Asthma and COPD – what’s new?

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February 2014
Ben Creagh-Brown

- Royal Surrey County Hospital
  Clinic Thursday pm
  Secretary - Jen Pritchard

- Nuffield Hospital, Guildford
  Clinic Thursday am
  Secretary - Sally Groves
Declarations of interest

• Travel expenses from Napp.
• Honoraria from GSK and Novartis for giving talks.
Overview

• Asthma
  1. Recent guidance
  2. Assessing control
  3. Current treatment options
  4. Newer therapies
  5. Treatments in development
  6. When to refer

• COPD
  1. Recent guidance
  2. Current treatment
  3. Controversies
    1. Spiriva
    2. ICS
    3. Cardiac co-morbidities
  4. Newer therapies
  5. Future therapies
  6. When to refer

Brief discussion of four cases
Asthma

British Guideline on the Management of Asthma
A national clinical guideline

May 2008
Revised January 2012

Updated 2012

www.brit-thoracic.org.uk/

www.ginasthma.org/
Asthma is still a problem

- 5.4 million people are on treatment for asthma in the UK
- National variability - 5-fold difference between PCT areas in the number of emergency admissions in adults
- International variability - Premature mortality from asthma was 1.5 times as high in the UK than in the rest of Europe in 2008 (~1000/yr, 90% considered preventable)
What are we aiming for with asthma control?

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Controlled (All of the following)</th>
<th>Partly Controlled (Any measure presented)</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>None (twice or less/week)</td>
<td>More than twice/week</td>
<td>Three or more features of partly controlled asthma*†</td>
</tr>
<tr>
<td>Limitation of activities</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Nocturnal symptoms/awaking</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Need for reliever/rescue inhaler</td>
<td>None (twice or less/week)</td>
<td>More than twice/week</td>
<td></td>
</tr>
<tr>
<td>Lung function (PEF or FEV₁)†</td>
<td>Normal</td>
<td>&lt; 80% predicted or personal best (if known)</td>
<td></td>
</tr>
</tbody>
</table>

The goal of management is for people to be free from symptoms and able to lead a normal, active life.
Asthma education. Environmental control.
(If step-up treatment is being considered for poor symptom control, first check inhaler technique, check adherence, and confirm symptoms are due to asthma.)

<table>
<thead>
<tr>
<th>As needed rapid-acting $\beta_2$-agonist</th>
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<tbody>
<tr>
<td><strong>Controller options</strong>*</td>
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</tr>
<tr>
<td>Select one</td>
<td>Select one</td>
</tr>
<tr>
<td>Low-dose inhaled ICS*</td>
<td>Low-dose ICS plus long-acting $\beta_2$-agonist</td>
</tr>
<tr>
<td>Leukotriene modifier**</td>
<td>Medium-or high-dose ICS</td>
</tr>
<tr>
<td>Low-dose ICS plus leukotriene modifier</td>
<td>Leukotriene modifier</td>
</tr>
<tr>
<td>Low-dose ICS plus sustained release theophylline</td>
<td>Sustained release theophylline</td>
</tr>
</tbody>
</table>

To Step 3 treatment, select one or more
To Step 4 treatment, add either

Oral glucocorticosteroid (lowest dose)
Anti-IgE treatment
- Step-up to gain control
- Step-down...
Why step-down?

- Dose-response curve means benefits of increased ICS dose may be minimal
- Side-effects – dysphonia, candida, purpura, skin thinning – dose response ≥400mcg/day
- Adrenal suppression ≥800mcg/day
- Osteoporosis occurs ≥800mcg/day
- Cost...

Combination inhaled corticosteroid and long acting bronchodilator (ICS/LABA) inhalers are now the most expensive drug class for the NHS.

Brown J. Seretide® is the most expensive drug prescribed nationally; but is it the most cost-effective combination inhaler on the market? NHS Prescriber 9, October 2010
Cost of treatment...

- Symbicort 400 ii bd £76
- Seretide 250 ii bd £59
- Seretide 500 i bd £41
- Flutiform 250 ii bd £46
- Symbicort 200 ii bd £38
- Seretide 125 ii bd £35
- Flutiform 125 ii bd £29
- Fostair 100 ii bd £29
- Symbicort 200 i bd £19
- Seretide 50 ii bd £18
- Flutiform 50 ii bd £18

Relvar Ellipta 184/22mcg £38.87
Relvar Ellipta 92/22mcg £27.80
Is it safe to step-down?

- RCT Scotland: 259 adult asthmatics, ≥800mcg
- Well controlled
- Step down (50%↓) vs. sham step down
- No difference in exacerbation rates

Adopting a stepdown approach to the use of high dose corticosteroids in patients with chronic stable asthma can lead to a significant reduction in the daily dose of inhaled corticosteroids without compromising asthma control

Hawkins et al. *BMJ* 2003;326:1115
Assessing asthma control

Clinicians frequently over-estimate asthma control and under-estimate the impact of asthma on patients’ lives

• Ask the patient
  – Unstructured – how are you?
  – Structured: RCP3, ACQ, ACT
• Measure PEF/FEV1
• FeNO
• Inhaler usage - heavy or increasing use of SABA is associated with asthma death

Prim Care Resp J 2009; 18(2): 83-88
RCP 3 questions – assess asthma control

1. Have you had difficulty **sleeping** because of asthma symptoms (including cough)?

2. Have you had your **usual asthma symptoms** during the day (cough, wheeze, chest tightness or breathlessness)?

3. Has your asthma interfered with your **usual activities** (e.g. housework, work, school, etc)?
Titrating the dose of ICS

Comparison of Physician-, Biomarker-, and Symptom-Based Strategies for Adjustment of Inhaled Corticosteroid Therapy in Adults With Asthma
The BASALT Randomized Controlled Trial

JAMA. 2012;308(10):987-997
BASALT

• 342 pts with mild-moderate asthma
• Randomised to 3 groups: (9 months)
  – symptom-based adjustment (SBA) of inhaled corticosteroids
  – biomarker-based adjustment (BBA) FeNO
  – physician assessment–based adjustment (PABA) based on NHLI guidelines
• The primary outcome was time to first treatment failure, a clinically important worsening of asthma
• Neither PABA nor BBA were superior to SBA

Newer treatments for asthma

1. Using symbicort - SMART
2. Xolair (Omalizumab)
3. (Bronchial thermoplasty)
4. Fostair (MART) and Flutiform
5. Relvar Ellipta
6. Spiriva(!)
1. Symbicort SMART (budesonide/formoterol)

• “In selected adult patients at step 3* who are poorly controlled or in selected adult patients at step 2, the use of budesonide/formoterol in a single inhaler as rescue medication instead of a short-acting β2 agonist, in addition to its regular use as controller therapy has been shown to be an effective treatment regime.”

* Step 3 = ICS/LABA; Step 2 = ICS
Symbicort SMART

Pro
• Convenient
• May offer lower ICS dosing, fewer exacerbations and fewer hospital admissions

Con
• May not adequately suppress airway inflammation
• Concerns about the supporting evidence
• Requires good patient understanding
• Associated with poor control in trials (17%)
2. Xolair (omalizumab)

Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201)

Issued: April 2013

1. Allergy to aeroallergen (SPT/RAST)
2. IgE 75-1000 IU/ml; pt can’t be too heavy
3. FEV1<80%
4. Optimal Rx plus >= 4 courses of OCS/y
5. Frequent symptoms
3. Bronchial thermoplasty

- Evidence of efficacy
- Specialist centres

Bronchial thermoplasty for severe asthma

Issued: January 2012

NICE interventional procedure guidance 419
guidance.nice.org.uk/ipg419
4. Fostair

- Beclomethasone/Formoterol
- 100mcg/6mcg
- 100mcg = 200-250mcg BDP equivalent (extrafine)
- 1-2 puffs BD, or 1-2 puffs BD and PRN (MART)
- Cheaper (£29) than Seretide (£35-£60)
- RCT evidence of non-inferiority

Flutiform

- Fluticasone/Formoterol
  - 50/5 mcg (£18)
  - 125/5 mcg
  - 250/10 mcg (£46)
- 2 puffs BD
- RCT evidence of non-inferiority

Flutiform vs Seretide
Flutiform vs Symbicort

BMC Pulm Med 2011;11:28
ERS abstract; 2011 Sep 24 - 28
Flutiform® inhaler for Asthma

The network were informed that Flutiform® is a recently launched combination inhaler and although recently launched it contains two established ingredients (Fluticasone & Formoterol). NICE guidance recommends that the least costly device that is suitable for an individual patient should be used if a combination inhaler is required. The network members concurred that Flutiform® is a cost effective alternative combination ICS/LABA. The network noted the price differential between the various combination ICS/LABA inhalers.

GP colleagues noted that if a spacer device is indicated for a patient, then the Aerochamber Plus® should be used as per the license (i.e. regular treatment of asthma where the use of a combination inhaled ICS/LABA is appropriate – currently not SMART)

The network members discussed possible solutions to support implementation and requested that the author of the review discuss this with the manufacturers of Flutiform®.

Recommendations:
The Network supported the use of Flutiform® (in line with the license) as a first line alternative to Seretide Evohaler® and Symbicort Turbohaler® in adults and children over 12 years where LABA/ICS is indicated as per BTS and NHS Surrey Asthma Guidelines. (NB 250mcg strength licensed only from 18 years).

Individual practices may consider actively switching patients on Seretide Evohaler® to an appropriate dose of Flutiform® MDI or to review patients when it is clinically appropriate to step up or step down the dose of ICS/LABA.
Medicines Management of Asthma in Adults and Adolescents over 12 years

Step up Step down: Aim to achieve early control, step up treatment as necessary and down when control is good.
Review patients using one or more β2 agonist devices monthly or using β2 agonist or symptomatic three times weekly or more.

Step 1 - Inhaled Short Acting β2 Agonist (SABA) as required
Short term reliever therapy
1st Choice: Salbutamol MDI 2 puffs pm + spacer (Aerochamber Plus®)
Alternative device: Easyhaler Salbutamol® 100 2 puffs pm

 Achieve early control and maintain by stepping up treatment as necessary. Step down when control is good.

Step 2 - Add Inhaled Corticosteroid (ICS) 200-800mcg/day *
Start at a dose appropriate to the initial severity.
Recommended starting dose 400mcg BDP© per day
Clenil Modulate® 100 MDI 2 puffs bd
or Qvar® 50 MDI 2 puffs bd
+ spacer (eg Aerocamber Plus®)
Alternative devices: Easyhaler Beclometasone® 200 1 puff bd
Qvar Easi-Breathe® 50 2 puffs bd
*BDP equivalent see overleaf for dose equivalences

Before starting new therapy check diagnosis, compliance with current medication and inhaler technique. Eliminate trigger factors including rhinitis.
Consider adding ICS if the patient:
- has had asthma exacerbations in the last 2 years
- is using a β2 agonist or is symptomatic 3 times weekly or more
- is waking one night per week with asthma
Qvar® contains extra fine particles, adjust dose as necessary.
For information on steroids and dose equivalences see overleaf
Titrade to the lowest dose at which control is maintained

Step 3 - Add Inhaled Long Acting β2 Agonist (LABA) to ICS
Consider LABA before going above 400mcg BDP/day
Starting doses when using combination ICS/LABA:
Flutiform® 50 MDI or Seretide Evohaler® 50 2 puffs bd + spacer (eg Aerocamber Plus®)
or Serotide Turbohaler® 100 1 puff bd
or Seretide Accuhaler® 100 1 puff bd

NO RESPONSE TO LABA - stop and increase steroid dose to 800mcg BDP/day
RESPONSE TO LABA but control still suboptimal - increase dose to 800mcg/day
Flutiform® 125 MDI or Seretide Evohaler® 125 2 puffs bd + spacer
or Serotide Turbohaler® 200 2 puffs bd (SMART regime in suitable patients)
or Seretide Accuhaler® 250 1 puff bd
Titrade the dose to the lowest dose at which effective control of asthma maintained
Control still inadequate: Montelukast 10mg nocte or Uniphyllin® 200mg bd
If there is no improvement after 4 weeks - review therapeutic range and dose

Step 4 - Consider Increasing ICS to 2000mcg/day (use spacer with high dose ICS)
Flutiform® 250 MDI (in adults over 18 years only)
or Seretide Evohaler® 250 2 puffs bd + spacer (Aerochamber Plus®)
or Seretide Accuhaler® 500 1 puff bd or Serotide Turbohaler® 400 2 puffs bd
Review at 4 weekly intervals. If still stable after 12 weeks consider stepping down.
Take individual patient factors into account eg winter months or allergy season
Consider referral to a specialist if on high dose ICS for more than 6 months

Symbicort Maintenance And Reliever Therapy (SMART®)
Symbicort 200/6® can be used as a rescue medication instead of SABA in addition to its regular use as a preventer at Step 3, in adults over 18 years.1, 2
Check BNF for dosing.
Review if rescue dose is used more than once daily on a regular basis. Educate suitable patients who can self manage.
http://www.medicines.org.uk

Step down when control is good.
Dose reduction should be slow to avoid deterioration.
Consider reduction every 3 months, decreasing the dose by approximately 25-50% each time.
See overleaf for more information on stepping down.
5. Relvar Ellipta

- A new once daily ICS/LABA (24-hour efficacy)
- Fluticasone *furoate* / Vilanterol
- Two strengths (92/22 and 184/22mcg)
- Studied in asthma (and COPD)
- As efficaceous as seretide
- Safe, without increased risk of pneumonia*
- New device
Asthma treatments in development

• Inhaled
  – LAMA/LABA (Ultibro)
  – Pitrakinra (IL-4 antagonist) Phase II trial
  – Tacrolimus
  – Tiotropium

• Injections
  – ...umabs, vs. IL-5, IL-4R, IL-13(R)

• Tablets
  • Mast cell TK-inhibitor
  • PDE4 inhibitors

http://www.ukmi.nhs.uk/applications/NDO/
When to refer

- Diagnosis unclear
- Unexpected clinical findings (ie crackles, clubbing, cyanosis, cardiac disease)
- Unexplained restrictive spirometry
- Suspected occupational asthma
- Persistent non-variable breathlessness
- Monophonic wheeze or stridor
- Prominent systemic features (myalgia, fever, weight loss)
- Chronic sputum production
- CXR shadowing
- Marked blood eosinophilia (> 1 x 10⁹/l)
- Poor response to asthma treatment
- Severe asthma exacerbation

Requiring frequent OCS
Asthma Case 1

• 25-year-old woman
• Asthma with night-time waking and some limitations to exercise
• Currently on Seretide 125 2 puffs BD

Options:

a) Seretide 250, 2 puffs BD
b) Relvar 184/22, 1 puff OD
c) Flutiform 250, 2 puffs BD
d) Montelukast
e) Theophylline
f) No change
Asthma Case 2

- 25-year-old woman
- Asthma
- No symptoms
- Currently on Seretide 250 2 puffs BD

Options:

a) Seretide 125, 2 puffs BD
b) Relvar 92/22, 1 puff OD
c) Flutiform 125, 2 puffs BD
d) No change
Any questions on asthma?
Differential Diagnosis: COPD and Asthma

COPD

• Onset in mid-life
• Symptoms slowly progressive
• Long smoking history

ASTHMA

• Onset early in life (often childhood)
• Symptoms vary from day to day
• Symptoms worse at night/early morning
• Allergy, rhinitis, and/or eczema also present
• Family history of asthma
COPD
Often treated like this:

1. SABA
2. (LABA)
3. LABA/ICS or LAMA
4. LABA/ICS and LAMA
5. + adjuncts theophylline / carbocysteine / antibiotics / OCS

Simple but likely excessive use of ICS

(NB: OCS not normally recommended)
BTS/NICE 2010

In people with stable COPD who remain breathless or have exacerbations despite use of short-acting bronchodilators as required, offer the following as maintenance therapy:

• if FEV$_1$ ≥ 50% predicted: either LABA or LAMA (can have ICS/LABA if remains symptomatic)
• if FEV$_1$ < 50% predicted: either LABA/ICS, or LAMA
GOLD 2013 added even more

<table>
<thead>
<tr>
<th>Patient Category C</th>
<th>Patient Category D</th>
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<tr>
<td>HIGH RISK, LESS SYMPTOMS</td>
<td>HIGH RISK, MORE SYMPTOMS</td>
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<tr>
<td><strong>GOLD</strong></td>
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<tr>
<td>3 or 4</td>
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<tr>
<td><strong>Exacerbations</strong></td>
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<tr>
<td>≥2/yr</td>
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<tr>
<td><strong>mMRC</strong></td>
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<tr>
<td>0-1</td>
<td>≥2</td>
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<tr>
<td><strong>CAT score</strong></td>
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<td>≥10</td>
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<tr>
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</tr>
<tr>
<td><strong>GOLD</strong></td>
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<td>1 or 2</td>
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In patients with FEV₁/FVC < 0.70:

GOLD 1: Mild \( \text{FEV}_1 \geq 80\% \text{ predicted} \)

GOLD 2: Moderate \( 50\% \leq \text{FEV}_1 < 80\% \text{ predicted} \)

GOLD 3: Severe \( 30\% \leq \text{FEV}_1 < 50\% \text{ predicted} \)

GOLD 4: Very Severe \( \text{FEV}_1 < 30\% \text{ predicted} \)

PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY)

mMRC Grade 0. I only get breathless with strenuous exercise. □

mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill. □

mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level. □

mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level. □

mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing. □
In patients with FEV₁/FVC < 0.70:

- **GOLD 1**: Mild
  - FEV₁ ≥ 80% predicted

- **GOLD 2**: Moderate
  - 50% ≤ FEV₁ < 80% predicted

- **GOLD 3**: Severe
  - 30% ≤ FEV₁ < 50% predicted

- **GOLD 4**: Very Severe
  - FEV₁ < 30% predicted

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<td>Patient group</td>
<td>First choice</td>
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<td>-----------------------</td>
<td>--------------------------------------------------------</td>
</tr>
<tr>
<td>A Low risk, less symptoms</td>
<td>Short-acting anticholinergic prn or Short-acting $\beta_2$-agonist prn</td>
</tr>
<tr>
<td>B Low risk, more symptoms</td>
<td>Long-acting anticholinergic or Long-acting $\beta_2$-agonist</td>
</tr>
<tr>
<td>C Higher risk, less symptoms</td>
<td>Inhaled corticosteroid + long-acting $\beta_2$-agonist or Long-acting anticholinergic</td>
</tr>
<tr>
<td>D Higher risk, more symptoms</td>
<td>Inhaled corticosteroid + long-acting $\beta_2$-agonist or Long-acting anticholinergic</td>
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Important non-inhaled interventions

- Smoking cessation
- Pulmonary rehabilitation; promotion of exercise
- Vaccines
- Self-management plans; with spare ABx/Steroids for IECOPD
- Oxygen alerts / Steroid cards
- Treat cardiac co-morbidities
Current controversies

1. Tiotropium may be harmful, particularly the respimat
2. ICS are probably overused, may be associated with harm
3. Cardiac co-morbidities and their treatment
1. Spiriva/tiotropium and risk of harm

• 2008 FDA warning following MA of 29 RCTs show increased mortality.
• UPLIFT study (largest single RCT) showed no such increased risk, but excluded those at high CV risk. Improved mortality vs. placebo.
• 2011 SR/MA of all Respimat COPD studies – 50% increased CV death.
• Others corroborate these findings.
• “Level 1 scientific evidence that tiotropium Respimat increases the risk of cardiovascular and all-cause mortality”.

Thorax. 2013 Jan;68(1):5-7
Autumn 2013

- RCT 17,000 pts
- Respimat 2.5mcg and 5mcg vs. handihaler
- Included CV patients
- No difference in safety or efficacy
- But no control group and study funded by BI
- Editorialist CoI

- Primary Care database (Holland)
- COPD and tiotropium
- Compared mortality, correcting for known confounders
- Excess mortality (27%) with respimat vs. handihaler

Tiotropium Respimat Inhaler and the Risk of Death in COPD

Robert A. Wise, M.D., Antonio Anzueto, M.D., Daniel Cotton, M.S., Ronald Dahl, M.D., Theresa Devins, Dr.Ph., Bernd Disse, M.D., Daniel Dusser, M.D., Elizabeth Joseph, M.P.H., Sabine Kattenbeck, Ph.D., Michael Koenen-Bergmann, M.D., Gordon Pledger, Ph.D., and Peter Calverley, D.Sc., for the TIOSPIR Investigators


Use of tiotropium Respimat Soft Mist Inhaler versus HandiHaler and mortality in patients with COPD

Katia M.C. Verhamme¹, Ana Afonso¹, Silvana Romio¹, Bruno C. Stricker², Guy G.O. Brusselle²,³ and Miriam C.J.M. Sturkenboom¹,²

Eur Respir J. 2013 Sep;42(3):606-15
2. Excessive use of ICS in COPD

- Guideline recommendations for the use of ICS in COPD are largely based on their preventive effect on exacerbations – although evidence is mixed
- No evidence of improved mortality; limited evidence of slowing FEV$_1$ decline; insignificant improvement in HRQoL
- Main risk – 70% increase in the rate of hospitalisation for pneumonia.
- “The indiscriminate use of ICS in COPD may expose patients to an unnecessary increase in the risk of side-effects such as pneumonia, osteoporosis, diabetes and cataracts, while wasting healthcare spending and potentially diverting attention from other more appropriate forms of management such as pulmonary rehabilitation and maximal bronchodilator use.”
3. Cardiac co-morbidities and COPD

- Commonly co-exist with COPD: IHD, AF, HT and heart failure
- Treatment including beta-blockers should be the same (β-1 selective: atenolol, bisoprolol, metoprolol, nebivolol) but often isn’t (BNF)
- CV death is the commonest cause of death in COPD and potentially treating co-morbidities will improve prognosis more than any COPD treatment!
Benefits of β-blockers

1. Treatment with βB may reduce the risk of exacerbations and improve survival in patients with COPD
   
   Arch Intern Med. 2010;170(10):880-887

2. Improved mortality in those with COPD who have an MI and are treated with β-blockers.
   
   BMJ 2013;347:f6650

3. βB may reduce mortality and AECOPD when added to established therapy, independently of overt cardiovascular disease and cardiac drugs
   
   BMJ 2011;342:d2549

4. The use of βB by inpatients with AECOPD is well tolerated and may be associated with reduced mortality
   
   Thorax 2008;63:301–305
Newer treatments for COPD

1. New LABA
   - Onbrez, Indacaterol
2. New LAMAs
   - Eklira, Aclidinium
   - Seebri, Glycopyrronium
3. New LABA/LAMA - Ultibro
4. New once daily ICS/LABA = Revlar
5. (Daxas, roflumilast, Mucolytics, Antibiotics)
1. Onbrez, Indacaterol

- Once daily LABA
- £29
- Evidence of
  - Non-inferiority to tiotropium (different class of drug but similar use)
  - Superiority to BD salmeterol
  - Superiority to BD formoterol

Thorax 2010;65:473e479
AJRCCM 2010; 182:155–162
ERJ 2011; 37: 273–279
2. New LAMAs

- Spiriva (tiotropium) was the only LAMA, now there are options
- They *may* be more effective
- They *may* be safer
- They *are* cheaper
Eklira (Aclidinium)

• Twice daily LAMA 400mcg
• £28
• Good things:
  – Good device
  – Best improvement in SGRQ (vs. Placebo)
  – Few side-effects and possibly no CV s/e
• Bad things:
  – No adequate trials vs. competitors
Seebri (Glycopyrronium)

- Once daily LAMA
- £28 (compared with spiriva £33)
- Evidence of non-inferiority to tiotropium
Due for review ...

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(Unless new published evidence becomes available before this date OR there is new published national guidance e.g. NICE)

Recommendations:
- Glycopyrronium (Seebri Breezhaler®) to be the first line LAMA of choice on the basis of evidence and cost effectiveness.
- Aclidinium (Eklira Genuair®) can be considered as an alternative device for patients who are unable to use the Seebri Breezhaler® / Spiriva Handihaler® devices
- Tiotropium Respimat® should no longer be recommended due to increasing reports of cardiovascular side effects and will be given a BLACK status on the prescribing advisory database.
3. Ultibro breezhaler

• Once daily LABA/LAMA (indacaterol and glycopyrronium bromide)
• Advantages of both onbrez and seebri in one package
• Costs £44
• Most suitable for patients with preserved lung function but very symptomatic
• Compared to individual constituents, spiriva or seretide, or placebo – all showed advantages of Ultibro
4. Relvar Ellipta

- A new once daily ICS/LABA (24-hour efficacy)
- Fluticasone \textit{furoate} / Vilanterol
- Two strengths (92/22 and 184/22mcg)
- Studied in asthma (and COPD)
- As efficaceous as seretide
- Safe, without increased risk of pneumonia*
- New device
COPD treatments in development

• Inhalers
  – Combination ICS/LABA/LAMA
  – More LABA/LAMA
  – Pan-selectin antagonist
  – Singel molucule LABA/LAMA
  – PDE3&4 inhibitor
When to refer COPD patients?

1. Diagnostic uncertainty
2. Suspected severe COPD
3. The patient requests a second opinion
4. Onset of cor pulmonale
5. Assessment for oxygen therapy, long-term nebuliser therapy or oral corticosteroid therapy
6. Bullous lung disease
7. A rapid decline in FEV$_1$
8. Assessment for pulmonary rehabilitation, lung volume reduction surgery or lung transplantation
9. Dysfunctional breathing
10. Onset of symptoms under 40 years or a family history of alpha-1 antitrypsin deficiency

NICE 2010
COPD Case 1

- 65-year-old woman
- COPD, ex-smoker
- 1 exacerbation in past year
- FEV$_1$ 60% predicted
- Complaining of excessive breathlessness
- Currently on ‘blue and brown’

Options:
- a) Relvar
- b) Ultibro
- c) LAMA
- d) LABA
COPD Case 2

- 65-year-old woman
- COPD, ex-smoker
- No exacerbations in past year
- SOB on walking up hills
- FEV\textsubscript{1} 65% predicted
- Currently on Seretide 250 2puffs BD

Options:

a) Change to LABA or LAMA
b) Add LAMA
c) No change
Summary

1. Increasing options for inhaled therapies for asthma and COPD
2. Reflected in increasing complexity of guidelines
3. Developments likely to offer real advantages
4. Allows more appropriate and effective treatment
ASTHMA
- The right amount of ICS
- Maybe no LABA
- Never LABA alone
- Rarely LT OCS

COPD
- Maximal LABA/LAMA
- Maybe no ICS
- Never ICS alone
- Hopefully never on LT OCS
Many thanks for listening

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ICS/LABA and licenses for COPD

• Initially FEV1<40%, then <50% and now <70% for Relvar.
• The only licensed formulation of seretide for COPD is seretide accuhaler 500, one BD.
• By contrast, the lower dose of ICS/LABA in Relvar has the COPD license