Responsible Respiratory Prescribing in Primary Care

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## Disclosures for Dr Vincent Mak

<table>
<thead>
<tr>
<th>Role</th>
<th>Details</th>
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<tr>
<td>Research Support/P.I.</td>
<td>No relevant conflicts of interest to declare</td>
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<td>Employee</td>
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<td>Consultant</td>
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<td>Major Stockholder</td>
<td>No relevant conflicts of interest to declare</td>
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<td>Speakers Bureau</td>
<td>No relevant conflicts of interest to declare</td>
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<td>Honoraria</td>
<td>AZ, GSK, Boehringer. Almirall, Novartis, TEVA Chiesi</td>
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<td>Scientific Advisory Board</td>
<td>No relevant conflicts of interest to declare</td>
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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 = \frac{\text{Health Outcomes}}{\text{Cost of delivering Outcomes}}

Porter ME; Lee TH NEJM 2010;363:2477-2481; 2481-2483
How do we achieve Value?

- **RIGHT CARE**
  - Do the right thing
  - Do the right thing right
  - Doing the right thing right first time should deliver quality and value
To understand VALUE – you have to know COST
What are the top 5 costliest drugs in the NHS (Dec 2015)?

- **5.** Sitagliptin 100mg - £80 million/yr
- **4.** Seretide 500 accuhaler - £91 million/yr
- **3.** Symbicort 200 - £96 million/yr
- **2.** Seretide 250 evohaler - £130 million/yr
- **1.** Spiriva - £175 million/yr

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

Total for high potency Seretide approx £220 million/yr

Source: NHSBSA last accessed Apr 2016
Trends in Prescribing of Seretide® inhaler by strength on an FP10 prescription form in England

Source: NHSBA
Who is prescribing high dose ICS?
Are we doing the right things?
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
Smoking prevalence in COPD
TORCH, Uplift Studies and ...POET-COPD

Salmeterol and Fluticasone Propionate and Survival in Chronic Obstructive Pulmonary Disease

Peter M.A. Calverley, M.D., Julie A. Anderson, M.A., Bartolome Celli, M.D., Gary T. Ferguson, M.D., Christine Jenkins, M.D., Paul W. Jones, M.D., Julie C. Yates, B.S., and Ioreen Vestbo, M.D., for the TORCH investigators

| Current smoker — no. (%) | 658 (43) | 651 (43) | 661 (43) | 660 (43) |

A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease

Donald P. Tashkin, M.D., Bartolome Celli, M.D., Stephen Senn, Ph.D., Deborah Burkhart, B.S.N., Steven Kesten, M.D., Shailendra Menjoge, Ph.D., and Marc Decramer, M.D., Ph.D., for the UPLIFT Study Investigators

| Current smoker (%) | 29.3 | 29.9 |

Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD

Claus Vogelmeier, M.D., Bettina Hederer, M.D., Thomas Glaab, M.D., Hendrik Schmidt, Ph.D., Maureen P.M.H. Rutten-van Mölken, Ph.D., Kai M. Beeh, M.D., Klaus F. Rabe, M.D., and Leonardo M. Fabbri, M.D., for the POET-COPD Investigators

| 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

© Copyright NHSRSA 2013
Trends in Prescribing of and Spending on Varenicline on an FP10 prescription form in England

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

© Copyright NHSBSA 2013
High Value Care in COPD

Pulmonary Rehabilitation

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Value of Pulmonary Rehabilitation

- Reduces admissions, improves exercise capacity, improves health related quality of life
- Post exacerbation PR v effective in avoiding admissions
- Numbers needed to Treat = 4
- The only intervention to date that has been shown to reduce the very high 3 month readmission rate seen in COPD (33% to 7%)
- Only costs £2,000-£8,000/QALY

Puhan et al 2011 Cochrane Database of Systematic Reviews 2011
Evidence Based Prescribing?
BTS/SIGN Asthma Guidelines

Grade D evidence
Dose-response curve for ICS\textsuperscript{1,2}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{dose_response_curve.png}
\end{figure}

Asthma – Getting it right?
B&H CCG
Asthma – Getting it right?

Low/moderate dose ICS/LABA inhalers as a % of all ICS/LABA inhalers

Average for latest 3 months (Dec 16 - Feb 17)
Source: PrescQIPP
Algorithm 2a: Use of inhaled therapies

Please note: This algorithm should be used within the wider context of the management of COPD, including algorithms 1, 2 and 3.

Breathlessness and exercise limitation

- SABA or SAMA as required*
  - FEV1 ≥ 50%:
    - LABA
  - FEV1 < 50%:
    - LABA + ICS

Exacerbations or persistent breathlessness

- LABA
- LAMA Discontinue SAMA
  - Offer LAMA in preference to regular SAMA four times a day
  - Consider LABA + LAMA if ICS declined or not tolerated
- LABA + ICS
  - Consider LABA + LAMA if ICS declined or not tolerated
- LAMA
  - Offer LAMA in preference to regular SAMA four times a day

Persistent exacerbations or breathlessness

- LABA + ICS
  - In a combination inhaler
- LABA + ICS
  - In a combination inhaler
- LAMA
  - LABA + ICS
  - In a combination inhaler

Abbreviations:
- SABA: Short-acting beta agonist
- SAMA: Short-acting muscarinic agonist
- LABA: Long-acting beta agonist
- LAMA: Long-acting muscarinic antagonist
- ICS: Inhaled corticosteroid

* SABA (as required) may continue at all stages
Offer therapy (strong evidence) Consider therapy (less strong evidence)
Evidence from UK

• Reviewed 3537 patients with a diagnosis of COPD\textsuperscript{1}
• Spirometry was recorded for 2458 (69%)
  • 709 (29%) inconsistent with COPD
  • 150 (6%) inconsistent with life

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

London Respiratory Team
COPD – Getting it right?

- Potential for Audit:
  - % of patients who have FEV1>50% (i.e. ICS unlikely to be indicated)
  - % of patients with FEV>50% and no exacerbations in past year (i.e. ICS even more unlikely to be indicated)
  - % of patients who had 0-1 exacerbations in past year regardless of FEV1
  - Referral rates for pulmonary rehab
  - % of patients who are still smokers
  - % of patients on both Asthma and COPD registers
Is it Safe?
### Is it safe - Evidence for the Side Effects of ICS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Randomised controlled trial</th>
<th>Observational study</th>
<th>Systematic review</th>
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</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 # risk)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Skin thinning/easy bruising</td>
<td>✓</td>
<td></td>
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<tr>
<td>Cataract</td>
<td></td>
<td>✓</td>
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<tr>
<td>Diabetes</td>
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<td>✓</td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Adrenal Suppression</td>
<td></td>
<td>✓</td>
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Are we getting the most from our inhaler spend?
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 ultrafine 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

• The most cost effective inhaled medication is one that the patient can and will take!

*Thorax 2010;65:A117

**Newman S. Chest 1985; 88: 152S-160S
• Often – use of high dose inhaled corticosteroid not appropriate for stage of disease for asthma and COPD
• In COPD – possible to use evidence based lower potency with same clinical efficacy
• Treatment rarely stepped down when stable or not effective
• Lack of awareness of potential harm of high potency inhaled corticosteroids – would patients use if fully informed?
• Poor inhaler technique and poor concordance often cause for treatment failure and not “fixed” by increasing the dose

If your patients knew the risks – what would they want/chose?
What can we do?

Do the wrong thing?
SIMPLE SWITCH

England – 2 million items/yr

Saves £30 million/year if you swop everyone
Same waste caused by poor inhaler technique
Same harm caused by high dose ICS
SIMPLE SWITCH

England – 2.2 million items/yr

Saves £16 million/yr if you swop everyone
Same harm caused by high dose ICS
What can we do?

Do the right thing?
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

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London Respiratory Team
Developed by London Respiratory Network

- Patient held card
- Warns about the potential side effects of high doses of ICS
- Warns not to stop an ICS suddenly
- Alerts HCP to the patient being on a high dose ICS
ICS Guidance for HCPs

- Reiterates side effect warnings
- Clarifies clinical evidence
- Reminds that
  - checking inhaler technique
  - using ICS through a spacer
  - changing inhaler device may be more effective than stepping treatment up
- Reminds to step treatment down when stable
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
• 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
Withdrawal of inhaled corticosteroids can be safe in COPD patients at low risk of exacerbation: a real-life study on the appropriateness of treatment in moderate COPD patients (OPTIMO)

Rossi A et al.
Respiratory Research 2014, 15:77
http://respiratory-research.com/content/15/1/77
• 914 COPD patients, on maintenance therapy with bronchodilators and ICS

• FEV1>50% predicted, and <2 exacerbations/year were recruited.

• Upon decision of the primary physicians, 59% of patients continued their ICS treatment whereas in 41% of patients ICS were withdrawn and regular therapy was continued with long-acting bronchodilators mostly (91% of patients)
OPTIMO STUDY RESULTS

• 816 patients (89.3%) concluded the study. Non-ICS group on tiotropium, indacaterol, formoterol, salmeterol, tio+indacaterol.

• FEV1, CAT and exacerbations history were similar in the two groups (ICS and no ICS) at T0 and at T6.

• No deterioration in lung function, symptoms, and exacerbation rate between the two groups at T0 and T6 observed.

CONCLUSION

• The withdrawal of ICS, in COPD patients at low risk of exacerbation, can be safe provided that patients are left on maintenance treatment with long-acting bronchodilators.
Asthma – Getting it right?
Surrey Downs CCG

Items for Low / moderate dose ICS/LABAs as a % of all ICS/LABAs

% low mod dose - 2014-15
% low mod dose - 2015-16
Avoiding inappropriate prescribing of high dose inhaled corticosteroid combination inhalers – is the message getting through?

VHF Mak¹,³, G D’Ancona²,³
¹Imperial College Healthcare NHSTrust, London.² Guy’s and St Thomas’ NHS Foundation Trust. ³NHSE London Respiratory Network

<table>
<thead>
<tr>
<th>Monthly Expenditure (NIC - £ millions) on high dose combinations</th>
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<tr>
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SAVING £2million/month

⁻⁻⁻⁻   14.5%  8.4%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%  0.0%

<table>
<thead>
<tr>
<th>Quarterly quantities of high dose ICS combinations</th>
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Seretide 250 Evohaler
Seretide 500 Accuhaler
Generic Fluticasone/Salmeterol 250/25 pMDI
Generic Fluticasone/Salmeterol inh 500/50 DPI
Flutiform 250/10
Sirdupla 250/25
Airlusal Forspiro 500/50
Relvar Ellipta 184/22
• Try to make right diagnosis

• Stop smoking, pulmonary rehabilitation, flu vaccine

• Keep it simple - treat predominant symptom

• Check concordance and inhaler technique

• Review all those on high dose inhaled steroids

• Consider commissioning Virtual Note Review Clinics
Rising to the challenge of improving respiratory care

Optimise – not Maximise

Do more of what is right - not what is easiest or cheapest!
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 FEV$_1$ >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)
Lambeth ICS prescribing pattern

17% reduction in high dose ICS
Virtual Note Review Clinics

GP+Consultant/Resp Pharmacist+Practice nurse in attendance

2-3 hours protected time – backfilled and incentivised

• Review of patient record
• Summarised the clinical evidence
• Review and offer advice for specific patients:
  • Ensure the correct diagnosis
  • Smoking cessation, PR, vaccination, ICS safety card
  • Review the appropriateness of & adherence to the inhaled therapy prescribed (e.g. gradually withdraw ICS or add LAMA if no exacerbations)
QIPP – but not that good!

Mak V et al ERS 2015
Impact of Virtual clinics

Mak V et al ERS 2015
Virtual Note Review Clinics

• Why it works?
  • See what needs to be done on your own patients – method sticks
  • 4C-ABLE framework keeps it simple – prioritises what needs to be reviewed
  • Support from pharmacist to manage medication changes/dose reductions
  • Face to face with consultant – forming “sticky” relationships!

• Once Bitten – Forever Smitten!
  • Excellent user feedback – “learnt lots”, “very useful”, “welcome back anytime”
The 4C-ABLE Framework

The 4C-ABLE framework for Asthma and COPD

4C (before seeing patient)
- 1. Confirm diagnosis and stage disease
- 2. Current treatment (pharmacological and non-pharmacological)
- 3. Control - assess level
- 4. Compliance - assess level

ABLE (when seeing patient)
- 5. Agree Aims
- 6. Barriers to success
- 7. Learning and self efficacy
- 8. Emend and agree management