** 10-15
- **Mild** 0-10

**Total score**: 2

**“Symptomatic” (weak and wheezy)**
Primary analysis: all-cause mortality at 3 years

HR 0.825, p=0.052
17.5% risk reduction
2.6% absolute reduction

Calverley et al. NEJM 2007
Rate of moderate and severe exacerbations over three years

Mean number of exacerbations/year

1.13

25% reduction

Placebo 0.97* 0.93* 0.85**†‡

SALM FP SFC

* p < 0.001 vs placebo; † p = 0.002 vs SALM; ‡ p = 0.024 vs FP

NNT to prevent 1 exacerbation in 1 year = 4

Calverley et al. NEJM 2007
Rate of exacerbations requiring systemic corticosteroids over three years

Mean number of exacerbations/year

* $p < 0.001$ vs placebo; † $p < 0.001$ vs SALM; ‡ $p = 0.017$ vs FP

Placebo: 0.80
SALM: 0.64*
FP: 0.52*
SFC: 0.46**‡

43% reduction

Calverley et al. NEJM 2007
TORCH: Results summary

SFC 50/500, in COPD patients with FEV$_1$ < 60% predicted

- Had a trend towards improved survival vs placebo
- Significantly maintains and improves health status vs placebo and components
- Significantly reduces the rate of exacerbations vs placebo and components
- Significantly improves lung function vs placebo and components
- Is generally well tolerated over 3 years with a lack of significant effect on systemic effects of steroids such as bone and eye disorders in COPD patients
- Led to increase in cases of pneumonia, but with no corresponding increase in mortality with SFC treatment

Calverley et al. NEJM 2007
Consequences of COPD exacerbations

- Increased Mortality
- Accelerated lung function decline
- Negative impact on quality of life
- Impact on symptoms and lung function
- Increased economic costs

EXACERBATIONS
A symptom based approach

- Smoking and aero-pollutant (dust) avoidance
- Yearly Flu vaccination, 5 yearly pneumococcal vaccination and regular exercise
- Exertional SOB - prn bronchodilators (SABA/SAMA)
- Fatigue + poor ET – reg bronchodilators (LABA and LAMA (*FEV1<60% predicted for Tiotropium))
- LRTI/bronchitis/AECOPD – Inhaled corticosteroids with LABA or LAMA (*FEV1<60% predicted)
- 2+ Hospitalisations/yr – triple therapy
COPD Phenotypes and treatment

• Mild disease (FEV1%pred >50%) - few Sx (SABA/SAMA)

• Mild disease (FEV1%pred >50%) - persisting Sx (LABA or LAMA) or 2+ exacerbations/yr (ICS/LABA)

• Mod-Sev disease (FEV1%pred ≤50%) - few Sx (ICS/LABA or LAMA)

• Mod-Sev disease (FEV1%pred ≤50%) - persisting Sx (ICS/LABA and LAMA) and 2+ exacerbations/yr (ICS/LABA and LAMA)
When to add the steroids

- ICS are needed when patients suffer recurrent exacerbations characterised by productive cough and SOB.
- ICS with LABA are superior to ICS alone and shown to improve lung function, quality of life and survival as do LAMA (TORCH/UPLIFT study).
- Oral steroids for 3-10 days are useful for exacerbations characterised by SOB with productive cough.
4. COPD - Beyond the airways

(Manage – future)
COPD - Beyond the airways

- Genetic factors
- Cigarette smoke
- Biomass fuel
- Lung cancer
- Peripheral lung inflammation
- "spill-over"
- Hypoxia
- Physical activity

- Skeletal muscle weakness
- Cachexia

- Systemic inflammation
  - Cytokines: IL-1β, IL-6, IL-18, TNFα
  - Acute phase proteins: CRP, SAA

- Cardiovascular diseases
  - IHD, CCF, hypertension

- Metabolic diseases
  - Diabetes
  - Metabolic syndrome
  - Obesity

- Bone disease
  - Osteoporosis
  - Osteopenia

- Depression
Beyond the airways

• Muscle fatigue, muscle weakness and cachexia (pulmonary rehab and optimised nutrition)
• Cardiovascular disease, stroke, CHF, pulmonary hypertension (aspirin, statin and β-blockers)
• Insulin resistance, metabolic syndrome, obesity (exercise, calorie restriction, wght loss)
• Osteoporosis (bisphosphonates)
Beyond the airways

- Future treatments will look to reduce [dynamic] hyperinflation measured as IC/TLC ratio rather than to use FEV$_1$ as a measure of outcome.

- Recent studies suggest that statins reduce hyperinflation and dilate small airways by reducing pulmonary inflammation, and improve endothelial function by reducing systemic inflammation (clinical trials underway).
COPD and lung cancer

• COPD increases the risk of lung cancer by 4-6 fold compared to smokers with normal lung function.
• 70-80% of lung cancer has pre-existing COPD
• 20-30% of deaths in COPD are from lung cancer
COPD overlap with lung cancer
Common pathogenic mechanisms and pathways in the development of COPD and lung cancer

Ian A Yang⁴, Vandana Relan, Casey M Wright, Morgan R Davidson,

Common pathogenic mechanisms and pathways in the development of COPD and lung cancer

Putative mechanism

Environmental toxins
(Cigarette smoke, air pollutants, carcinogens)

COPD

Epithelial–mesenchymal transition (EMT)
- TGFβ
- Wnt, Notch

Infection

Oxidative stress

↓ Angiogenesis

Ineffective repair

Lung cancer

Self-sustaining growth

Matrix degradation
- MMPs

Inflammation
- NF-κB
- STAT3
- IL-6
- Neutrophil elastase

Wound repair

Cell proliferation

Angiogenesis
- EGFR
- HIF
- VEGF
- nAChR

Evade immune surveillance

Limitless replication

↑ Angiogenesis

Underlying susceptibility:
Lung cancer gene associated with COPD: triple whammy or possible confounding effect? 2008

R.P. Young*, R.J. Hopkins*, B.A. Hay*, M.J. Epton†, P.N. Black* and G.D. Gamble*

**Loci from GWA studies**

**COPD (Lung Function)**
- 1q23-IL6R
- 5q33- ADAM19/HTR4
- 6p21-AGER
- 6q24- GPR126

**Lung Cancer**
- 1q21-CRP
- 5p15- CRR9/TERT
- 6p21-BAT3
- 6q24- RGS17§

**Overlapping Loci**

Chromosome 4q31 locus in COPD is also associated with lung cancer


2010

FAM13A locus in COPD is independently associated with lung cancer – evidence of a molecular genetic link between COPD and lung cancer

2011

Abstract: Recent genome-wide association studies have reported chromosome 4q22.1 is associated with lung function and COPD in a case-control study of current or former smokers with chronic obstructive pulmonary disease (COPD, n = 458), lung cancer (n = 454), or normal lung function and smoking history. Confirmed loci (rs7671167) confer a protective effect on smoking-related COPD risk. The effect was independent of smoking status at the 4q22.1 locus.
Lung cancer risk score: Very High Risk (6 or more)

In addition to smoking, the risk of lung cancer is further increased by:

- genetic factors
- how much you smoked
- age
- COPD.

Respiragene Test* identifies those at greatest risk based on the above factors.

Life-long Smoker – has on average a 1 in 10 (10%) lifetime chance of getting lung cancer.

Non-smoker – has on average a 1 in 200 (0.5%) lifetime chance of getting lung cancer.

Daily cigarette consumption pre- and post genetic testing

After genetic testing changes in cigs/day:
Overall 78% decreased cigs/day (blue), 13 (28%) Quit smoking, 2 lost to follow up, while 9 (20%) no change (orange) and 1 (2%) increased (red) consumption

* diagnosed Prostate cancer after testing)
CT screening for lung cancer

NLST trial (NEJM August, 2011)

- RCT of >50,000 current and former smokers in the US aged 55-74 yr and with 30+ pack year history
- Compared yearly CT screening with CXR screening over 3 years
- Showed a 20% reduction in lung cancer mortality
- Concerns remain over low pick up rates, costs and harms from radiation and unnecessary investigation of low risk smokers → need to better target high risk smoker
Diagnosis and management of COPD

- **Diagnose** - assess airflow limitation (spirometry, PEFR)
- **Assess** - symptoms (CAT and MRC score)
- **Assess** - risk of exacerbations (PHx of exacerbation)
- **Assess** - COPD comorbidities (anxiety/depression, muscle wasting/fatigue)
- **Assess** - COPD-related comorbidities (CHD/CHF, lung cancer, osteoporosis)
- **Manage** - reduce risk and reduce symptoms

**Diagnose** – spirometry

**Assess** – CAT or mMRC score

**Manage** – reduce Sx/exacerbations
New GOLD-defined patient groups

Poor spirometry (FEV\%pred\leq50\%) or 2+ exacerbations/yr (AB/pred/yr) but ET= manages hills ok Good QOL CAT<10

“Exacerbator” (wet and wheezy)

Reduced spirometry (FEV\%pred\geq50\%) or 0-1 exacerbation/yr (AB/pred/yr) but ET=manages hills ok Good QOL CAT<10

Mild (early)

Poor spirometry (FEV\%pred\leq50\%) or 2+ exacerbations/yr (AB/pred/yr) and ET≥ SOB up slight hills Poor QOL CAT\geq10

Severe (combined-www)

“Symptomatic” (weak and wheezy)

Reduced spirometry (FEV\%pred\geq50\%) or 0-1 exacerbation/yr (AB/pred/yr) and ET≥SOB up slight hills Poor QOL CAT\geq10

“Symptoms”† (mMRC or CAT score)

ICS/LABA or LAMA

SABA or SAMA prn

LABA or LAMA

ICS/LABA and LAMA

mMRC 0-1
CAT <10

mMRC \geq 2
CAT \geq 10

(Risk Classification of Airflow Limitation)

2 or more

Less than 2

RISK* (Exacerbation history)
Management of COPD - summary

At risk patients
- Spirometry
- Smoking cessation

Mild – Intermitant Sx
- CAT questionnaire
- Vaccinations
- Prn SABA

Mild – Persistant Sx
- Reg LABA or LAMA
- “Symptomatic”
  (weak and wheezy)

“Exacerbator”
(wet and wheezy)

“Infective exacerbators”

Mild – Persistant Sx
- LABA + ICS
- ± LAMA

Mod – Persisting Sx
- LABA + ICS
- ± LAMA

Significant Disability
- LTOT
- Volume reduction/valve surgery

Significant Co-morbidity
- CVS risk
- Lung cancer sx

Volume reduction/valve surgery
Lung cancer sx
Lung Health Clinic (Auckland)

For assessment of patients with breathlessness or suspected of asthma or COPD (especially those exposed to smoking or aero-pollutants).

For lung function testing, medication review, smoking cessation, inhaler technique, COPD unresponsive to treatment and lung cancer screening.

Associate Professor Robert Young,
Consultant Physician (FRACP, PhD)

Contact us: Ph 0800 789999 or 09 630 9967
or Fax 09 623 6456
or email: lunghealthclinic@adhb.govt.nz