

## SIGN 158: British guideline on the management of asthma

### Results of expert group scoping exercise

The principal results of the scoping exercise are detailed in Table 1.

A total of nine group members responded: Chris Barber (CB), Anne Boyter (AB), Toby Capstick (TC), Erol Gaillard (EG), Natalie Harper (NH), James Paton (JP), Hilary Pinnock (HP), Stephen Scott (SS), Steve Turner (ST).

HSR, health services researcher (SIGN)

*Table 1: Scoping feedback by guideline section from expert group members*

Section	Proposed action	Rationale	Suggested new key questions
<b>4 – Monitoring asthma</b>	Revalidate (JP)	Not much new information	
<b>5 – Supported self-management</b>	Refresh (NH)		
	Revalidate (HP) - 'no new evidence review' but will be 'editorially refreshed' <ul style="list-style-type: none"> <li>• 5.1 Effectiveness of supported self-management</li> <li>• 5.3 Schoolchildren</li> <li>• Limited health literacy</li> <li>• 5.4 Adherence</li> <li>• 5.5.2 Implementation of interventions</li> </ul> I am assuming that we need to go through the SIGN process to include	<ul style="list-style-type: none"> <li>• <b>5.1 Effectiveness of supported self-management.</b> We ought to include Hodkinson (a network meta-analysis) and my meta-review which with the implementation systematic review (which is already cited in SIGN 158) provide a comprehensive overview of supported self-management for people with asthma.</li> <li>• <b>5.3 Schoolchildren.</b> See below under organisation of care – there are two new SRs on school-based interventions.</li> </ul>	

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	<p>new references and I fear that an editorial 'refreshing' does not allow this. It would seem unfortunate not to include these systematic reviews.</p>	<ul style="list-style-type: none"> <li>• <b>Limited health literacy.</b> Health literacy does not have a section at the moment, but does need to be highlighted. There is a SR exploring the challenge of supported people with limited health literacy to 'self-manage' their asthma, which I don't think we mention at the moment.</li> <li>• <b>5.4 Adherence.</b> See below under organisation of care – there is a new Cochrane review on digital interventions to improve adherence. The text under <i>Electronic monitoring</i> needs to be 'refreshed' (as well as the section on IT strategies (in 14.4.3) which needs to cross reference to section 14.4)</li> <li>• <b>5.5.2 Implementation of interventions.</b> This can be refreshed with some developmental evidence for the different strategies, but the message is still correct.</li> </ul>	
<p><b>6 – Non-pharmacological management</b></p>	<p>Refresh but may be some new questions (JP)</p>	<p>Recent information on use of masks, indoor air filtration, complex interventions. Lots of papers about filters indoor, breathing exercise and vitamin D – much it of low quality. However, a synthesis of this information is not likely to be found elsewhere More importantly, this is an important section because it brings together information about the place and effectiveness of non-pharmaceutical approaches, including allergen exclusion and desensitisation</p>	<p>May be new questions around environmental factors and how to mitigate their impact</p>

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	Refresh, especially KQ4: environmental exposure (EG)	Recent developments and media coverage around fungal allergen exposure in the home and air pollution contributing to asthma deaths	
	Refresh (NH)		
	Refresh (TC)	Large volume of studies including systematic reviews that could add to this section	
	Refresh (AB)	The searches look to have found new information and studies that could change recommendations	
	Refresh (HP) – Update: 6.2.14 Breathing exercises 6.2.19 Exercise and pulmonary rehabilitation	These sections have a growing evidence base – including diverse modes of delivery (so cross reference with organisation of care.	
	Refresh (SS)	<p>The overall recommendations do not change from first impressions due to the quality of studies however further critical review of the evidence presented is warranted. On first appearance there looks to be positive (but mixed) signals for air purification. There is more evidence to review for rehab and breathing exercises and mixed reports for Vitamin D.</p> <p>There is more evidence available for air purification in the abstracts presented that may suggest a recommendation which is a change from previous. Most of the evidence in the abstracts is positive warranting further critical exploration of the data.</p> <p>Review of evidence for yoga therapy / breathing exercises / rehab also warranted in view of the number of abstracts available focussed on this aspect.</p>	

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		<p>May even warrant a spinoff section on physio recommendations. There is quite a lot on inspiratory muscle training esp in children.</p> <p>There is additional evidence for Vitamin D supplementation that also requires more critical exploration. Especially in vit D supplementation in pregnancy and future risk of wheeze in children. This may revalidate or refresh the current understanding</p> <p><b>CAUTION:</b> Thorsteinsdottir F, Walker KC, Runstedt SE, Jacobsen R, Maslova E, Backer V, Heitmann BL and Handel MN. <b>The role of prenatal vitamin D on the development of childhood asthma and wheeze: An umbrella review of systematic reviews and meta-analyses.</b> Clinical Nutrition. 2022;41(8):1808-1817. This review states that all other studies are of poor quality and therefore cannot be used.</p>	
	<i>HSR – possibly refresh</i>	<i>Papers that may warrant potential change</i>	
<b>7 – Pharmacological management</b>	Refresh (JP)	This is closely linked to the difficult asthma section, particularly around the issue of new biologics. There will be overlap in the papers for both key questions. Importance of new drugs in the management of difficult asthma	
	New (EG)	Rapid developments in last few years in the field of biologics management. Clinicians need to understand who is eligible – phenotype – and the options that are available to match the phenotype.	<p>Which patients should be referred for biologics</p> <p>Phenotypes associated with a good response to specific biologics</p>

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	Refresh data on anti-IL5 MABs (TC)	<ul style="list-style-type: none"> <li>Significant volume of new data. Update data on anti-IL5 MABs, particularly comparative data from systematic reviews, and oral corticosteroid reduction</li> </ul>	
	New (TC)	Need information on anti-IL4/13 MAB (dupilumab) and anti-TSLP MABs (Tezepelumab) - no data in literature search (but is in section 10: difficult asthma - should be here), so needs to be repeated.	Potentially need a new key questions on role of anti-IL4/13 and anti-TSLP MABs, similar to previous key questions on the role of anti-IgE and anti-IL5 MABs
	Refresh (AB)	Biologics. This is linked to the difficult asthma section and there is significant new information about new products and their use. There is some overlap with difficult asthma	
	New – biologics (SS)	Although the data for Omalizumab, Mepo and Benra remain the same with some ongoing supportive evidence there is now good data and availability of Bupilumab and Tezepelumab that will need to be incorporated into guidance. Recommendations for Dupilumab and Tezepelumab need to be included as they are not present in the 2019 guideline. Also the data on comparison studies needs to be considered.	
	Refresh – Bronchial thermoplasty (SS)	There is more evidence although it does not change the current recommendation it updates long term safety data Also some “real world” data.  Bronchial thermoplasty may not be available soon due the company who make the equipment discontinuing due to the rise of biologics replacing the	

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		need for the intervention. This will obviously have an impact on the recommendations going forward (I was surprised how positive the abstracts provided for it were).	
	<i>HSR - refresh</i>	<i>Updates warranted for omalizumab, dupilumab, tezepelumab, benralizumab</i>  <i>Thermoplasty – papers that may warrant refresh</i>	
<b>8 – Inhaler devices</b>	Refresh (NH) – could be linked with environmental section		
<b>9 – Management of acute asthma</b>	Refresh (JP)	There looks to be some new information. The most significant is the increasing evidence for the use of SMART therapy. There is little new information. This is another important section because it summarises the evidence and provides widely-used evidence-based algorithms for the treatment of asthma attacks.	
	Revalidate (EG)	To me there has not been much new in this area, maybe in the context of virtual wards but that is maybe a little stretch	
	Refresh (NH)		
	Refresh (TC)	Minor update and low priority. <ul style="list-style-type: none"> <li>Minor update to ketamine and Sevoflurane/isoflurane section 9.9.5 - only minor updates and no substantive change to current section 9 is likely, so would not be a priority.</li> </ul>	
	Refresh (AB)	There is potentially new information but this might not be a priority area	

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	Revalidate (SS)	<p>New papers noted but do not alter the current guideline recommendations.</p> <p>There is some low-grade evidence to review to confirm the current recommendations on Ketamine. A study requires critical review regards isoflurane and ECMO</p> <p>New study for Magnesium in children</p>	
	<i>HSR - refresh</i>	<i>Potential update to ketamine but unlikely to result in a recommendation</i>	
<b>10 – Difficult asthma</b>	Refresh (JP)	<p>There is significant new information since the last guideline particularly on the use of biologics. There is significant new information and new medicines since the last guideline particularly around the use of biologics. This includes information about the use of mabs in children. Bronchial thermoplasty looks to be clearly effective.</p> <p>The management of difficult asthma is changing a lot with the introduction of the new biologic agents. GINA now has very good advice in this area, The BTS/SIGN guideline will need updating on regular basis to reflect the changes that are coming through</p>	
	Refresh (TC)	<p>Minor update and low priority.</p> <ul style="list-style-type: none"> <li>• Only a couple of studies relevant (pollen, adherence). Probably would not add much, so would not be a priority</li> <li>• Most of the studies identified overlapped with section: biologics and fit better there (especially Tezepelumab)</li> </ul>	

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	Refresh (AB)	There is significant new information and new medicines since the last guideline was published on the biologics used in this area. This includes information about the use of mabs in children	
	New (ie complete redraft) (HP) - Pathways for assessing people with uncontrolled asthma (in primary or secondary care) and appropriate referral to a severe asthma clinic	<p>A huge issue at the moment are pharma-funded initiatives in primary care identifying and reviewing people with uncontrolled asthma (with a view to increasing referrals to severe asthma clinics and prescribing of biologics). <u>Unbiased</u> evidence on optimal pathways would be very helpful for healthcare managers who are currently accepting/promoting these services as well as for clinicians – and patients, of course. This needs to cross reference with section 14.1.</p> <p>There are some papers in the scope that might inform this pathway (e.g studies about adherence in this group) but I think a search would need to look specifically for ‘pathway-relevant ‘evidence. We may find very little (unbiased) evidence but then we need to highlight the research gap. Without this evidence, implementing the clinical recommendations in a way that identifies all the people with uncontrolled asthma who would benefit without referring everyone with uncontrolled asthma who could be managed in primary care. Evidence on defining ‘response/non-response’ to biologics might also inform pathways, as knowing when to stop therapy is as important as knowing when to start it.</p>	What is an appropriate pathway for identification of people with uncontrolled asthma (typically in primary care) who would benefit from a referral to a severe asthma clinic?



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	New (SS) - Severe Asthma: To combine with biologics recommendations also	This section, abstracts crosses over with the biologic section so needs to use both sets of references. The addition of new biologics that were not in the 2019 guideline need adding: Dupilumab and Tezepelumab. Evidence and recommendations for Dupilumab and Tezepelumab require adding. This is also crossing over into the biologic section recommendations and needs to be combined. Otherwise no change otherwise to the severe asthma section.	
	<i>HSR – revalidate/refresh</i>	<i>Recommendations unlikely to change</i>	
<b>Phenotyping (part of biologics)</b>	Refresh (EG)	Rapid developments in last few years in the field of biologics management. Clinicians need to understand who is eligible – phenotype – and the options that are available to match the phenotype.	Which patients should be referred for biologics  Phenotypes associated with a good response to specific biologics
	Revalidate (SS)	There are no studies in the scoping list “phenotyping” that change the current guideline recommendations. However there are areas for future research and may need to be mentioned in section 4.5 “other approaches” and maybe stronger evidence that blood eosinophils are a marker of future asthma attack risk.  Approached worthy of a mention include Breathomics, Microbiome, Aspergillus sensitisation and plasma proteomics. All are research tools but show potential for future use.	

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		Although this does not change current recommendations it is useful to highlight future possibilities and areas for research that may be useful subsequently.	
	<i>HSR – possibly refresh</i>	<i>Some papers may warrant potential change</i>	
<b>12 – Asthma in pregnancy</b>	Refresh (NH)		
<b>14 – Organisation of care</b>	Revalidate (HP) - ‘no new evidence review’ but will be ‘editorially refreshed’ <ul style="list-style-type: none"> <li>• 14.3 Asthma clinics</li> <li>• 14.4 Telehealthcare</li> <li>• 14.5 School-based interventions</li> </ul> I am assuming that we need to go through the SIGN process to include new references and I fear that an editorial ‘refreshing’ does not allow this. It would seem unfortunate not to include these systematic reviews.	<ul style="list-style-type: none"> <li>• <b>14.3 Asthma clinics.</b> There is currently no mention of templates as a strategy for facilitating the recommended ‘structured review’. We have published a SR showing that templates increase adherence to guideline recommended task, though may compromise patient-centred care.<sup>4</sup></li> <li>• <b>14.4 Telehealthcare.</b> This is a fast moving area accelerated by the COVID pandemic and needs considerable ‘refreshing’. We don’t even mention AI – and we probably need to change the name to ‘Digital care’ which seems to be the latest umbrella term! <i>Remote consultations.</i> One of my PhD students is completing a systematic review on asynchronous consulting and has found more papers than I expected; we have also done a realist review on delivering supported self-management in remote consultations.<sup>5</sup> <i>Digital support for adherence.</i> There is an important Cochrane review showing that digital technology (especially smart inhalers) can improve adherence and (for the first time)</li> </ul>	

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		<p>conforms that this can improve asthma outcomes.<sup>6</sup></p> <p><i>Will the diagnosis section look at CDSS?</i></p> <ul style="list-style-type: none"> <li>• <b>14.5 School-based interventions.</b> There is now a Cochrane review.<sup>7</sup> and our systematic review. These both support school-based interventions.</li> </ul>	
<b>Sputum cell counts</b>	Refresh (EG)	Don't think there has been much new in itself, but this fits with phenotyping to identify the most suitable biologic so would go with refresh in the context of phenotyping	
	Revalidate (SS)	There is no new evidence to support sputum cells counts in the abstracts provided. No change to current guideline required	
	<i>HSR – revalidate/refresh</i>	<i>Cochrane review may lead to stronger recommendation</i>	
<b>Severe asthma</b>	New (EG)	This is again tightly linked to biologics as the scoping review shows and needs to be part of the new section. Again not much new evidence in severe asthma as such in isolation.	
	New (NH)	This needs to be differentiated from what "Difficult asthma" is listed as (which has modifiable elements)	
<b>Digital technology linked with asthma</b>	New (NH)	The use of digital technology in its various forms including SMART digital inhalers and digital platforms	
<b>Environmental impact</b>	New (NH)		
<b>Air quality; indoor/outdoor air pollution</b>	New (NH)		
	New (CB)	<p>This area is relevant to asthma management as per multiple publications:</p> <ul style="list-style-type: none"> <li>• Every breath we take: the lifelong impact of air pollution. RCP London 2016.</li> </ul>	These will likely relate to what advice should be given to asthma patients with exposure.

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		<ul style="list-style-type: none"> <li>Air pollution: outdoor air quality and health NICE guideline [NG70] Published: 30 June 2017</li> <li>Indoor air quality at home. NICE guideline NG149. Published 08 Jan 2020</li> <li>BTS Position Statement on Air Quality and Lung Health Published 2022</li> </ul>	

#### Additional comments

We may want to think about a slight restructure given that biologics play such an important part.	EG
Technology and asthma has seen an explosion since covid and may need a new section	EG
Adherence and adherence monitoring is becoming a central part of non-severe asthma management and maybe deserves its own section, tied in with technology	EG
The elements that are not being covered by the NICE/BTS/SIGN document should be addressed with some guidance to all (and not specifically to one population of HCPs, such as primary care as this is presuming that primary care are not in receipt of the knowledge and other HCPs working in other areas are), we know that there are knowledge gaps throughout the whole system	NH
I am not sure that the inclusion of “sputum cell counts” and “thermoplasty” is relevant for the vast majority that will be utilising national guidance and so this may be better served by a “link to evidence” such as was discussed at the scoping meeting. Sections such as phenotyping could be linked with severe asthma.	NH
We should consider including a section on asthma in children and young people.	NH
We can adopt one of 2 approaches: Continue with the current layout in which case the answer to all questions is “yes” as people are very familiar with this and feel comfortable in locating information. Or we can align any new layout with the joint NICE/BTS/SIGN so that there is uniformity throughout. This is something that should be discussed by the group.	NH
Concern that NICE scope includes Occupational Asthma, but no intention to update it, or expand to include work-aggravated asthma which is much more common? Unclear how this all fits with recent BTS OA Clinical Statement.	CB
I think the main area to focus on is the biologics section, unless the new guideline is going to refer to existing NICE technology appraisals, otherwise will need an update here.	TC

Overall there are no major changes/reviews required except for the biologic section: The two biologics: Dupilumab and Tezepelumab are not included in the 2019 guideline.	SS
Severe/difficult asthma is the greyest of the grey in children and I'd be happy to be part of this group if that helped – I am not aware of any major leaps forwards in this area.	ST

### Recommendations

The working group recommends updating SIGN 158 as part of the pathway of care with the following approach:

- Revalidate and reformat 'Management of acute asthma' (existing section 9) as a standalone guideline, with further review in 3 years' time.
- Review and refresh 'Non-pharmacological management' (section 6) and 'Occupational asthma' (section 13) and produce as standalone guidelines, with further review in 3 years' time. These sections would be updated to reflect new evidence in environmental factors, air purification and breathing.
- Produce a new standalone guideline on uncontrolled asthma that includes guidance on pharmacological management (specifically biologics), assessment, phenotyping, high-risk patients, biomarkers and monitoring (replacing the existing sections 7 and 10).
- Review and update accompanying patient booklet.

### Decision

The recommendations were ratified by Healthcare Improvement Scotland Evidence Senior Management Team on 7 February 2024.