

## Online supplementary Table S8b

### QUESTION

#### Can measuring blood eosinophil count help diagnose asthma in adults with episodic/chronic suggestive symptoms?

**POPULATION:** Population of adults (>18 yrs old) with diagnostic uncertainty of asthma

**INTERVENTION:** Blood eosinophil count (BEC)

#### **GOLD STANDARD:**

1. Peak flow variability > 20% or spontaneous variation in FEV<sub>1</sub> > 12%- and 200-ml between several clinic visits
2. Bronchodilation > 12% AND > 200 ml improvement
3. Airway hyperresponsiveness: PC20 < 16 mg/ml (or 8 mg/ml) of Methacholine (or Histamine) or PD mannitol < 625 mg or fall in FEV<sub>1</sub> > 10% after exercise
4. Improvement in FEV<sub>1</sub> > 12% and 200 ml after a 2-week course of OCS or a 4-week course of ICS

### ASSESSMENT

#### Test accuracy

How accurate is the test?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very inaccurate <input checked="" type="radio"/> Inaccurate <input type="radio"/> Accurate <input type="radio"/> Very accurate <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Low test sensitivity (ranging from 0.15 to 0.59)</p> <p>High test specificity (ranging from 0.39 to 1.0)</p> <p>No data on blood eosinophils expressed as absolute value. Studies have concentrated on blood eosinophils expressed as % of leucocytes</p> <p>One study (Nekoe et al) provided the 95% specificity at 5.9%</p>	<p>Two large studies (one prospective from primary care and one retrospective from secondary care) providing similar AUC.</p> <p>AUC around 0.6. Thresholds ranging between 4-6%</p>

#### Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Trivial</li> <li>○ Small</li> <li>X Moderate</li> <li>○ Large</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	<p>BEC might be useful to endotype asthma and establish eligibility to biological treatment (particularly anti-IL-5) in severe forms of the disease. Recent evidence suggest also that it might be a marker for the necessity to use ICS.</p> <p>Blood eosinophils is better to phenotype than diagnose asthma</p>	

### Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Large</li> <li>○ Moderate</li> <li>○ Small</li> <li>X Trivial</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	<p>No major undesirable effects. Pain and concerns related to venipuncture</p>	

### Certainty of the evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Very low</li> <li>X Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>		

### Certainty of the evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<ul style="list-style-type: none"> <li>○ Very low</li> <li>X Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>	Recent data (included in the narrative section) suggest that blood eosinophils > 150 $\mu$ l in newly diagnosed mild asthma makes ICS treatment necessary to prevent asthma exacerbation (Pavord I, Lancet Respir Med 2020)	
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### Certainty of the evidence of test result/management

How certain is the link between test results and management decisions?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Very low</li> <li>X Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>		

### Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>X Favors the comparison</li> <li>○ Probably favors the comparison</li> <li>○ Does not favor either the intervention or the comparison</li> <li>○ Probably favors the intervention</li> <li>○ Favors the intervention</li> <li>○ Varies</li> <li>○ Don't know</li> </ul>	<p>Results of the test not known immediately, as opposed to FeNO</p> <p>Statistical performance not better than FeNO</p> <p>Bronchial challenge tests show better PPV and NPV</p>	

### Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input checked="" type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input type="radio"/> Varies <input type="radio"/> Don't know	Non-expensive and easy to perform test	
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## Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input checked="" type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		

## Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Some patient may experience adverse event during venepuncture.	

## Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes	Non-expensive and easy to perform test	

X Yes o Varies o Don't know		
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TYPE OF RECOMMENDATION

Strong recommendation against the intervention o	Conditional recommendation against the intervention ●	Conditional recommendation for either the intervention or the comparison o	Conditional recommendation for the intervention o	Strong recommendation for the intervention o
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CONCLUSIONS

Recommendation

The TF suggests not measuring blood eosinophil count for asthma diagnosis (conditional recommendation, low quality of evidence)

Blood eosinophil count does not define asthma but rather contributes to phenotyping

Justification

BEC lacks sensitivity to diagnose asthma, with sensitivities ranging between 21% to 59% in the reported studies. A BEC does not provide immediate results at the time of the consultation in order to directly help the clinician, although as blood leukocyte differential is a test frequently performed for several indications in routine practice, it may be that a previous test is available at the time of the consultation. BEC cut-offs above 4% and 6% have a specificity greater than 80% and 95% respectively and may help the clinician to be confident in their diagnosis in patients with suggestive symptoms.