Assessment of patient centred outcomes in COPD

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• Global Medical Expert; GSK*

* Financial conflict of interest
Lung Disease

- Expiratory Airflow limitation
- Over-inflation
- Dynamic hyperinflation
- V/Q mismatch

Breathlessness

- Exercise Limitation

Health Impairment

- Impaired Mood
- Sleep Disturbance

Cough

Exacerbations

Cytokines

- Muscle Wasting

Fatigue

Exercise Limitation

Unknown

Impaired Mood

V/Q mismatch
FEV$_1$ as a correlate of symptomatic outcomes

**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**
The simple question
– “How are you?”

- Very well
- Quite well
- OK
- Quite poor
- Very poor
Patients judge overall asthma severity using different criteria

Two patient clusters when judging asthma severity

These patients judge asthma severity only using symptoms

These patients judge asthma severity using 4 different factors

Barley & Jones ERJ 2005: 25: 671
Symptoms - the simple question: how bad is your COPD?

Patient’s answer to “how are you?” may be unreliable

- 75% have to stop even when walking at my own pace or walk slower than people of my age
- 60% have to stop every few minutes when walking on level ground
- Too breathless to leave the house

MRC Dyspnoea Scale

mMRC Dyspnoea Scale for Breathlessness

Grade 0  Breathless with strenuous exercise

Grade 1  Short of breath when hurrying on the level
  or walking up a slight hill

Grade 2  Walk slower than people of the same age on the level
  or stop for breath while walking at own pace on the level

Grade 3  Stop for breath after walking about 100 yards
  or after a few minutes on the level

Grade 4  Too breathless to leave the house
  or breathless when dressing or undressing
St George’s Respiratory Questionnaire (SGRQ) - examples of item weights

**Symptoms Section**

- I cough for several days of the week  
  Weight (mean ± sd): 63 ± 25

**Activity Section**

- I take a long time to have a wash  
  Weight (mean ± sd): 74 ± 27

**Impacts Section**

- I am not in control of my chest problem  
  Weight (mean ± sd): 90 ± 16
### COPD Assessment Test (CAT)

<table>
<thead>
<tr>
<th>Item</th>
<th>Score Options</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td>012345</td>
<td>I cough all the time</td>
</tr>
<tr>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>012345</td>
<td>My chest is completely full of phlegm (mucus)</td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td>012345</td>
<td>My chest feels very tight</td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>012345</td>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td>012345</td>
<td>I am very limited doing activities at home</td>
</tr>
</tbody>
</table>

**Two recent systematic reviews of CAT**

Gupta et al ERJ 2014; 44: 873-884  
Karloh et al Chest 2015; epub

Scoring range 0-40

Jones et al; Eur Respir J 2009; 34: 648–654
CAT vs SGRQ total in 4 Asian countries

Kwon et al. Chest 2013; 143: 703
CAT score

Walk slower than people of the same age on the level or stop for breath while walking at own pace on the level.

Jones et al. ERJ 2013, 42(3):647-54

mMRC vs CAT score

CAT: Medium impact

- COPD is one of the main problems in life
- Wake up with breathlessness most days
- Walk up 1 flight of stairs slowly
- Housework done slowly or with rests

CAT ≥ 10 is equivalent to mMRC Grade 1

- Short of breath when hurrying on the level or walking up a slight hill
- Walk slower than people of the same age on the level or stop for breath while walking at own pace on the level

Jones et al. BMC Pulmonary Medicine. 2011;11(1):42
CAT scores in clinical practice

*Kwon et al Chest 2013; 143:703-710
†Tsuda et al Respir Investig 2012;50:34-9
Relationship between CAT score and exacerbations in preceding year (prospectively measured in a routine clinic)

Kelly et al Respiration 2012;84:193–199
### Change in CAT score with exacerbations

<table>
<thead>
<tr>
<th></th>
<th>Stable median [range]</th>
<th>Exacerbation median [range]</th>
<th>Change median [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>With exacerbation (n=3 studies)</td>
<td>16.0 [15.8-17.2]</td>
<td>21.3 [20.7-22.4]</td>
<td>+6.1 [4.7-6.6]</td>
</tr>
</tbody>
</table>

Gupta et al Eur Respir J 2014; 44: 873-884
CAT and risk of moderate-severe exacerbation in patients with a history of a treated exacerbation in preceding year

Baseline CAT score 0-9
Baseline CAT score 10-19
Baseline CAT score 20-29
Baseline CAT score 30-39

p=0.001
Correlation between long-term change in FEV$_1$ and change in SGRQ score

Nagai et al Int J COPD 2015; 10: 745
Minimum clinically important difference (MCID) for the CAT

- Mapping onto SGRQ (MCID = 4)
  - CAT MCID = 1.6
  - Only works at a population level
  - (CAT scores don’t have decimals)

- Individual patient MCID
  - CAT MCID = 2
## Change in CAT score with rehabilitation

<table>
<thead>
<tr>
<th>Rehabilitation (n=4 studies)</th>
<th>Change median [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-2.9</td>
</tr>
<tr>
<td></td>
<td>[range -2.2 to -3.0]</td>
</tr>
</tbody>
</table>

### Improvement with rehabilitation

<table>
<thead>
<tr>
<th>CAT</th>
<th>Improvement with rehabilitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using MCID = 1.6</td>
<td>1.8 x MCID</td>
</tr>
<tr>
<td>Using MCID = 2</td>
<td>1.5 x MCID</td>
</tr>
</tbody>
</table>

### Improvement with rehabilitation

<table>
<thead>
<tr>
<th>CAT</th>
<th>Improvement with rehabilitation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGRQ</td>
<td>1.6 x MCID</td>
</tr>
<tr>
<td>CRQ</td>
<td>1.9 x MCID</td>
</tr>
</tbody>
</table>

* Lacasse et al 2009 Cochrane Review

Gupta et al Eur Respir J 2014; 44: 873-884
Comparison of responsiveness of SGRQ and CAT in response to pharmacological therapy

-6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6

Change in SGRQ

Umec/Vilanterol Salmeterol/Fluticasone

MCID

Change in CAT

Umec/Vilanterol Salmeterol/Fluticasone

MCID

MCID†

† Mapping from SGRQ

Singh et al BMC Pulm Med 2015;15:91

Odds Ratios for responder rates vs placebo calculated using different SGRQ scores for response threshold

40% greater odds of benefit compared to placebo

Estimate of efficacy is almost independent of the responder cutpoint

Jones et al ATS 2013 (Abstract)
Jones et al J COPDF 2017 (accepted for publication)
SGRQ responder analysis: ICS/LABA vs Triple Therapy (pooled data from 4 trials)

Odds ratio 1.6 (95% CI: 1.3, 2.0; p<0.001)

60% greater odds of a clinically significant improvement with Triple Therapy compared with ICS/LABA

Summary

• FEV$_1$ correlates poorly with
  – Dyspnoea, exercise capacity and health status
• Simple global questions e.g.: “How are you?”
  – May under-estimate severity
• mMRC dyspnoea scale
  – Too insensitive
• Health status questionnaires
  – SGRQ – complex and time consuming
  – CAT – simple and designed for routine use
• Responder analysis
  – Largely independent of the cutpoint chosen
  – Provides meaningful measurement for clinicians