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Rapid Diagnostic Tests

Dr. Annette Plüddemann
Director: Diagnostic Horizon Scan Programme

18 May 2015

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6 March 2013 Last updated at 00:13

Stomach cance

By Michelle Roberts
Health editor, BBC News online

A quick and simple breath test diagnose stomach cancer, stud reveal.

Scientists from Israel and China fou was 90% accurate at detecting anc distinguishing cancers from other s complaints in 130 patients.

The British Journal of Cancer says could revolutionise and speed up t cancer is diagnosed.

About 7,000 UK people develop st have an advanced stage of the dis

Two-fifths of patients survive for at alive after five years, despite treatr

Currently doctors diagnose stomac stomach lining using a probe and a down the gullet.

The new test looks for chemical pr to patients with stomach cancer.

Volatile organic compounds

Cancer appears to give off a signa compounds that can be detected u and **perhaps even dogs**.

The science behind the test itself is been working on the possibility of b

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17 January 2013 Last updated at 12:19

Phone apps may delay skin cancer diagnosis

Using a smartphone app to decide whether a mole is cancerous could delay sometimes life-saving treatment, according to American researchers.

Researchers say you must seek medical advice if you are concerned about a mole

The University of Pittsburgh scientists put four applications to the test by showing them 188 pictures of cancers and less concerning skin conditions.

Three of the apps wrongly labelled the cancerous lesions as unproblematic in almost a third of cases.

Doctors warn using phones rather than seeking expert help could be harmful.

The research, published in the journal JAMA Dermatology, looked at four commonly used applications.

The images selected to test the apps were all of skin lesions that were later removed and checked for an accurate diagnosis.

Three of the apps analysed the pictures using automated algorithms, without the involvement of doctors.

But users submitting pictures to the fourth app had their images reviewed by a qualified skin specialist.

In this case only one out of 53 cancerous legions was misdiagnosed, but this app cost $5 (£3.10) per use.

Prof Laura Ferris, lead researcher of the study, said: "It is important that

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The Oxford Diagnostic Horizon Scan Programme identifies new and emerging diagnostic technologies relevant to primary care in the NHS.

The horizon scanning reports summarise why the technology is important, provide an overview of the current available evidence and assess whether it could be adopted in the NHS and if so, what the requirements are for the delivery of the technology into practice.

These **reports are freely accessible** and disseminated to the NIHR Health Technology Assessment Programme (HTA), the National Institute for Health and Clinical Excellence (NICE) and commissioners of health care services to facilitate adoption and identify further research requirements.

We are funded by the **National Institute for Health Research** (NIHR) and collaborate with the Health Economics Research Centre at Oxford University.

Find out more about our research

www.oxford.dec.nihr.ac.uk/horizon-scanning

What is the evidence?

- Is it accurate (enough)?
- Is it feasible and who would use it?

  e.g. GP, nurse, patient…
- Will it change practice? e.g. Does it help decision making, reduce referrals, etc.?
- How do patients/doctors feel about using it?
- Is it cost effective?

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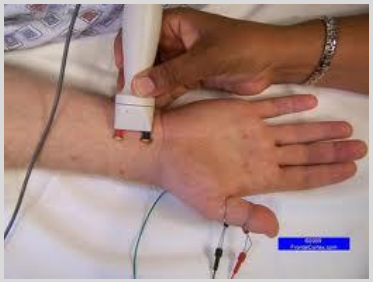

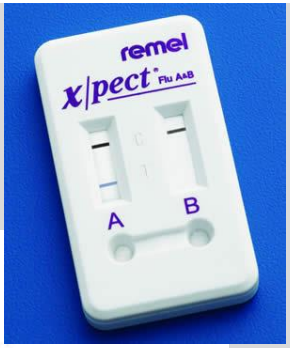

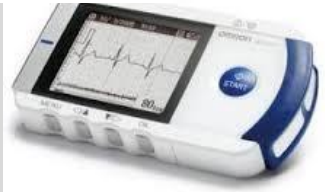

Self-monitoring of INR

✓Accuracy:
Systematic review of the accuracy of 3 commonly available point-of-care coagulometers: accuracy is comparable to laboratory measures and adequate for clinical use

✓ Clinical impact:
Systematic reviews including individual patient data analyses (over 5000 patients)

❖ Self-management (i.e. self-testing and self-adjusting warfarin) – reduces thromboembolic events (RR = 0.47) and all-cause mortality (RR = 0.55) but no effect on major bleeds

❖ Self-monitoring (i.e. self-testing and warfarin adjustment by clinician) – significant reduction in thromboembolic events (HR = 0.51), but not for major bleeds or death

✓ Patient acceptability:
UK trials suggest 24% of patients would agree to carry out self-monitoring, of which 70% could be successfully trained and would be able to do so

What do the guidelines say?

The 2014 NICE guideline on self-monitoring coagulation status (DG14):

"In patients with AF who require long-term anticoagulation, self-monitoring should be considered if preferred by the patient and the following criteria are met:

- *the **patient** is both physically and cognitively **able** to perform the self-monitoring test, or in those cases where the patient is not physically or cognitively able to perform self-monitoring, a designated carer is able to do so*
- *an **adequate supportive educational programme** is in place to train patients and/or carers*
- *the patient's ability to self-manage is **regularly reviewed***
- *the **equipment** for self-monitoring is **regularly checked** via a quality control programme."*

What is currently happening?

Recent data from the Churchill Hospital in Oxford:

160 “self-testers” (out of about 8,500 patients) but none who self-manage

D. Keeling, personal communication

Bottom line?

- Patients who self-monitor or self-manage can improve the quality of their warfarin therapy
- Self-monitoring reduces the rate of clot-related events and is a safe option for suitable patients of all ages
- Patients should be offered the option to self-manage, with health-care support as back-up

Point-of-care tests for coeliac disease

Boots

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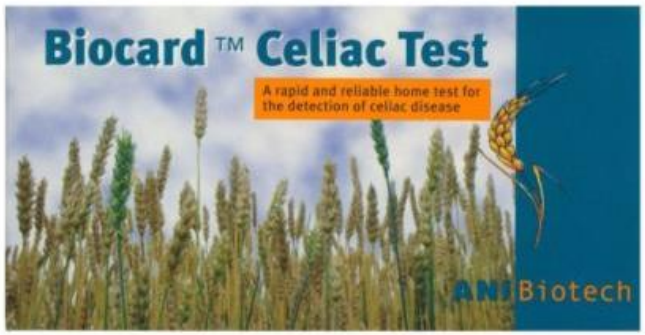
pharmacy & health | beauty | fragrance | mother & baby | toiletries | men | electrical | photo | opticians | toys | gift | sun & holiday | offers

Home > Beauty > Electrical > Electrical Health > Screening kits > Biotech Biocard Celiac Test



Biotech Biocard Celiac Test

5351065

£20.42

Collect in store

Home delivery

Quantity 1

Add

Check store availability

★★★☆☆ (14) Write a review

Biotech Biocard Celiac Test is a rapid and reliable home test for the detection of celiac disease from a fingertip blood sample. Celiac disease is an intolerance to gluten.

✓Accuracy:

- 5 case-control studies in biopsy-confirmed coeliac disease patients and lab controls
- Sensitivity 90%-97% and specificity 79%-100%
- No studies in primary care

✓ Clinical impact:

- Accuracy may be overestimated due to study design and selective populations
- Sensitivity in asymptomatic children was much lower (65-79%) – ability to rule out coeliac disease in children is reduced
- ~8% of coeliac disease patients are IgA deficient, test may give a false negative result
- Patients self-testing may begin gluten-free diets without confirmation testing or additional advice (and investigations for potential comorbid conditions)

✓ Patient acceptability:

- No research evidence
- Comments suggest they like the rapid and immediate result but some do have reservations regarding the accuracy

What do the guidelines say?

The 2009 NICE guideline on coeliac disease (CG86):
Do not use self-tests and/or point-of-care tests for coeliac disease as a substitute for laboratory-based testing. Patients with positive self- or POC-tests are sent for further serological testing.

Bottom line?

- The evidence for point-of-care tests is limited
- In the future they may be helpful in the diagnostic work-up of coeliac disease in primary care settings by increasing speed of results or access to testing in some settings, as sensitivity and specificity are comparable with laboratory-based serology. However, a negative result does not safely rule out coeliac disease

Autoimmune markers for the diagnosis of rheumatoid arthritis

✓**Accuracy:**

Meta-analysis of the diagnostic accuracy of rheumatoid factor (50 studies) and anti-cyclic citrullinated peptide antibody (37 studies):

- RF: sensitivity 69%, specificity 85%
- ACPA: sensitivity 67%, specificity 95%
- Setting: Hospital arthritis clinics, no large studies based in primary care

✓ **Clinical impact:**

- 60–70% patients with RA have a positive RF, which is predictive of disease severity, but not useful for diagnosis
- Only 11–20% of people with musculoskeletal symptoms and a positive RF actually have RA
- Unclear whether adding ACPA to RF provides any added benefit
- No evidence to support use of RF or ACPA as diagnostic tests for RA in primary care

What do the guidelines say?

The 2009 NICE guideline on rheumatoid arthritis (CG79):

- "Refer for specialist opinion any person with **suspected persistent synovitis of undetermined cause**. Refer urgently if any of the following apply:
  - the small joints of the hands or feet are affected
  - more than one joint is affected
  - there has been a delay of 3 months or longer between onset of symptoms and seeking medical advice.

- Refer urgently any person with suspected persistent synovitis of undetermined cause, **even if their blood tests show a normal acute-phase response or negative rheumatoid factor**."

What is currently happening?

Cohort study and retrospective analysis of RF requests made to hospital immunology lab between 2003 and 2009:

- 67% of requests were from primary care
- substantial variation between practices

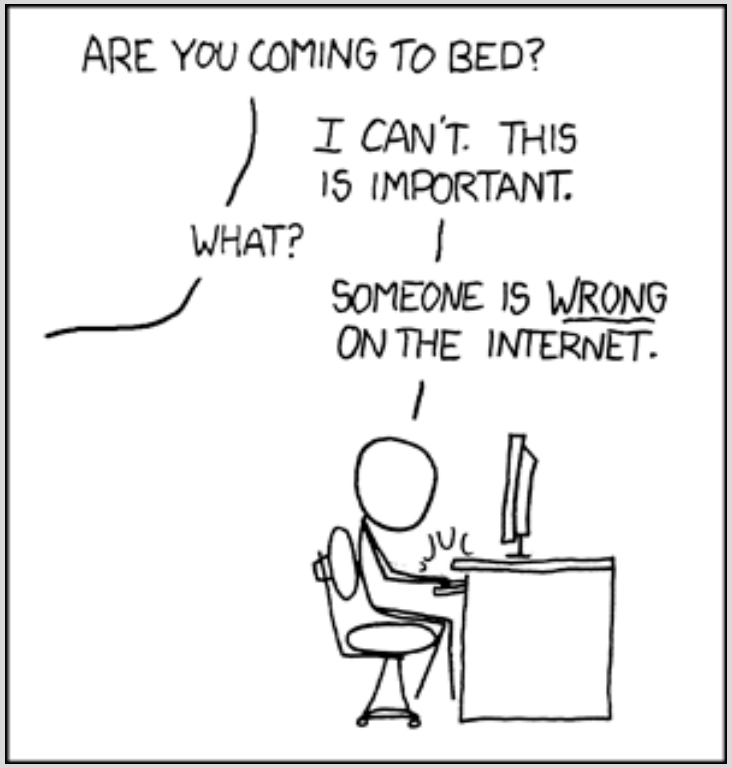
From: Is rheumatoid factor useful in primary care? A retrospective cross-sectional study (2013) http://link.springer.com/article/10.1007/s10067-013-2236-0/fulltext.html

Bottom line?

- Role of RF in diagnosing RA in primary care remains unclear
- Newer tests (e.g. ACPA), are emerging with higher specificity and positive predictive values, but similar sensitivity
- Currently GPs should base diagnostic and referral decisions on clinical features. A positive RF or ACPA has value in supporting these decisions, but a negative test does not rule out disease

What is the ONE thing I need to remember from today?

Don’t believe everything you are told,
Ask for the Evidence!



www.xkcd.com

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If you come across a new test or are thinking about implementation:

Have a look at our website
http://www.oxford.dec.nihr.ac.uk/

If we haven't assessed it, please let us know about it!
dec@phc.ox.ac.uk

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Point-of-care tests in airways disease

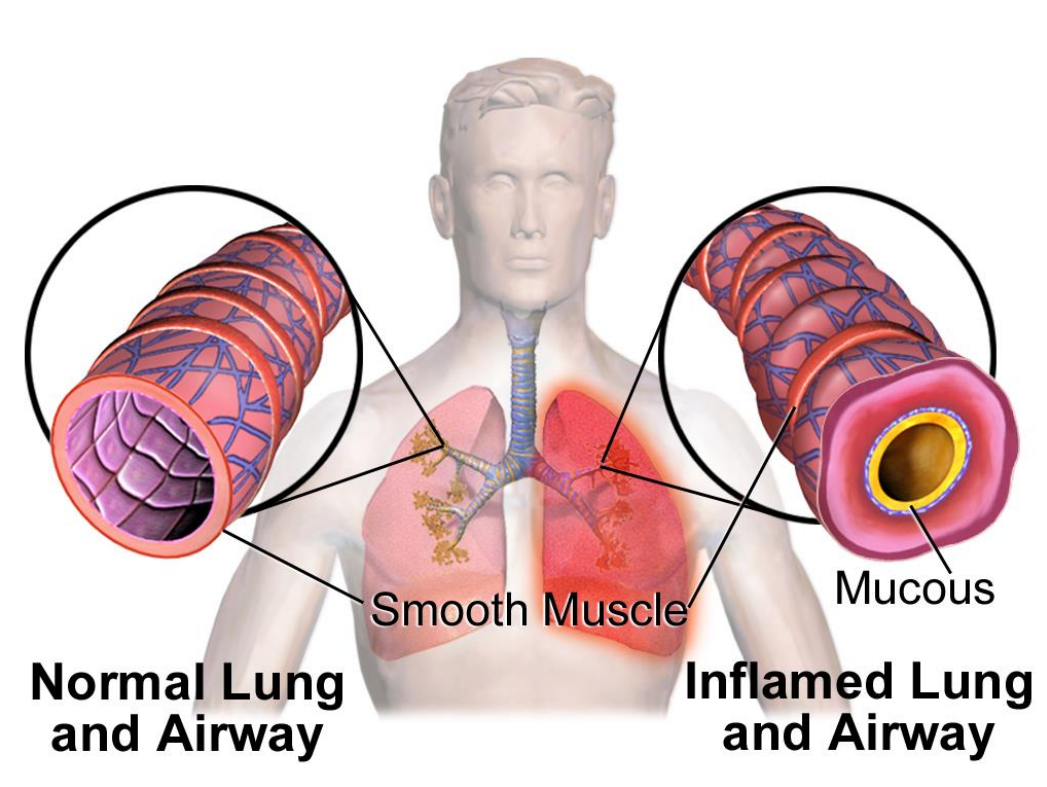
Dr Helen Ashdown. 18 May 2015
GP and NIHR Doctoral Research Fellow

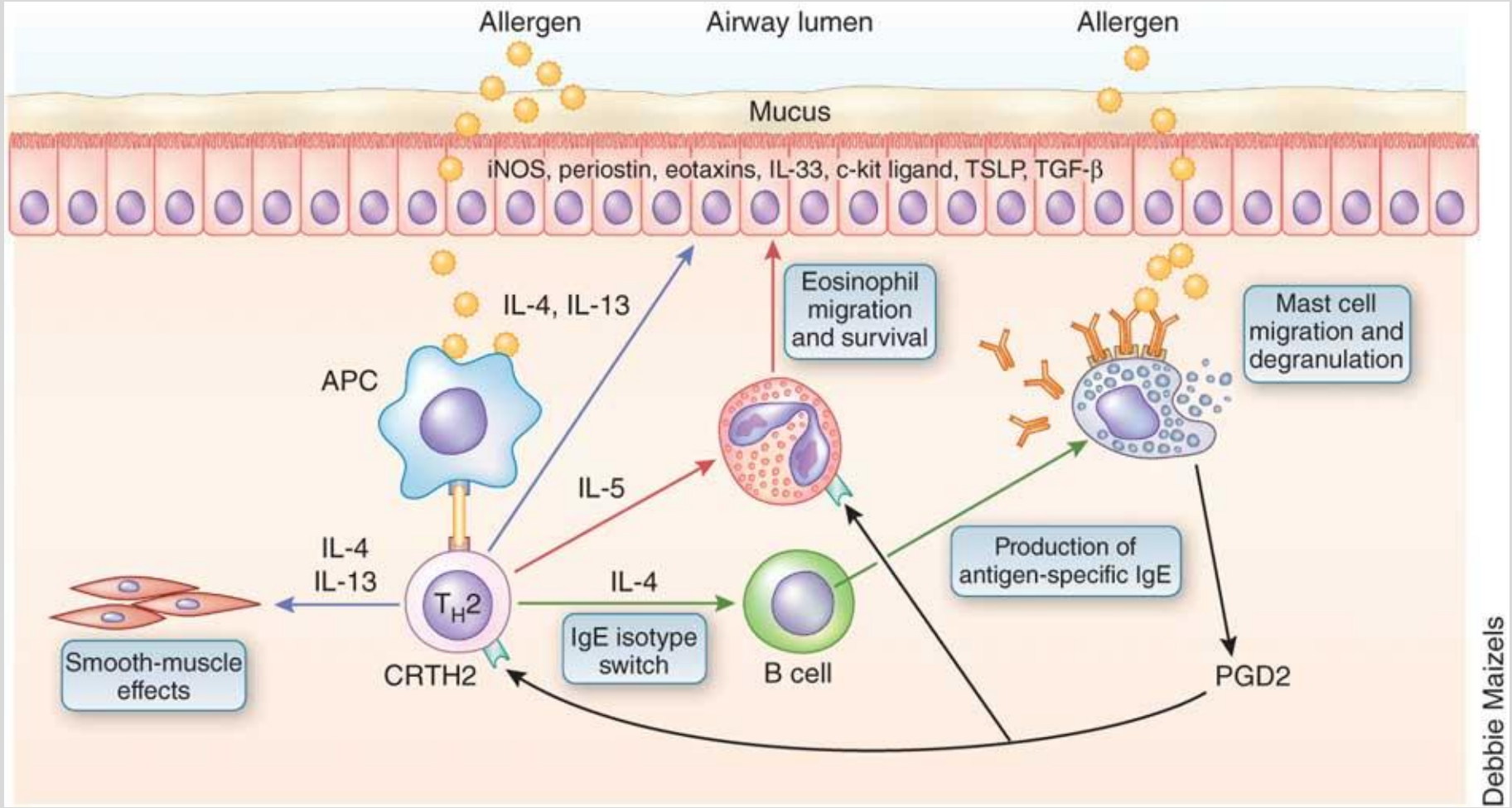
Outline

- Eosinophils, FeNO and steroid responsiveness in asthma and COPD
- Immediate horizons: FeNO in asthma
- More distant horizons: Eosinophils in COPD
- Primary care studies on the horizon

Airways disease

- Inflammation and bronchoconstriction
- T_H2-mediated
  - Eosinophils
  - Nitric oxide





From: Wenzel, S.E. (2012). Asthma phenotypes: the evolution from clinical to molecular approaches. *Nature Medicine* **18**, 716–725.

- NO and eosinophils increased in airway
- Steroid treatment targets this T_H2 response

Steroid responsiveness

- Eosinophilic airway inflammation (NO, sputum and blood eosinophils) is a reliable predictor of response to steroids, regardless of underlying diagnostic label
- Management strategies which seek to minimize eosinophilic airway inflammation substantially reduce exacerbation frequency in asthma and COPD

Pavord, I. D., et al. (2008). Inflammometry to assess airway diseases. *Lancet* **372**(9643): 1017-1019.

Over-diagnosis of asthma

- Non-specific symptoms – GORD, post-viral bronchial hyper-responsiveness, anxiety
- Trials of inhaled steroid treatment likely to be positive
  - Self-limiting
  - Fluctuation over time
  - Observer bias

Pavord, I. D., et al. (2015). Asthma diagnosis: addressing the challenges. *Lancet Respir Med.*

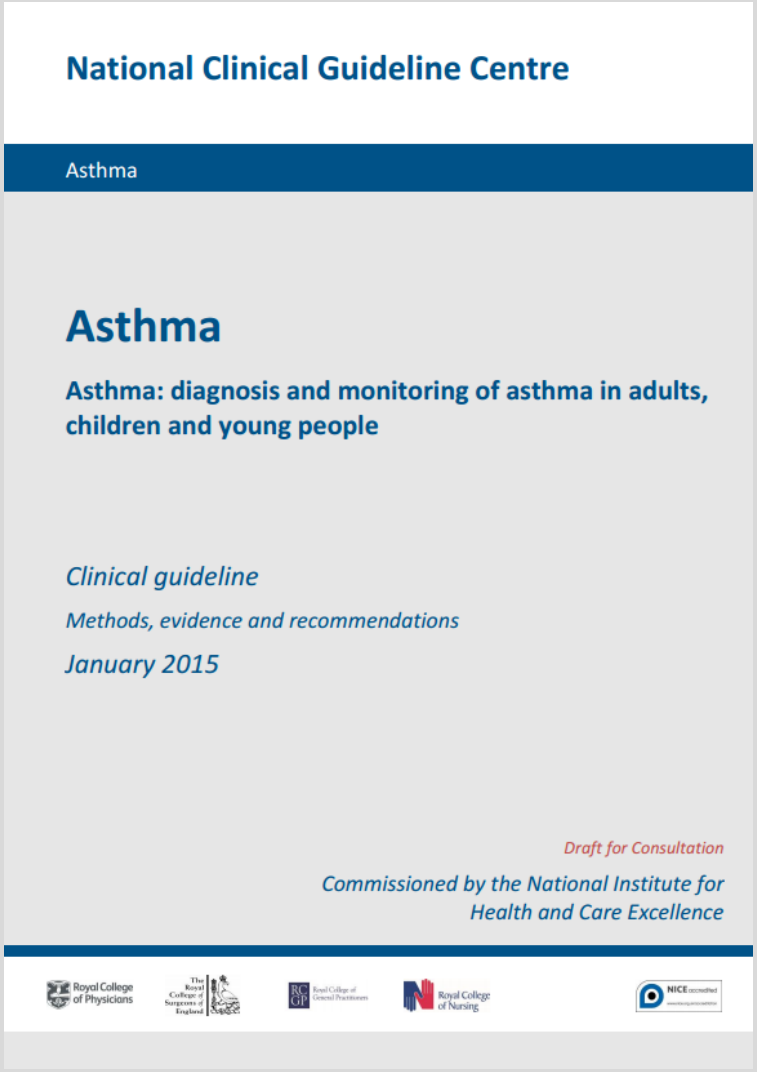
Immediate horizons: FeNO

- Portable easy-to-use breath test
- FeNO correlates with airway eosinophilic inflammation
- Reliably predicts response to steroids

Bjermer, L., et al. (2014). Current evidence and future research needs for FeNO measurement in respiratory diseases. *Respir Med* **108**(6): 830-841

NICE

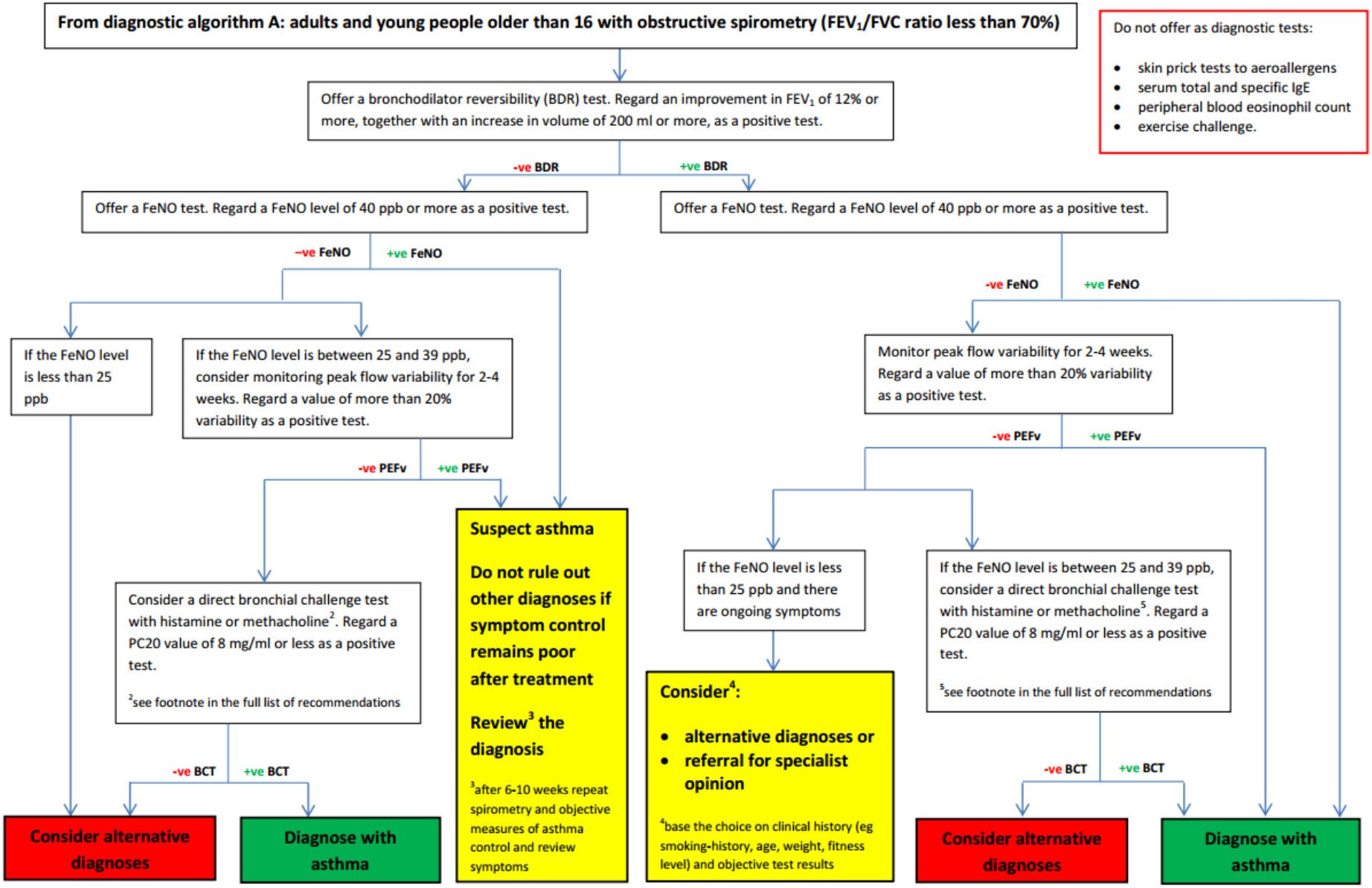
- Add-on test to diagnostic pathway
- Sensitivity ~80%, specificity ~90% (FeNO cut-off 40ppb vs. physician)
- £10-13 per use (£6.36 equipment cost)



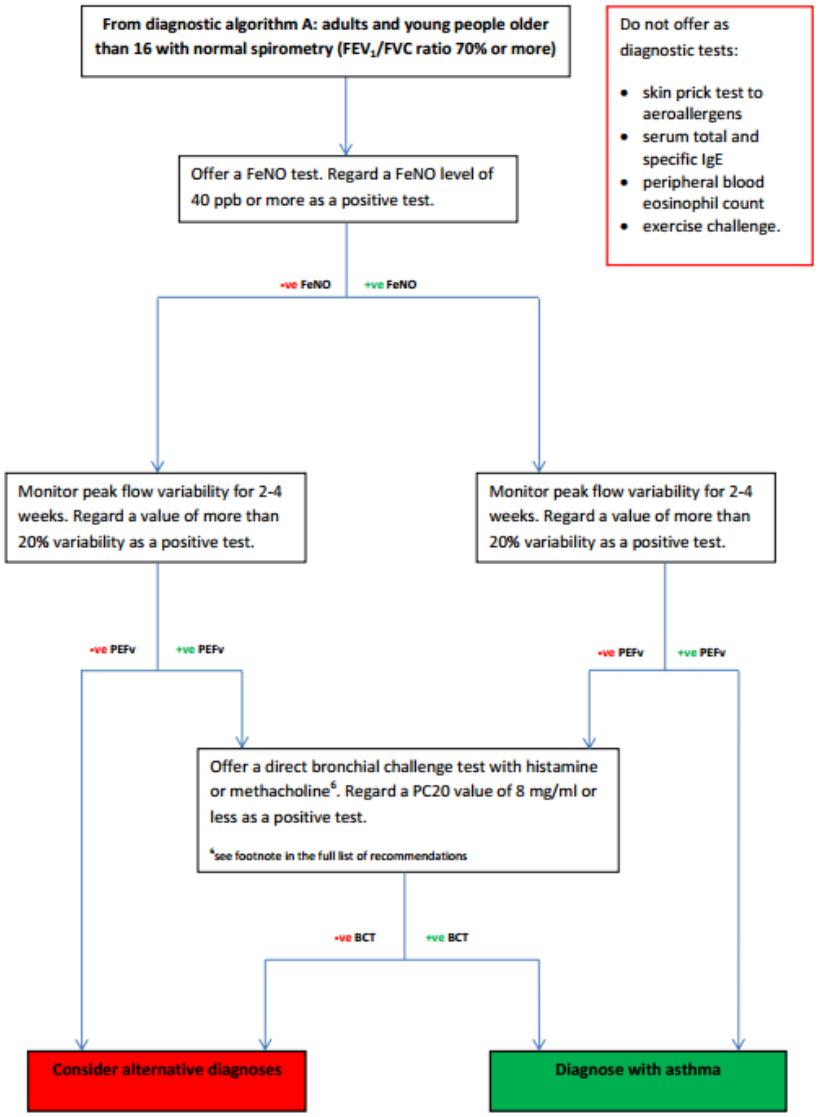
NICE Clinical Guideline (draft for consultation, January 2015). Asthma: diagnosis and monitoring of asthma in adults, children and young people.

DRAFT FOR CONSULTATION (January 2015)

Diagnostic algorithm B1 – objective tests for adults and young people older than 16 with obstructive spirometry



Diagnostic algorithm B2 – objective tests for adults and young people older than 16 with normal spirometry

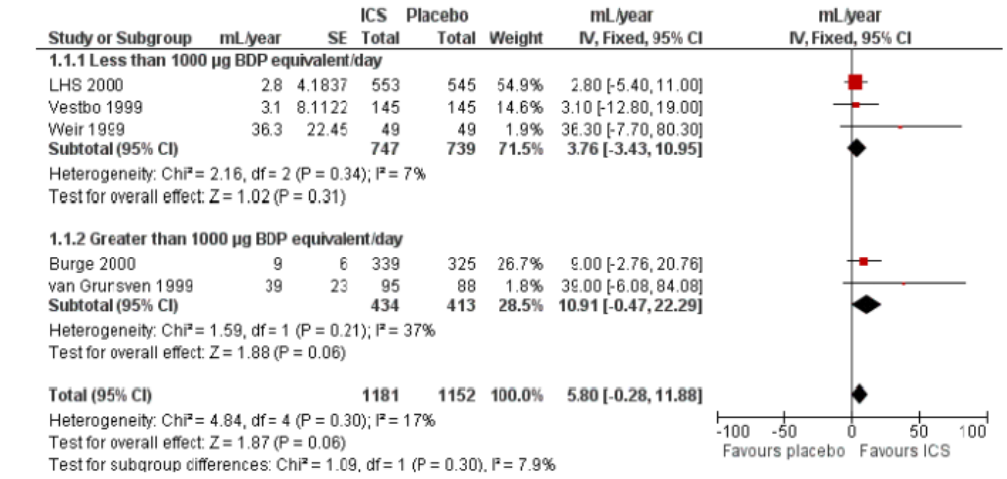


NICE Clinical Guideline (draft for consultation, January 2015). Asthma: diagnosis and monitoring of asthma in adults, children and young people.

Distant horizons: COPD

- Inhaled steroid treatment in asthma well-established
- Less consistent benefit in COPD

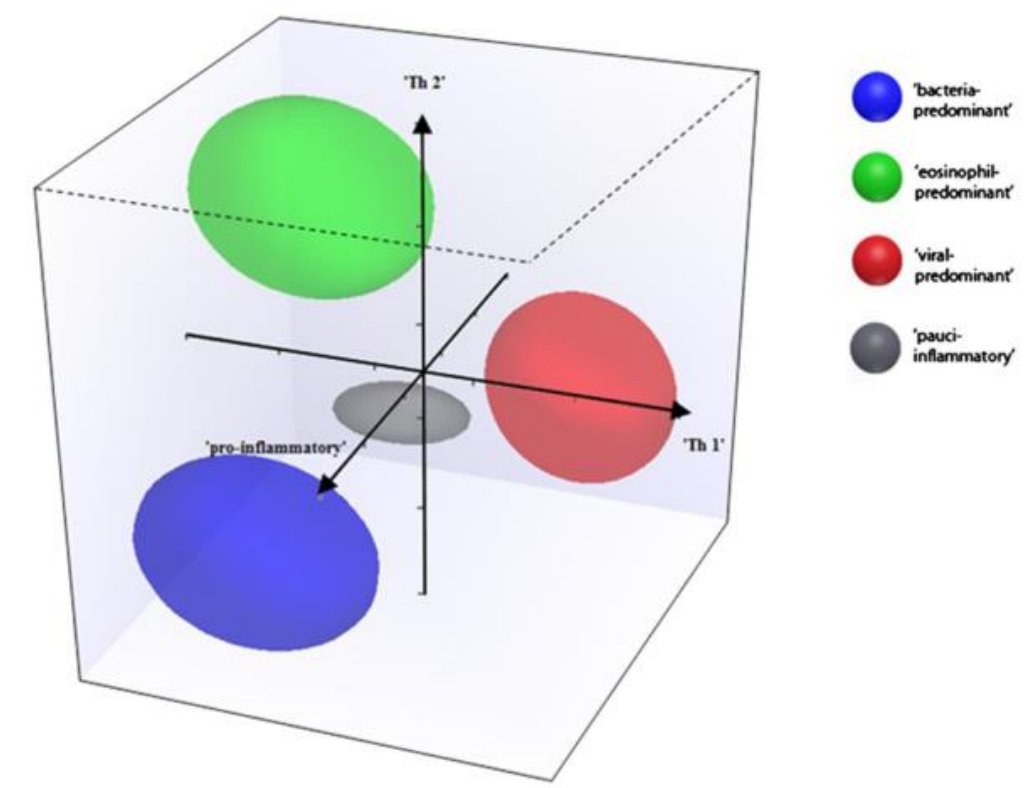
Figure 2. Forest plot of rate of decline of post-bronchodilator FEV1 (mL/yr), using generic inverse variance analysis



Yang IA, Clarke MS, Sim EH, Fong KM (2012). Inhaled corticosteroids for stable chronic obstructive pulmonary disease. *The Cochrane database of systematic reviews* **7**: CD002991.

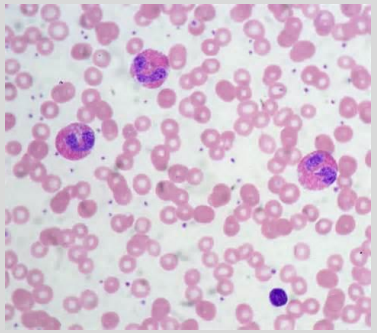
Eosinophil subgroup in COPD

- T_H2/eosinophil-predominant subgroup of COPD patients – blood and sputum
- May account for inconsistent response to steroids



Bafadhel M, McKenna S, Terry S, Mistry V, Reid C, Haldar P, et al (2011). Acute exacerbations of chronic obstructive pulmonary disease: identification of biologic clusters and their biomarkers. *American journal of respiratory and critical care medicine*. **184(**6): 662-71.

COPD exacerbations



- RCT of eosinophil-directed vs. standard therapy with oral prednisolone
  - Blood eosinophils ≤ or >2%
- Patients who were eosinophil-negative
  - More treatment failures when given steroids
  - Improved symptom scores when given placebo

Bafadhel, M., et al. (2012). Blood eosinophils to direct corticosteroid treatment of exacerbations of chronic obstructive pulmonary disease: a randomized placebo-controlled trial. *Am J Respir Crit Care Med* **186**(1): 48-55.

Long-term COPD

- Steroid treatment improved symptoms, lung function and quality of life scores in more 'eosinophilic' patients (sputum)
- Reduction in exacerbations when managed by sputum eosinophil count (Siva 2007)

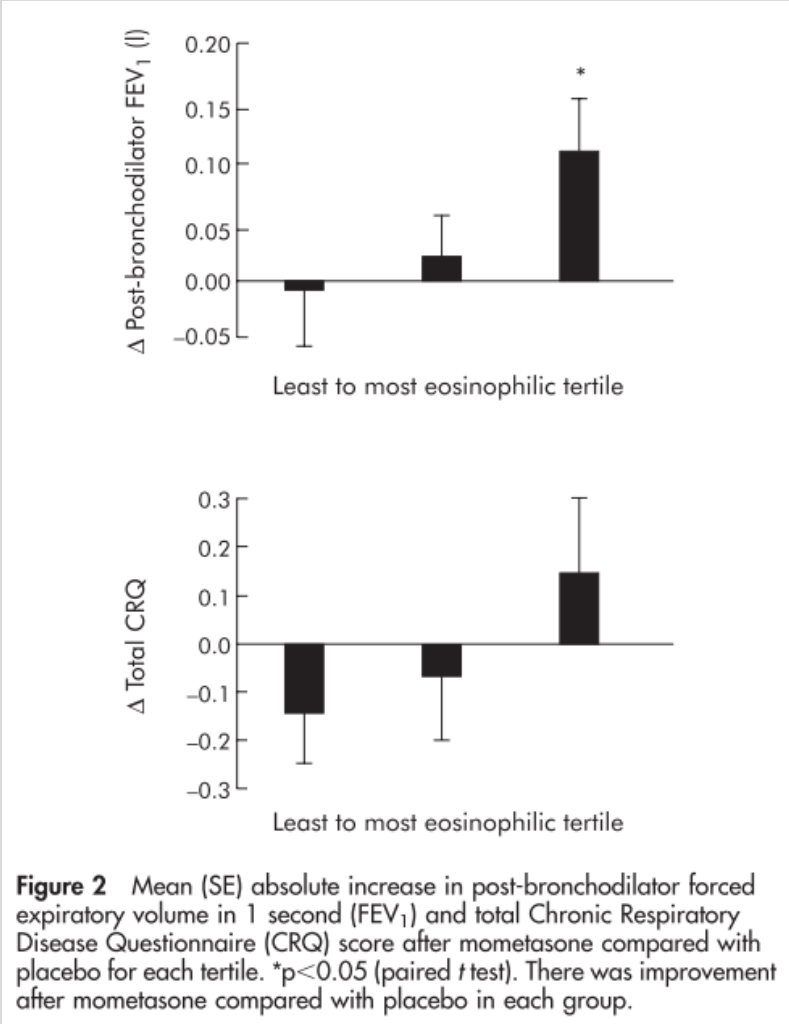


Figure 2 Mean (SE) absolute increase in post-bronchodilator forced expiratory volume in 1 second (FEV_1) and total Chronic Respiratory Disease Questionnaire (CRQ) score after mometasone compared with placebo for each tertile. *$p<0.05$ (paired *t* test). There was improvement after mometasone compared with placebo in each group.

Brightling CE, McKenna S, Hargadon B, Birring S, Green R, Siva R, et al. (2005). Sputum eosinophilia and the short term response to inhaled mometasone in chronic obstructive pulmonary disease. *Thorax.* **60**(3): 193-8.

Future questions

- Translating secondary care research into primary care setting – earlier disease/steroid-naive
- POC blood eosinophils in exacerbations
- Long-term management in steroid-naïve patients
  - Blood eosinophils
  - FeNO

White cell count differential (eosinophils)

Coming soon to Thames Valley…

- COPD exacerbations
  - RCT of point-of-care eosinophils and CRP to target antibiotics/steroids
  - RCT of point-of-care CRP testing to target antibiotic prescribing (PACE)
- Long-term COPD management
  - Establishing variability of FeNO and blood eosinophils in stable steroid-naïve patients

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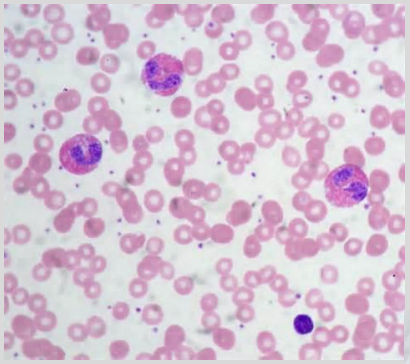

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