Dr Laura Waters
Mortimer Market Centre, London

<table>
<thead>
<tr>
<th>Speaker Name</th>
<th>Statement</th>
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<tbody>
<tr>
<td>Dr Laura Waters</td>
<td>Has received advisory board fees or fees for speaking at company sponsored events from: ViiV, Gilead, BMS, AbbVie and Janssen.</td>
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<tr>
<td>Date</td>
<td>April 2015</td>
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</tbody>
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Top 5 general medical tips

Laura Waters
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Mortimer Market Centre, London
5 tips/themes

1. Reviewing the history
2. Drug interactions
3. Sending the right tests
4. Questioning treatment
5. Questioning diagnoses
Introduction

• Our patients may see us more frequently than any other HCP
• Many of our patients have co-morbidities (and the proportion will continue to increase)
• We need to know enough about general medicine to order the right tests and make appropriate management suggestions
REVIEWING THE HISTORY
The history over 8 days

- 68 year old woman admitted to a large AMU
- Admitted with severe exacerbation COPD
- Started on antibiotics
- Reviewed by 2 medical SpRs, medical consultant, and 2 ITU registrars
- Admitted to HDU
- Deteriorated
- Family called in
The history revisited

- From daughter
  - Worsening SOBOE and ‘breathlessness when lying flat’ for several weeks
- Known aortic stenosis
- Raised JVP on examination
- High dose furosemide administered
- Sat up drinking tea the next morning
Preventable deaths due to problems in care in English acute hospitals: a retrospective case record review study

Helen Hogan,¹ Frances Healey,² Graham Neale,³ Richard Thomson,⁴ Charles Vincent,³ Nick Black¹
Contributors to preventable patient deaths

<table>
<thead>
<tr>
<th>Type of problem in care (%)</th>
<th>Preventable deaths n=52</th>
<th>Non-preventable deaths n=79</th>
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<tbody>
<tr>
<td>Clinical Monitoring*</td>
<td>40 (31.3)</td>
<td>25 (18.0)</td>
</tr>
<tr>
<td>Diagnosis†</td>
<td>38 (29.7)</td>
<td>30 (21.6)</td>
</tr>
<tr>
<td>Drug or fluid related‡</td>
<td>27 (21.1)</td>
<td>30 (21.6)</td>
</tr>
<tr>
<td>Technical problem§</td>
<td>8 (6.3)</td>
<td>26 (18.7)</td>
</tr>
<tr>
<td>Infection related</td>
<td>9 (7.0)</td>
<td>22 (15.8)</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>0 (0)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (4.7)</td>
<td>3 (2.2)</td>
</tr>
</tbody>
</table>

*Failure to act upon results of tests or clinical findings, set up monitoring systems or respond to such systems or increase intensity of care when required.
†Missed, delayed or inappropriate diagnosis as a result of failure to perform an adequate assessment of patient’s overall condition including appropriate tests or lack of focused assessment when required.
‡Side effects, inappropriate use, failure to give prophylactic care, anaphylaxis, etc.
§Related to an operation or procedure whether on ward, in a diagnostic suite or in theatre and including inappropriate or unnecessary procedures.
What had gone wrong?
What does this mean for us?

• The initial diagnosis was not questioned
• Prior senior reviews were assumed to be correct
• Nobody went back to the beginning to take a history
• If she had been HIV+ with well controlled HIV would you?
• Always revisit the history and investigations in deteriorating patients
DRUG INTERACTIONS
HIV-Druginteractions.org

Now Includes Cobicistat
Access our comprehensive, user friendly, free, drug interactions charts

Providing clinically useful, reliable, up-to-date evidence-based information
Non-HIV drug interactions

Drug-disease and drug-drug interactions: systematic examination of recommendations in 12 UK national clinical guidelines

Siobhan Dumbreck,1 Angela Flynn,1 Moray Naim,2 Martin Wilson,3 Shaun Treweek,4 Stewart W Mercer,5 Phil Alderson,6 Alex Thompson,7 Katherine Payne,7 Bruce Guthrie1

Dumbreck S et al. BMJ 2015;350:h949
Methodology

• Systematic identification, quantification, and classification of potentially serious drug-disease and drug-drug interactions for drugs recommended by NICE clinical guidelines for:
  – Type 2 diabetes
  – Heart failure
  – Depression

in relation to 11 other common conditions and drugs recommended by NICE guidelines for those conditions

Dumbreck S et al. BMJ 2015;350:h949
Methodology

• All guidelines reviewed by a GP and two pharmacists
• Treatments divided into:
  – **First line:** If recommended for all/nearly all with the condition (eg ACEI in heart failure)
  – **Second line:** If recommended only for some patients/circumstances (eg. spironolactone for heart failure)
Overlap of chronic co-morbidities

Fig 1 | Proportion of people with three index conditions who have each of other conditions. Morbidity data were not available for osteoarthritis or neuropathic pain; “painful condition” data shown are defined by receipt of four or more prescriptions for non-over the counter analgesics in previous 12 months.

Dumbreck S et al. BMJ 2015;350:h949
Drug-disease interactions

Most associated with chronic kidney disease:
- 27/32 identified drug-disease interactions for drugs recommended for type 2 diabetes
- 6/6 of the drug-disease interactions for depression*
- 10/10 of the drug-disease interactions for heart failure

*the depression guidelines did not discuss any potential drug-disease interactions

Dumbreck S et al. BMJ 2015;350:h949
Drug-drug interactions

- **133** potentially serious interaction pairs in the type 2 diabetes guideline:
  - 25 (19%) involved one of the four drugs recommended as first line treatments for all or nearly all
- **89** potentially serious drug-drug interaction pairs in the depression guidelines
  - 19 (21%) involved the one drug class recommended as first line (SSRIs)
- **111** potentially serious drug-drug interaction pairs identified in the heart failure guidelines
  - 21 (19%) involved the two classes recommended as first line

Dumbreck S et al. *BMJ* 2015;350:h949
Types of harm

<table>
<thead>
<tr>
<th>Index condition</th>
<th>Cardiovascular*</th>
<th>Bleeding</th>
<th>Renal/potassium</th>
<th>Central nervous system</th>
<th>Other†</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td><strong>Type 2 diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line recommended drug</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Second line recommended drug</td>
<td>54</td>
<td>11</td>
<td>18</td>
<td>1</td>
<td>29</td>
<td>113</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line recommended drug</td>
<td>1</td>
<td>9</td>
<td>0</td>
<td>7</td>
<td>2</td>
<td>19</td>
</tr>
<tr>
<td>Second line recommended drug</td>
<td>10</td>
<td>13</td>
<td>0</td>
<td>27</td>
<td>20</td>
<td>70</td>
</tr>
<tr>
<td><strong>Heart failure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line recommended drug</td>
<td>15</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>Second line recommended drug</td>
<td>17</td>
<td>34</td>
<td>17</td>
<td>0</td>
<td>22</td>
<td>90</td>
</tr>
</tbody>
</table>

*Includes effects on heart rate or rhythm or effects on blood pressure.
†Includes myopathy with statin treatment, or clinically relevant altered plasma concentration (for example, of digoxin, lithium, ciclosporin, or theophylline), which might require dose alteration or closer monitoring.
Conclusions

• Many guidelines suggest starting a drug but rarely considered drug-disease or drug-drug interactions
• Limiting the chronic guidelines considered and not including short-term treatment for intercurrent problems may have underestimated interactions

Dumbreck S et al. BMJ 2015;350:h949
What does this mean for us?

• We need to accurately document all medical conditions and concomitant medications
• We are excellent at reviewing ART DDI and should routinely extend this to non-ART DDI
SENDING THE RIGHT TESTS
Diarrhoea

• Acute diarrhoea is often infective
• Organic aetiology suggested by:
  – copious watery diarrhoea
  – nocturnal diarrhoea
• Frequent, small amounts of faeces suggest functional bowel disease such as IBS (NICE criteria)
• Bloody diarrhoea implies colonic disease:
  – Inflammatory bowel disease or carcinoma, or an invasive infective diarrhoea, e.g. Campylobacter jejuni
NICE IBS guidelines: red flags

- **History**
  - Rectal bleeding
  - A family history of bowel or ovarian cancer
  - A change in bowel habit to looser and/or more frequent stools >6 weeks in a person aged >60

- **Examination/investigation**
  - Anaemia
  - Abdominal masses
  - Rectal masses
  - Raised inflammatory markers (?IBD)

**Investigations:**
- FBC, ESR, CRP
- Coeliac screen (EMA or TTG)
- +/- CA-125 in women
- Faecal calprotectin....
Faecal calprotectin

Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel

Issued: October 2013

NICE diagnostics guidance 11
www.nice.org.uk/dg11
Pancreatic exocrine function

• Several tests, faecal elastase simplest
• Chelsea & Westminster cohort\(^1\):
  – Retrospective analysis of 233 faecal elastase results
  – 104 (45%) had evidence of pancreatic exocrine insufficiency (faecal elastase < 200 mcg/g)
  – Predictive factors: HCV, alcohol misuse, steatorrhoea
  – Not-predictive: didanosine, stavudine
  – 77% of those treated reported symptom improvement

Bile acid malabsorption

• An often overlooked cause of chronic diarrhoea
• Prevalence:
  – 4-5% in chronic diarrhoea\(^1\)
  – Approximately 1/3 of patients meeting IBS-D criteria\(^1\)
• In one retrospective SeHCAT series (n=373)\(^2\):
  – 51% had bile acid malabsorption (including 40% of those with no risk factors)
  – Of 77 patients with ‘IBS-D’ 27% tested positive
• Trial of cholestyramine effective in 70-96%\(^1\)

What does this mean for us?

• Diarrhoea is a common symptom
• Patients may have been investigated a long time ago or suboptimally
• Ensure the PMH includes details.... “chronic diarrhoea, investigated by gastroenterology”
British Thoracic Society
Scottish Intercollegiate Guidelines Network

British guideline on the management of asthma
Quick Reference Guide

Revised October 2014
Not all steroids are CYP450 substrates

- Most are and chance of significant interaction depends on half life:
  - Fluticasone
  - Budesonide
  - Mometasone
  - Ciclesonide

- Beclomethasone is not
NICE: inhaled steroids

• Beclomethasone and budesonide:
  – Approximately equivalent in clinical practice (1:1 dose ratio)
  – May be variations with different delivery devices
  – Limited evidence from two open studies of suboptimal design that budesonide via the turbohaler is more clinically effective

• Fluticasone equal clinical activity to beclomethasone and budesonide at half the dosage
  – Evidence for fewer side effects at doses with equal clinical effect is limited

• Mometasone appears to provide equal clinical activity to beclomethasone and budesonide at half the dosage. Relative safety not fully established
Cochrane review: Fluticasone vs beclomethasone vs budesonide.

Fluticasone at half day dose yields slightly greater improvement in airflow. More side effects.
Co-formulations

• ‘But fluticasone and budesonide are available co-formulated with LABA’

• LABA are the next step up from inhaled steroids and should NOT be given without inhaled steroids

• Seretide = fluticasone + salmeterol

• Fostair = beclomethasone + formoterol

• Benefits are driven by ADHERENCE
QUESTIONING DIAGNOSES
The diagnosis of asthma is based on the recognition of a characteristic pattern of symptoms and signs
and the absence of an alternative explanation for them. The key is to take a careful clinical history.

- Base initial diagnosis on a careful assessment of symptoms and a measure of airflow obstruction:
  - in patients with a **high probability** of asthma move straight to a trial of treatment. Reserve
    further testing for those whose response to a trial of treatment is poor.
  - in patients with a **low probability** of asthma, whose symptoms are thought to be due to an
    alternative diagnosis, investigate and manage accordingly. Reconsider the diagnosis of
    asthma in those who do not respond.
  - in patients with an **intermediate probability** of asthma the preferred approach is to carry
    out further investigations, including an explicit trial of treatments for a specified period,
    before confirming a diagnosis and establishing maintenance treatment.
Draft NICE guidance on asthma

- Consultation period closed March 2015
- Final guidance expected July 2015
- Draft advises **spirometry for all** to diagnose asthma
- May have a significant impact on historical asthma diagnoses
Methacholine & mannitol challenges

NICE draft:
offer a direct bronchial challenge test with histamine or methacholine....if diagnostic uncertainty after a normal spirometry potentially MIS-DIAGNOSED
Conclusion: top tips

1. Always go back to the history
2. Review ALL potential drug-drug interactions
3. Ensure you request/suggest the right tests (and review investigation history)
4. Question if your patient’s treatment is the right one
5. Question if your patient’s diagnosis is the right one
Acknowledgements

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