

Supplementary table S12b

QUESTION

Can bronchial challenge testing help diagnose asthma in adults with episodic/chronic suggestive symptoms?

POPULATION:	Secondary Care
INDEX TEST:	Bronchial Challenge (Methacholine, Histamine, Mannitol)
GOLD STANDARD	BDR Reversibility (>12% and 200ml improvement)

ASSESSMENT

Test accuracy

How accurate is the test?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very inaccurate <input type="radio"/> Inaccurate <input checked="" type="radio"/> Accurate <input type="radio"/> Very accurate <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Bronchial challenge has high sensitivity but lower specificity when compared against BDR as the reference 'gold standard'.</p> <p>Bronchial challenge testing has sensitivity between 0.63 (Porpodis study) to 1.07 (Ulrik study).</p>	<p>BDR more likely to be positive in lower FEV₁ (<90%)</p> <p>Sensitivity/Specificity much greater if high pre-test probability.</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input checked="" type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Making a correct diagnosis with a more sensitive and specific test is highly desirable.</p>	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none">○ Large○ Moderate○ Small○ Trivial○ Varies○ Don't know	No major undesirable effects of bronchial challenge testing. Mannitol is known to cause cough. Histamine can cause flushing, rashes. These are short lasting and reversible.	

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">○ Very low○ Low○ Moderate○ High○ No included studies	<p>For diagnosing asthma – moderate certainty.</p> <p>For excluding asthma – low certainty, but sensitivity % are much higher than specificity which is highly variable from 0.07-0.95</p>	Having a test which is highly sensitive helps to exclude asthma if the test is negative, so is a desirable test characteristic.

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
<ul style="list-style-type: none">○ Very low○ Low○ Moderate○ High○ No included studies	In the presence of a current symptoms, a positive bronchial challenge test will give a high confidence of initiating asthma management.	

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">○ Very low○ Low○ Moderate		

<input type="radio"/> High <input type="radio"/> No included studies		
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	No major undesirable effects of bronchial challenge testing. Mannitol is known to cause cough. Histamine can cause flushing, rashes.	
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Large costs <input type="radio"/> Moderate costs <input 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	Bronchial challenge testing requires more resources (staff, equipment, training, time) and cost of methacholine, histamine is greater. Mannitol kits are easier as they require no air source so can be performed in a low resource setting with a spirometry. Cost need to be balanced against the cost of a delayed or missed diagnosis, and inappropriate use of inhalers.	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input type="radio"/> Probably no impact <input type="radio"/> Probably increased	None Identified	

<input type="radio"/> Increased <input type="radio"/> Varies <input checked="" type="radio"/> Don't know		
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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	<p>The tests are acceptable and safe. Patient's more likely to get a better indication whether or not they have asthma.</p> <p>Many patients taking long term ICS/LABA are often reluctant to withdraw from ICS/LABA – fearful of bronchoconstriction and cough (mannitol).</p>	

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 <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Hospitals: Increased cost for consumables, staff, training, time in physiology lab, space for equipment</p> <p>Patients: Need to ensure withdrawn off medication. Potentially takes longer time than BDR.</p> <p>Physiologist: Increased workload</p>	

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

The TF suggests bronchial challenge testing should be performed in secondary care to confirm asthma diagnosis in adults (Conditional recommendation for the intervention, low quality of evidence)

A provocative concentration of methacholine (PC20-M) or histamine (PC20-H) <8 mg/ml in steroid-naïve patients and <16 mg/ml in patient receiving regular inhaled corticosteroids supports a diagnosis of asthma

Indirect challenges such as mannitol or exercise may be considered in patients who remain negative with direct constricting agents

Justification

In making a conditional recommendation the TF balanced the desirable effects of making a diagnosis, against any undesirable effects, risks to patients and the resources required to implement and make bronchial challenge testing a feasible test. Although methacholine, histamine and mannitol are very safe, these tests require additional equipment, reagents, time in the laboratory, air source, and trained staff, with access to resuscitation facilities and medical personnel in rare cases of severe bronchoconstriction. This will undoubtedly increase the costs in comparison to BdR testing. Mannitol challenge appeared slightly more specific than methacholine challenge, albeit one study.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities