PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Diagnosis and management of asthma in children
AUTHORS	Martin, Joanne Townshend, Jennifer Brodlie, Malcolm

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Prof. Ian Sinha Institution and Country: Alder Hey Children's Hospital, United Kingdom of Great Britain and Northern Ireland Competing interests:None
REVIEW RETURNED	21-Mar-2022

GENERAL COMMENTS	Dear Dr Martin and colleagues This is a really excellent review and I have little to add. I think you have covered the main areas very well, and the paper is very well written A couple of thoughts: 1) I would add air pollution as a risk factor for development of asthma in children , BMJ . 2020 Aug 19;370:m2791. doi: 10.1136/bmj.m2791. 2) In our asthma clinic, teh ethos is that managing asthma is "33% ICS, 33% healthy living, 33% self-esteem, 1% everything else".... although this obviously doesn't cover all children, who do need something else, it would I think be worth mentioning the importance of good diet and exercise somewhere (self management section maybe?) 3 On this point it may be worth mentioning in the referral to a specialist section that there is a need for an MDT approach (at least in tertiary services) 4 I would make a mention in the ICS paragraph about the shift in GINA towards symptoms-drivern rather than daily steroids for mild asthma. This has been evaluated in children (and we are running an RCT about this - ASYMPTOMATIC). If it helps, we have written an editorial about this: https://pubmed.ncbi.nlm.nih.gov/31972134/ 5 I couldn't see a summary of biologics in the text itself - I wonder if one is warranted to discuss the developments in this field (or at least a nod to them - they probably only help a handful of children, but a reader may want to see your views on this... perhaps again in the "referral to specialist" section 6 Alongside PAAP I would discuss inhaler technique as an important aspect of self-management (the two tend to go together) - we know for example MDI without spacer is a suboptimal way to manage asthma

	Overall, congratulations on a lovely paper. Best wishes Ian

REVIEWER	Reviewer name: Dr. Aidan Searle Institution and Country: UHBristol Educ Ctr, United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	02-Mar-2022

GENERAL COMMENTS	I appreciate the opportunity to review this concise and well presented review of the Diagnosis and management of asthma in children. Although I am not a clinician I appreciate that the review provides a coherent overview of diagnostic procedures in the context of guidelines at the national and international level. However, as a qualitative researcher I am concerned that there has been little attention paid to the contribution that qualitative data can bring to understanding the management of children with asthma. Indeed, there is an existing body of work that has explored parental perceptions of childhood asthma and the implications for patient-practitioner communication that if included in the present review would serve to better understand and contextualise the implications for clinical practice. For example, health professionals' awareness of child and parent perceptions of asthma can influence asthma management decisions and the provision of information for families. Moreover, there have been attempts to consolidate the informational needs of parents with regard to the management of childhood asthma. Some of these issues are highlighted and discussed in this paper: https://www.nature.com/articles/s41533-017-0053-7

REVIEWER	Reviewer name: Dr. Simon Craig Institution and Country: United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	22-Mar-2022

GENERAL COMMENTS	Thank you for the opportunity to review this interesting (non-systematic) review article on the diagnosis and management of asthma in children. The authors stated aims include to provide an "overview of good clinical practice in the diagnosis and management of paediatric asthma" and suggest that the paper may be a useful tool for health care providers working in a range of child health settings. Major suggestions (1) The discussion around diagnostic testing is interesting, but I was left unsure as to what the authors recommend. In particular, what testing should be done in a child who was diagnosed (clinically) with asthma when they were 3-4 years of age who is now 6 or 7? Do they need any tests? If so, when? How often? Does every child with a history of asthma / wheeze need lung function testing when they turn 6? Or is this only necessary for new-onset symptoms at this age? Which children require FeNO testing? When is it specifically indicated? How many children currently have objective lung function testing? Are there costs and practical considerations related to this? How does access compare across different settings (not only within the

	UK but internationally)? There are many different recommendations provided in Table 4. What do the authors recommend in primary care? Which tests should only be done by specialists? (2) Treatment discussions are not completely resolved. A number of options are presented in Table 5. Is there evidence to support the choice of one option over another? Some indication of the relative levels of evidence (or lack of any evidence) supporting each option would be useful Table 6 – SABA can be given by inhalation (with or without a spacer), by a nebuliser, or as an oral liquid (less useful). Please provide recommendations on the preferred route of administration. Biologic agents can be quite costly. It would be useful to present some data on the magnitude of the benefit (i.e. how many asthma attacks per year are reduced by omalizumab?), as well as some indication of the cost of a usual course of treatment (or a year of treatment) (3) Some comment on relative access to specialist care, advanced diagnostic testing would be useful. Poverty (at a local, regional and national level) plays a significant part in access to optimal asthma care. Minor suggestions (4) Introduction, page 4 of PDF< line 24. The authors state that "paediatric asthma outcomes are poor overall." Which outcomes? How bad are they? Is this a UK or global perspective? (5) What does "T2" stand for (page 7, line 36) Overall, the paper is clearly written. There are some examples where things may be said more concisely. E.g. Abstract, page 3 of PDF, line 26 – remove "asthma" from "promoting good asthma outcomes" Page 5 of PDF, line 5 – consider removing "for health care professionals" Page 5, line 50 – consider removing "of asthma attacks in children" Page 6, line 5 – consider removing "in providing good asthma care" Page 9, line 44 – "rarely practical out with a research setting" - ? replace with "rarely practical outside a research setting" Page 17, line 10 – "improve" rather than "improved" and "reduce" rather than "reduced" Please provide a definition for abbreviations in table 4 (e.g. LABA, ICS, LTRA, etc) It appears that the referencing software has introduced a few errors in the referencing. In particular, the following references should be reviewed for accuracy of the author / organisation involved: 5, 21, 24, 28, 31, 32, 38, 44, 45.

VERSION 1 – AUTHOR RESPONSE

Dear Imti,

Thank you for the opportunity to submit a revised version of our review article 'Diagnosis and management of asthma in children'. We are grateful to the reviewers for their comments and have endeavoured to respond constructively to each of the points and suggestions raised. A point-by-point response is provided below (our responses are in blue text). Please do not hesitate to contact me if you have any questions or if any clarification is required – we would be pleased to respond to any queries. Yours sincerely Malcolm Brodlie BSc (Hons), MB ChB, PhD, FRCPCH Director of the North East NIHR Integrated Academic Training Programme for Doctors and Dentists Clinical Senior Lecturer and Honorary Consultant in Paediatric Respiratory Medicine Reviewer 1 I appreciate the opportunity to review this concise and well presented review of the Diagnosis and management of asthma in children. Although I am not a clinician I appreciate that the review provides a coherent overview of diagnostic procedures in the context of guidelines at the national and international level. Thank you for these positive comments. However, as a qualitative researcher I am concerned that there has been little attention paid to the contribution that qualitative data can bring to understanding the management of children with asthma. Indeed, there is an existing body of work that has explored parental perceptions of childhood asthma and the implications for patient-practitioner communication that if included in the present review would serve to better understand and contextualise the implications for clinical practice. For example, health professionals' awareness of child and parent perceptions of asthma can influence asthma management decisions and the provision of information for families. Moreover, there have been attempts to consolidate the informational needs of parents with regard to the management of childhood asthma. Some of these issues are highlighted and discussed in this paper: https://www.nature.com/articles/s41533-017-0053-7 Thank you for highlighting the importance of understanding the perceptions of young people and their caregivers, and the influence this may have on engagement and clinical outcomes in asthma. We fully agree and have now highlighted this in the 'Non-pharmacological management' section where we also cite the paper above on pages 17-18. We have added the following sentence: "Taking time to understand the perceptions of young people and their caregivers in relation to their asthma diagnosis and management is important and exploring such perceptions may enhance engagement during consultations, subsequently improving outcomes for young people." Reviewer 2 This is a really excellent review and I have little to add. I think you have covered the main areas very well, and the paper is very well written Thank you for these comments. A couple of thoughts: 1) I would add air pollution as a risk factor for development of asthma in children , BMJ . 2020 Aug 19;370:m2791. doi: 10.1136/bmj.m2791. Thank you for pointing this out, we agree, and air pollution has now been added to Table 2 as a risk factor and the above paper cited. 2) In our asthma clinic, the ethos is that managing asthma is "33% ICS, 33% healthy living, 33% self-esteem, 1% everything else".... although this obviously doesn't cover all children, who do need something else, it would I think be worth mentioning the importance of good diet and exercise somewhere (self management section maybe?) We also agree on this point and have added a section on the role of good diet and exercise in the 'Self-management' section on page 18 with the following paragraph: "Diet and exercise are additional important self-management aspects within paediatric asthma care. A number of short term exercise interventions have demonstrated improvements in lung function and symptom control(55). Healthy eating interventions can help reduce BMI and improve the quality of

life of both young people and their caregivers.” 3 On this point it may be worth mentioning in the referral to a specialist section that there is a need for an MDT approach (at least in tertiary services) We have highlighted the importance of an MDT approach in ‘When to refer to a specialist’ section on page 23. An extra sentence now reads: “A key element of specialist care is a multidisciplinary team consisting of a number of professionals, including specialist nurses, psychologists, physiologists and pharmacists.” 4 I would make a mention in the ICS paragraph about the shift in GINA towards symptoms-driven rather than daily steroids for mild asthma. This has been evaluated in children (and we are running an RCT about this - ASYMPTOMATIC). If it helps, we have written an editorial about this: https://pubmed.ncbi.nlm.nih.gov/31972134/ Thank you, we have now highlighted this change in management approach and the evidence behind this in the ‘Pharmacological management’ section on page 14. An extra sentence now reads: “As seen in Table 7, GINA recommends symptom-driven ICS use, compared to daily ICS use, as initial therapy in children over 6 years of age. In comparison to daily ICS use, symptom-driven use has demonstrated a similar exacerbation risk and reduces the risk of ICS adverse effects.” We have also now cited the editorial mentioned above. 5 I couldn't see a summary of biologics in the text itself - I wonder if one is warranted to discuss the developments in this field (or at least a nod to them - they probably only help a handful of children, but a reader may want to see your views on this... perhaps again in the "referral to specialist" section Thank you for pointing this out. We have added an additional paragraph on page 15 in the ‘Pharmacological management’ section covering the role of biologics, their targeted use and their associated costs and citing Table 8. This now reads: “There are a number of biologic agents (Table 8) that may be used in the management of paediatric asthma. These are endotype specific, targeted therapies that should be used only under the supervision of specialists. Their availability and cost varies between countries and different healthcare systems.” 6 Alongside PAAP I would discuss inhaler technique as an important aspect of selfmanagement (the two tend to go together) - we know for example MDI without spacer is a suboptimal way to manage asthma This is another excellent point. We have now highlighted the importance of assessing inhaler technique on page 17. This now reads: “Annual asthma reviews are also opportunities to assess inhaler technique (including spacer use) and provide education on this if necessary. Poor inhaler technique is common in young people with asthma and associated with poor disease control.” Overall, congratulations on a lovely paper. Thank you

VERSION 2 – REVIEW

REVIEWER	Reviewer name: Institution and Country: Competing interests:
REVIEW RETURNED	

GENERAL COMMENTS	

REVIEWER	Reviewer name: Institution and Country: Competing interests:
REVIEW RETURNED	

GENERAL COMMENTS	

REVIEWER	Reviewer name: Institution and Country: Competing interests:
REVIEW RETURNED	

GENERAL COMMENTS	

VERSION 2 – AUTHOR RESPONSE

VERSION 3 – REVIEW

REVIEWER	Reviewer name: Institution and Country: Competing interests:
REVIEW RETURNED	

GENERAL COMMENTS	

REVIEWER	Reviewer name: Institution and Country: Competing interests:
REVIEW RETURNED	

GENERAL COMMENTS	

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REVIEW RETURNED	

GENERAL COMMENTS	

VERSION 3 – AUTHOR RESPONSE