Responsible Respiratory Prescribing

Dr Vincent Mak
Consultant Physician in Respiratory Integrated Care
Imperial College Healthcare and Central London Community Healthcare NHS Trust

Respiratory Clinical Leadership Group

Sep 2014

Disclosures for Dr Vincent Mak

<table>
<thead>
<tr>
<th>Category</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Support/P.I.</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Employee</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Consultant</td>
<td>Secondary Care Consultant in Primary Care</td>
</tr>
<tr>
<td>Major Stockholder</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Speakers Bureau</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Honoraria</td>
<td>AZ, GSK, Boehringer. Almiral, Novartis</td>
</tr>
<tr>
<td>Scientific Advisory Board</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
</tbody>
</table>

Presentation includes discussion of the following off-label use of a drug or medical device: Nil
Responsible Prescribing should be based on:

- Evidence-Based Efficacy (Grade A)
- Safety (primum non nocere)
- Value (cost effectiveness)

"clinicians will need to accept that they are responsible for the stewardship of resources and not just their use"
Sir Muir Gray BMJ Oct 6 2012

Value Framework

Value = Health Outcomes / Cost of delivering Outcomes

Porter ME; Lee TH NEJM 2010;363:2477-2481; 2481-2483
RIGHT CARE

- Do the right thing
- Do the right thing right
- Doing the right thing right first time should deliver quality and value

ADDING VALUE by RIGHT CARE

- High Value
  - Low Value
  - Added value from doing things right (quality improvement)
- High Value
  - Low Value
  - Added value from doing the right things (making the right decisions)
To understand VALUE – you have to know COST
Awareness of respiratory inhaler costs in HCPs

Survey of healthcare professionals by creating an online SurveyMonkey questionnaire concerning the costs of some commonly prescribed inhalers.

Respondents were able to click on an approximate of range for costs for one month’s treatment at the normal recommended dosage (choice of 5).

We also asked about awareness of evidence for the effective use of metered dose inhalers (MDIs) by patients and HCPs.

The survey was disseminated by email from various community and hospital databases within NHS London and beyond, especially to those with an interest in respiratory care.

RESULTS

- We had 1274 respondents
  
<table>
<thead>
<tr>
<th></th>
<th>N= 1274</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctors</td>
<td>21%</td>
</tr>
<tr>
<td>Nurses</td>
<td>38%</td>
</tr>
<tr>
<td>Pharmacists</td>
<td>21%</td>
</tr>
<tr>
<td>AHPs</td>
<td>15%</td>
</tr>
</tbody>
</table>

- 70% had a respiratory interest
- 89% were clinicians
RESULTS 2

- Overall, the correct price range was identified by fewer than 50% of respondents (see table). Having a respiratory interest or having attended a London Respiratory Team event were more likely to choose the correct price range.

- The correct price range for the most expensive and most commonly prescribed combination inhaler had the second lowest correct responses (36% correct)

What are the top 5 costliest drugs in the NHS (Mar 2014)?

- **5. Sitagliptin 100mg** - €89 million/yr
- **4. Seretide 500 accuhaler** - €122 million/yr
- **3. Symbicort 200** - €130 million/yr
- **2. Tiotropium** - €183 million/yr
- **1. Seretide 250 evohaler** - €190 million/yr

Thus, of the top 5 costliest drugs to the NHS currently, 4 ARE RESPIRATORY INHALERS

Total for high potency Seretide approx €330 million/yr

Source: [www.drugtariff.co.uk](http://www.drugtariff.co.uk) = last accessed Sep 2014
Who is prescribing high dose ICS?

Variation Between North of England Clinical Commissioning Groups in Spending on Seretide®, Symbicort®, Foradil® and Flutiform® (Quarter to June 2013).
Who is prescribing high dose ICS?

How are you doing in the Netherlands?
Medicines as % of Health Expenditure

1.12 Expenditure on pharmaceuticals dispensed by pharmacies and general practitioners as a share of the total expenditure on health care in 2012

Source: Dutch Foundation for Pharmaceutical Statistics (SFK) 2013

Medicines cost per capita

1.11 Per capita expenditure on medicines dispensed by pharmacies and general practitioners in 2012 (in €)

Source: Dutch Foundation for Pharmaceutical Statistics (SFK) 2013
What are the top 5 costliest drugs in the NHS (Mar 2014)?

- 5. Sitagliptin 100mg - €89 million/yr
- 4. Seretide 500 accuhaler - €122 million/yr
- 3. Symbicort 200 - €130 million/yr
- 2. Tiotropium - €183 million/yr
- 1. Seretide 250 evohaler - €190 million/yr

Thus, of the top 5 costliest drugs to the NHS currently, 4 ARE RESPIRATORY INHALERS

Total population of England 53 million

Source: www.drugtariff.co.uk = last accessed Sep 2014

What were the top 5 costliest drugs in the Netherlands in 2013?

- 5. Metoprolol - €50 million/yr
- 4. Rosuvastatin - €61 million/yr
- 3. Formoterol+Bud/Bec - €83 million/yr
- 2. Tiotropium - €94 million/yr
- 1. Seretide - €108 million/yr

Thus, the top 3 costliest drugs to the Netherlands currently ARE RESPIRATORY INHALERS

Total population 17 million

Source: Dutch Foundation for Pharmaceutical Statistics (SFK) 2013
Are we doing the right thing?

COPD London Respiratory Team Value Pyramid - Cost/QALY

- Telehealth: £92000/QALY
- Long term Oxygen Therapy: £11-16000/QALY
- LABA: £5-8000/QALY
- Tiotropium/LAMA: £7000/QALY
- Pulmonary Rehabilitation: £2000-8000/QALY
- Stop Smoking Support with pharmacotherapy: £2000/QALY
- Flu vaccination? £1000/QALY in “at risk” population
Smoking prevalence in COPD
TORCH, Uplift Studies and POET-COPD

Current smoker — no. (%) 658 (43) 653 (43) 661 (43) 660 (43)

Current smoker (%) 29.3 29.9

Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD

Current smoker (%) 48.0 48.3

London Respiratory Team
Doing the right thing?

Trends in Prescribing of and Spending on Nicotine Replacement Therapy on an FP10 prescription form in England

N.B. Prior to April 2013 prescriptions the data only relates to prescribing in GP practices

Doing the right thing 2?

Trends in Prescribing of and Spending on Varenicline on an FP10 prescription form in England

N.B. Prior to April 2013 prescriptions the data only relates to prescribing in GP practices
Why commissioners should care about smoking …

- For every 1% increase in prevalence of smoking in your COPD population there is a 1% increase in COPD admission rates.

- For every 1% increase in prevalence of smoking in your asthma population there is a 1% increase in asthma admission rates.

Expenditure on smoking cessation products in Netherlands 2013: €9 million

Source: SFK 2013
Pulmonary Rehabilitation
‘Breathe Better, Feel Good, Do More’

High Value Care in COPD

Evidence Based Prescribing?
Does this mean majority of asthmatics are at Step 4+ of BTS guidelines?

UK COPD NICE Guidance
Evidence of Overuse of Inhaled Corticosteroids in COPD

De la Rosa et al. ERJ 2011: P4627

<table>
<thead>
<tr>
<th></th>
<th>GOLD I (n=46)</th>
<th>GOLD II (n=129)</th>
<th>GOLD III (n=71)</th>
<th>GOLD IV (n=88)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABA (%)</td>
<td>37</td>
<td>35.7</td>
<td>41.3</td>
<td>87.5</td>
<td>28.1</td>
</tr>
<tr>
<td>LABA (%)</td>
<td>37</td>
<td>57.4</td>
<td>81.7</td>
<td>87.5</td>
<td>41.7</td>
</tr>
<tr>
<td>ICS (%)</td>
<td>47.5</td>
<td>61.2</td>
<td>80.3</td>
<td>100</td>
<td>44.5</td>
</tr>
<tr>
<td>Combination (%)</td>
<td>32.6</td>
<td>43.4</td>
<td>67.6</td>
<td>87.5</td>
<td>32</td>
</tr>
<tr>
<td>ICS/LABA (%)</td>
<td>26.1</td>
<td>25.6</td>
<td>32.4</td>
<td>25</td>
<td>21.6</td>
</tr>
<tr>
<td>Tiolbudesonide (%)</td>
<td>17.4</td>
<td>31</td>
<td>46.5</td>
<td>62.5</td>
<td>35.9</td>
</tr>
<tr>
<td>tiotropium (%)</td>
<td>-</td>
<td>3.1</td>
<td>8.4</td>
<td>25</td>
<td>1.8</td>
</tr>
<tr>
<td>Long-term o2 (%)</td>
<td>-</td>
<td>-</td>
<td>1.4</td>
<td>12.5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Evidence from UK

Combination inhalers increase COPD admissions?

Harries T et al. Primary Care Respiratory Journal: doi: 10.1038/npjpcrm.2014.6

COPD London Respiratory Team Value Pyramid - Cost/QALY

- Telehealth £92000/QALY
- Triple Therapy £7000-£187000/QALY
- Long term Oxygen Therapy £11-16000/QALY
- LABA £5-8000/QALY
- Tiotropium/LAMA £7000/QALY
- Pulmonary Rehabilitation £2000-8000/QALY
- Stop Smoking Support with pharmacotherapy £2000/QALY
- Flu vaccination? £1000/QALY in “at risk” population
The low value pyramid?

- LAMA + LABA +ICS – TRIPLE THERAPY
- LABA
- LAMA
- PR
- Stop Smoking
- Flu Vaccine

Representation based on national GP contract data and locally retrieved data

Is it Safe?
### Risks of high dose ICS

<table>
<thead>
<tr>
<th>Risk</th>
<th>Randomised controlled trial</th>
<th>Observational study</th>
<th>Systematic review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Bone fracture</td>
<td>(No effect on fracture risk)</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Skin thinning/easy bruising</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cataract</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>HPA suppression</td>
<td></td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>


---

### Inhaler Technique
Doing the Right Things Right – Inhaler Technique

- In some studies, up to 90% of patients may not be able to use an MDI effectively
- 91% of healthcare professionals who teach use of an MDI cannot demonstrate it correctly*
- Even with effective technique, lung deposition from an MDI is at best 12% (excluding newer fine particle inhalers)**
- Large volume spacer may be easier to use and may increase deposition to over 20%**
- If used incorrectly – a lot of the drug from MDI is wasted

*Thorax 2010;65:A117
** Newman S. Chest 1985; 88: 152S-160S
Responsible Respiratory Prescribing

Key Messages

1. Respiratory medications are expensive

**Doing the Right Things:**
2. When prescribing any new respiratory inhaler, ensure that the patient has undergone NICE-recommended support to stop smoking
3. Pulmonary rehabilitation is a cost effective alternative to stepping up to triple therapy and should be the preferred option if available and the patient is suitable.

**Doing the Right Things Right:**
4. When prescribing any inhaled medication, ensure that the patient has undergone patient centred education about the disease and inhaler technique training by a competent trainer
5. When prescribing an MDI (except salbutamol), ensure that a spacer is also prescribed and will be used
6. When prescribing high dose inhaled corticosteroids (>1000ug BDP equivalent?), ensure that the patient is issued with an inhaled steroid safety card

---

**Inhaled Corticosteroid Safety Card**

- Increase awareness amongst prescribers of:
  - Waste
  - Risk
  - Value

- Make prescribers aware of alternatives before high dose ICS

- May change prescribing behaviour as uncomfortable discussion with patient about risk vs benefit
Warn about high dose ICS side effects:
- Pneumonia
- Diabetes
- Bone Loss
- Adrenal Suppression

In COPD – moderate dose ICS (800µg BDP equivalent) same clinical efficacy as very high dose ICS (2000µg BDP equivalent).

In asthma – little evidence for efficacy of ICS above 800µg/day (BTS/SIGN Grade D evidence)

Checking inhaler technique, using ICS through a spacer or changing inhaler device may be more effective than increasing the dose or stepping up treatment

If dose of ICS has been stepped up in the treatment of asthma and patient is well controlled – consider stepping down after 3 months.
Minimise Risk : Involve Patients

Inhaled Corticosteroid Safety Information for Adults

Inhaled corticosteroids are very important in the treatment of respiratory conditions such as asthma and eosinophilia, chronic obstructive pulmonary disease (COPD). They act by reducing inflammation and improving symptoms and their development. Corticosteroids are also used for nasal conditions such as sinusitis and hayfever. Generally, they are very safe and free from serious side effects when used in standard doses. Inhaled corticosteroids can result in adverse effects such as sore throat, hoarse voice or cough. Rarely these adverse effects may be reduced by using a spacer device with metered dose inhalers that contain corticosteroids. The key to reducing these effects is by using the right type of inhaler for the right condition, the right dose and the correct technique. If you are taking ICS regularly for a long time, especially if you are allergic to pollen or other allergens, then you may develop avoidable respiratory side effects such as throat irritation.

- Warn about potential for adrenal suppression on high doses of ICS
- Warn about not stopping high dose ICS suddenly

Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD (WISDOM)

Magnussen H et al. NEJM Sept 2014
DOI: 10.1056/NEJMoa1407154
WISDOM STUDY

• 2485 patients with moderate to severe COPD with exacerbations
• Randomised after 6 week run in to either ICS continuation of stepwise withdrawal to dual bronchodilatation with LAMA/LABA (tio/salm) over 52 weeks
• Mean FEV1 34%  Mean mMRC 1.8
• Primary end point – time to first moderate or severe COPD exacerbation

WISDOM STUDY RESULTS

• 2027 patients completed study
• No difference in exacerbation rate between 2 groups  (HR 1.06  CI 0.94-1.19)
• At week 18, ICS group had 38ml greater trough FEV1 (p<0.001) and week 52 - 43 ml (p<0.001)
• Slight difference in SGRQ at weeks 52 in favour of ICS continuation )1.22 difference p=0.047

CONCLUSION

• Many patients with severe to very severe COPD and exacerbations may not benefit from addition of ICS on top of LAMA+LABA
Evaluation of an ICS withdrawal programme in patients with Mild/Mod COPD in Lambeth CCG

Grainne d’Ancona, National Institute of Health Research (NIHR) Masters Research Fellow; Irem Patel, Consultant Respiratory Physician, KCH
Cathrine McKenzie, Consultant Pharmacist, GSTT
Tariq Sethi, Head of Respiratory Medicine, KCH

Lambeth CCG ICS stepwise withdrawal programme

• Feasibility study in one CCG (48 practices)
• Withdrawal by GP upon recommendation by the multidisciplinary Integrated Respiratory Team in a “Virtual Clinic”
• 370 patients with FEV₁ >50% reviewed – 320 had COPD
• 2/3 patients had a change in medicines recommended
• Of these, 76% to gradually stop or step down ICS dose
• 60% attempted (95% patient acceptance)
Virtual Clinic

- Many years of primary care education sessions, practice support sessions, workshops, community clinics etc, have not produced improvements
- 2-3 hours dedicated time with GP and practice nurse – GP reimbursed for time spent
- Supported by specialist respiratory pharmacist
- 12-15 patient case records reviewed – all patients with mild/moderate COPD on register who are on high dose ICS
- Confirm diagnosis, severity, exacerbation rate and appropriateness of treatment
- Care plan agreed with stepwise reduction or withdrawal of ICS as appropriate
- Re-review within 3 months by pharmacist

Lambeth ICS prescribing pattern

17% reduction in high dose ICS
It can be done!

Summary

- Respiratory Medications are expensive
- Respiratory Medications, especially high dose inhaled corticosteroids are often over prescribed in both asthma and COPD
- This is causing both waste and potential harm
- A stepwise approach to reduction and withdrawal of high dose inhaled can be successful in conjunction with educating and alerting prescribers about potential harm and evidenced based alternatives
Table 1. Proposal of pharmacological treatment of COPD based on clinical phenotypes and severity

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>A High-risk exacerbator</td>
<td>LABA</td>
<td>LABA</td>
<td>LABA</td>
<td>LABA</td>
</tr>
<tr>
<td>B Deteriorating COPD asthma</td>
<td>LABA + ICS</td>
<td>LABA + ICS</td>
<td>LABA + ICS</td>
<td>LABA + ICS</td>
</tr>
<tr>
<td>C Exacerbator with emphysema</td>
<td>LABA</td>
<td>LABA</td>
<td>LABA</td>
<td>LABA</td>
</tr>
<tr>
<td>D Exacerbator with chronic bronchitis</td>
<td>LABA</td>
<td>LABA</td>
<td>LABA</td>
<td>LABA</td>
</tr>
</tbody>
</table>

Reproduced with permission from Serina et al.°

ICS—inhaled corticosteroids; LAMA—long-acting anticholinergic; LABA—long-acting β₂-agonist; PDE4—inhibitor; SABA—short-acting β₂-agonist; SAMA—short-acting anticholinergic. *In case of intermittent symptoms.