Dr Laura Waters

Mortimer Market Centre, London

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Speaker Name	Statement
Dr Laura Waters	Has received advisory board fees or fees for speaking at company sponsored events from: ViiV, Gilead, BMS, AbbVie and Janssen.
Date	April 2015

Top 5 general medical tips

Laura Waters
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5 tips/themes

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

Introduction

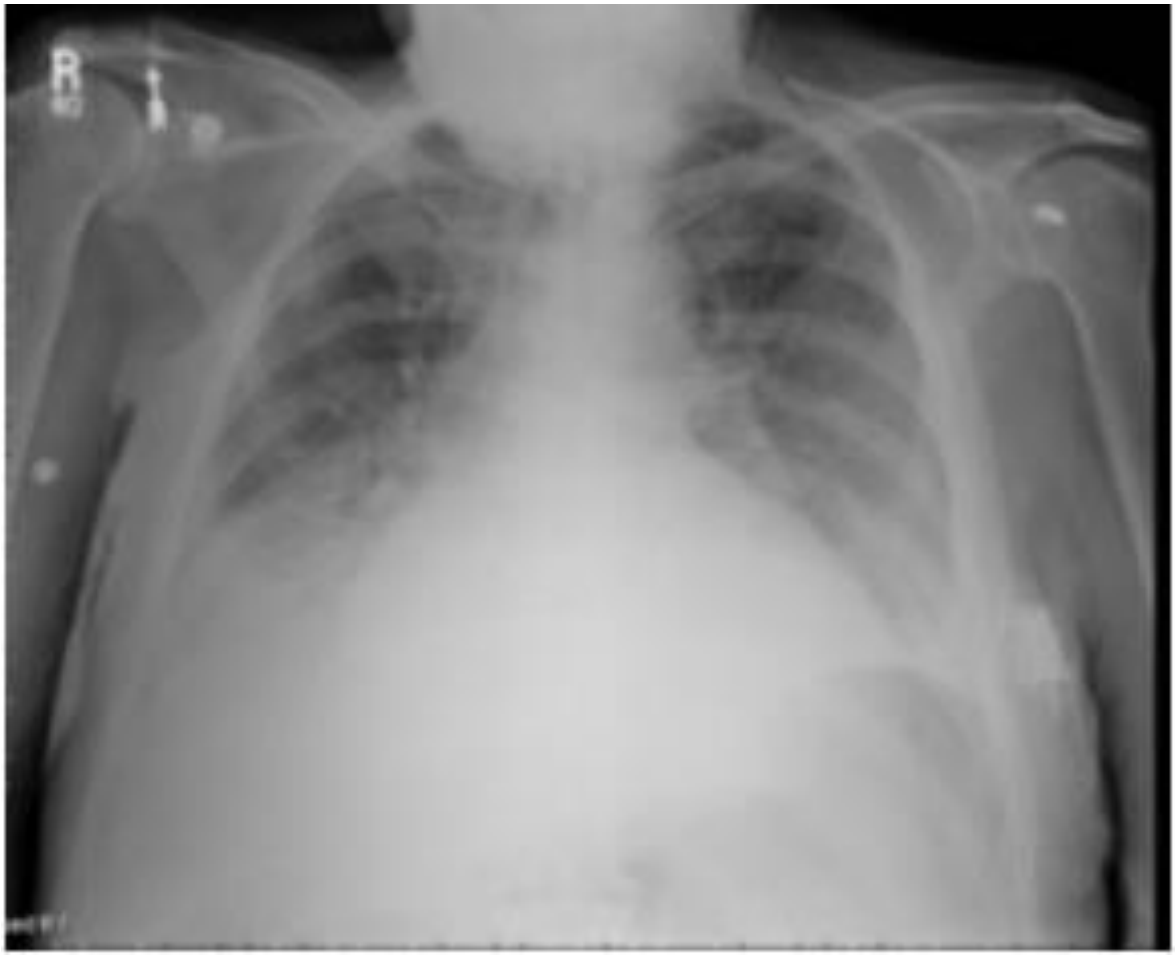
- Our patients may see us more frequently than any other HCP
- Many of our patients have co-morbidities (and the proportion will continue to increase)
- We need to know enough about general medicine to order the right tests and make appropriate management suggestions

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

CXR



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

Inpatient mortality revew (n=1000)

Original research

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 Black[1]

Hogan H et al. BMJ Qual Saf 2012;21:737–745.

Contributors to preventable patient deaths

Table 5 Types of problems in care that contribute to patient death (More than one option may apply for each patient).

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

*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.

Hogan H et al. BMJ Qual Saf 2012;21:737–745.

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

Non-HIV drug interactions

RESEARCH

OPEN ACCESS

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

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

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)

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

Overlap of chronic co-morbidities

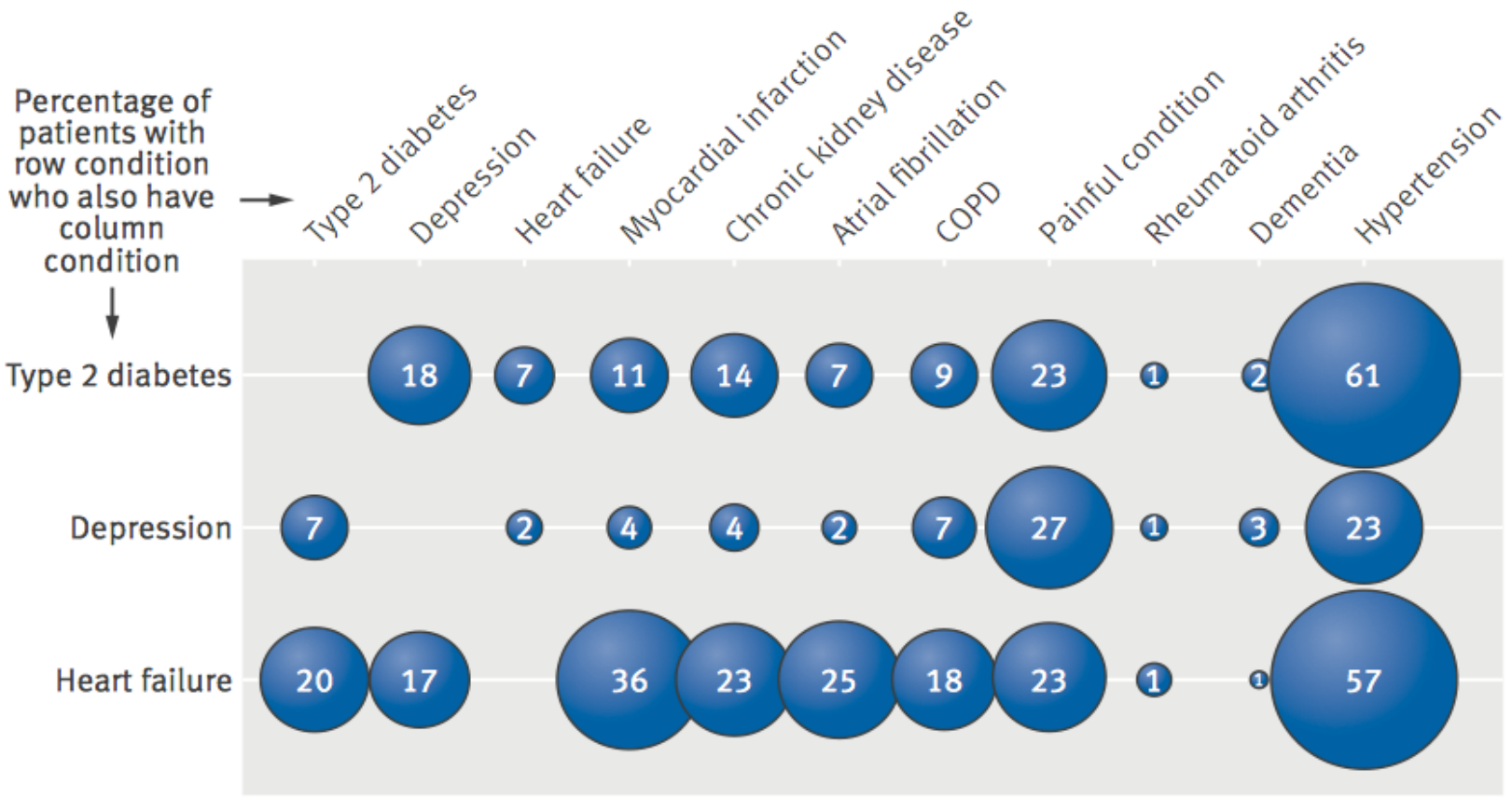


Fig 1 | Proportion of people with three index conditions who have each of other conditions. Morbidity data were not available for osteoarthritis or neuropathic pain; "painful condition" data shown are defined by receipt of four or more prescriptions for non-over the counter analgesics in previous 12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

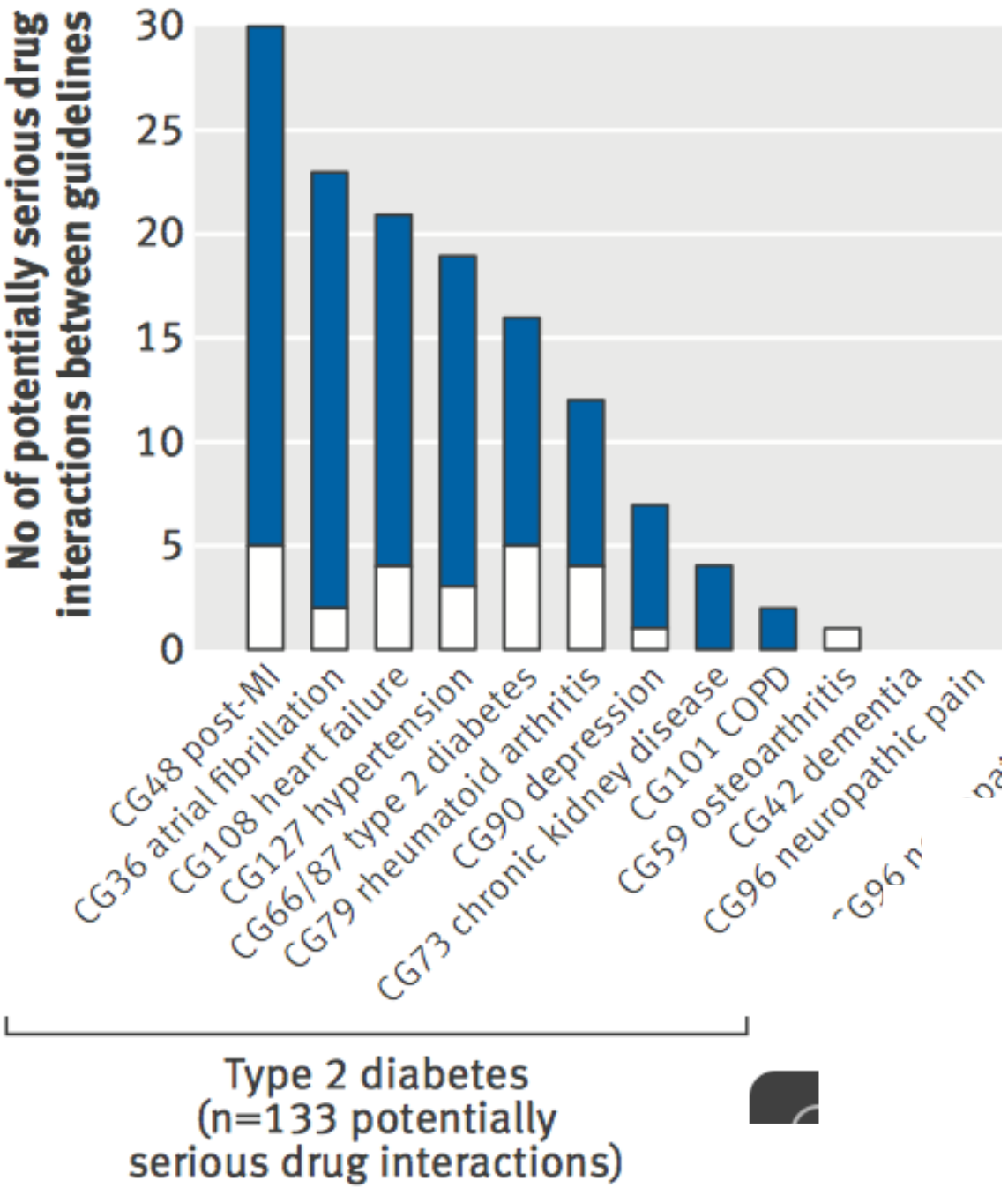
*the depression guidelines did not discuss any potential drug-disease interactions

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



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

Types of harm

Table 3 | Type of harm expected from potentially serious drug-drug interaction for each index condition

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

*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.

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

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**
  - Recta
  - A fam
  - A cha frequent stools
- **Examin**
  - Anae
  - 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

1. Martin T et al. HIV Medicine 2013;14(3):161-6.

Bile acid malabsorption

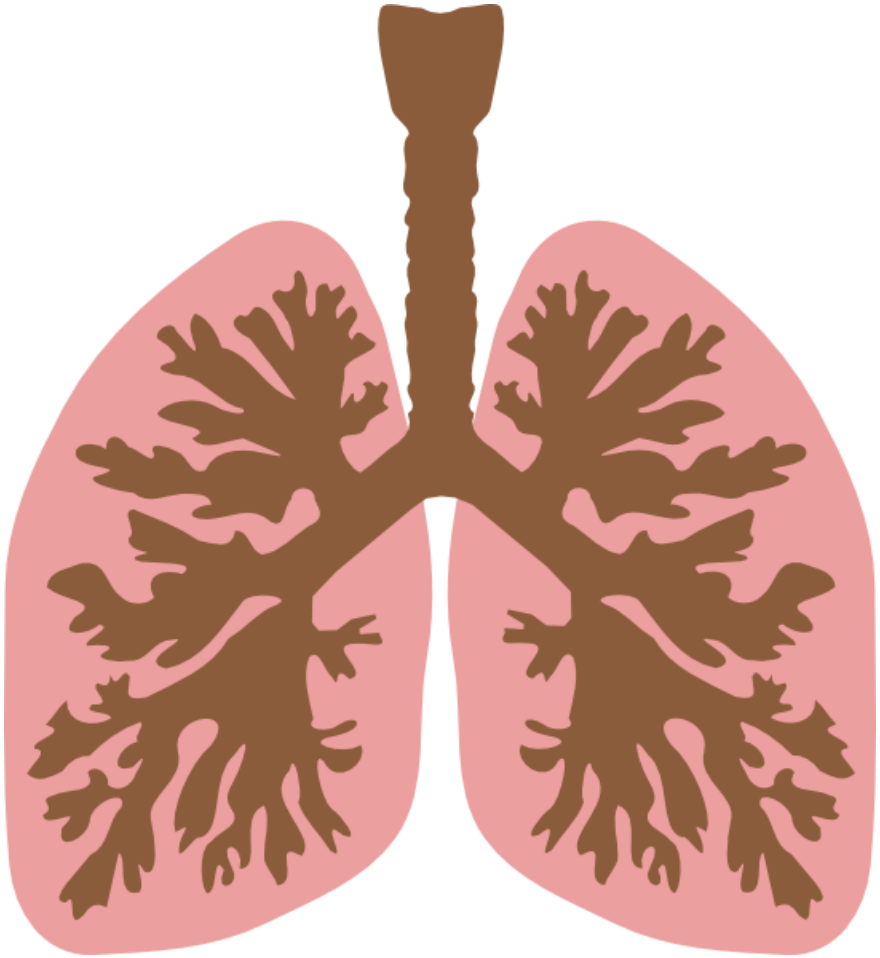
- An often overlooked cause of chronic diarrhoea
- Prevalence:
  - 4-5% in chronic diarrhoea[1]
  - Approximately 1/3 of patients meeting IBS-D criteria[1]
- In one retrospective SeHCAT series (n=373)[2]:
  - 51% had bile acid malabsorption (including 40% of those with no risk factors)
  - Of 77 patients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

1. Barkun AN et al. Can J Gastroenterol. 2013 Nov;27(11):653-9.
2. Wong BS et al. Clin Gastroenterol Hepatol. 2012;10:1009–15.
3. Gracie DJ et al. Neurogastroenterol Motil. 2012 Nov;24(11):983-e538.

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"*

QUESTIONING TREATMENT



Lungs

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 bud ide

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD002310.

Fluticasone versus beclomethasone or budesonide for chronic asthma in adults and childr

Adams N[1], Lasserson TJ, Cates CJ, Jones PW.

Author information

Abstract

BACKGROUND: Beclomethasone dipropionate (BDP) and budesonide (BUD) are commonly prescribed inhaled c r the treatment of asthma. Fluticasone propionate (FP) is newer agent with greater potency in in-vitro assays.

OBJECTIVES: To compare the efficacy and safety of Fluticasone to Beclomethasone or B nic asthma.

SEARCH STRATEGY: We searched the Cochrane Airways Group trial register (Ja contacted trialists and pharmaceutical companies for additional studies and searched abstracts o

SELECTION CRITERIA: Randomised trials in children and adults compari e treatment of chronic asthma.

DATA COLLECTION AND ANALYSIS: Two reviewers independently a er extracted data. Quantitative analyses were undertaken using RevMar

MAIN RESULTS: Seventy-one studies (14,602 participants) represe al quality was fair. Dose ratio 1:2: FP produced a significantly greater nt and change in morning PEF, but not change in FEV1 or evening PEF. T ce between FP and BDP/BUD were seen for trial withdrawals. FP led t dose of BDP/BUD, FP led to a greater likelihood of pharyngitis. There was hour urinary cortisol was measured frequently but data presentation was li morning PEF, evening PEF, and FEV1 over BDP or BUD. The effects ncidence of hoarseness, pharyngitis, candidiasis, or cough.

AUTHORS' CONCLUSIONS: Fluticasone given at half the daily dose of be measures of airway calibre, but it appears to have a higher risk of causing sore throat and oarseness. There are concerns about adrenal suppression with Fluticasone given to children omised trials included in this review did not provide sufficient data to address this issue.

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

Diagnosis: BTS/SIGN recommendations

DIAGNOSIS IN ADULTS

INITIAL ASSESSMENT

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 chall es

Clin Exp Allergy. 2014 Oct;44(10):1240-5. doi: 10.1111/cea.12352.

The potential role of direct and indirect bronchial challenge testing to identify overtreat mmunity managed asthma.

Manoharan A[1], Lipworth BJ,

⊕ Author information

Abstract

BACKGROUND: Although challenge testing is not routinely used in primary c

OBJECTIVE: The aim of th sting in community managed asthma.

METHODS: Patients curre ited to take part in the study. At screen de (FeNO); Asthma Control Questionn

RESULTS: A total of 3388 percent had either a positive metha allenges. Fourteen percent of metha e to methacholine. Spirometry, FeNO, ACQ and AQLQ were significantly nhaled corticosteroids and frequent long-acting beta-agonists.

CONCLUSIONS AND CLINICAL RELEVANCE: We found that 30% of allenge negative and could be potentially misdiagnosed or overtreated, in turn su

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

- Professor Martin Fisher
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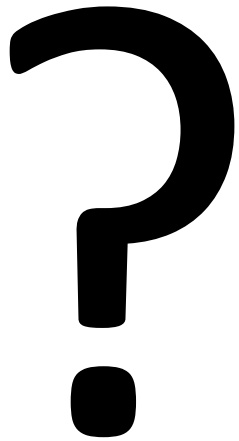
Thank you



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British HIV Association

BHIVA

21st Annual Conference of the British HIV Association (BHIVA)

#BHIVA2015

21–24 April 2015

The Brighton Centre, Brighton, UK