National Institute for Health and Clinical Excellence

Asthma
Scope Consultation Table
10 April 2013-8 May 2013

Type (NB this is for internal purposes – remove before posting on web)

SH = Registered Stakeholders. These comments and responses will be posted on the NICE website after guideline development begins.
NICE = Comments from NICE. These are added to this table for convenience but will not be posted on the web.
Non Reg = Comments from organisations and people who have not registered as stakeholder. These are added for convenience but will not be posted on the web.

ID No	Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
1	SH	Faculty of Sports and Exercise Medicine	5	(Objective tests)	Possible role for FEV0.75 in young children (<8yrs)	Thank -you. Both spirometry and flow-volume loops are in the Scope, and if the GDG agree with your suggestion this can include consideration of FEV0.75.
2	SH	Roche Products Ltd	1	2	The remit has been outlined as covering 'diagnosis and management…', however as outlined in section 4, the decision was made that the guideline will only cover 'diagnosis and monitoring'. For clarity on the remit, could this rationale also be added to section 2?	Thank you. We agree. However the scope template is fixed by NICE and as such we are unable to add this wording to the remit section. NICE are currently in discussion with NHS England about editing the remit to 'diagnosis and monitoring' and in due course this title will be altered accordingly.
3	SH	Faculty of Sports and Exercise Medicine	1	3.1	Breathlessness on exercise due to general lack of cardiovascular fitness ,often associated with obesity, can be misinterpreted as bronchial hyper responsiveness associated with asthma	Thank you.
4	SH	Faculty of Sports and Exercise Medicine	2	3.1	In extreme exercise, particularly in cold dry conditions, a form of airflow obstruction associated with neutrophilic airway inflammation may be confused with allergic asthma.	Thank you.
5	SH	NAPP Pharmaceuticals	2	3.1	In the epidemiology section we suggest including further information on the incidence of poor asthma control. For example it would be useful to highlight the number of avoidable deaths from asthma. In a report by Asthma UK it suggests that there were 1,143 deaths from asthma in the UK in 2010 (16 of these were children aged 14 and under). An estimated 75% of hospital admissions for asthma are avoidable and as many as 90% of the deaths from asthma are preventable. It would also be useful to highlight poor adherence to asthma therapy and the importance of inhaler technique for control.	Section 3.1 is part of the Introduction, and intended only as a brief outline of the problem which the Guideline will address.
6	SH	Group of Occupational	2	3.1	There is consistent published evidence that occupational exposures cause a significant proportion of adult-onset asthma, accounting for	Please note that this section is intended only as a brief outline of the problem which the

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		Respiratory Disease Specialists (GORDS)			around 1 in 6 cases. The majority of this is caused by an allergic mechanism, with a minority following high dose irritant exposures. The proportion of asthma cases caused by work is not widely appreciated in primary care [7-9], and we believe should be highlighted in Section 3 on asthma epidemiology in the NICE document.	Guideline will address. However, although excess detail is inappropriate we have added a sentence to highlight the importance of work exposures.
7	SH	London Respiratory Team	1	3.1	We still have a considerable volume of avoidable admissions and deaths from asthma – these should be addressed as part of the guideline	We agree that this is an important problem, but the remit of this guideline is to cover diagnosis and monitoring only.
8	SH	Royal College of Nursing	2	3.1	We wondered why the epidemiology only gave global figures for Asthma and no UK figures.	Thank you. We have added add a few numbers pertinent to the UK, although please note that this section is intended only as a brief outline of the problem which the Guideline will address
9	SH	Royal College of Nursing	3	3.1 b	Do we know what percentage of the 235 million people quoted that are children and could UK figures be included too?	Thank you. We have added a few numbers pertinent to the UK, although please note that this section is intended only as a brief outline of the problem which the Guideline will address
10	SH	Novartis Pharmaceuticals UK Ltd	1	3.1 b	Estimates are given for the worldwide prevalence of asthma - can a UK estimate be included to give an indication of the scale of the problem facing the NHS?	Thank you. We have added a few numbers pertinent to the UK, although please note that this section is intended only as a brief outline of the problem which the Guideline will address
11	SH	Boehringer Ingelheim	1	3.1 b	While asthma is a chronic condition, it can be life threatening.	Thank you.
12	SH	Royal College of Nursing	4	3.1 c	Suggest change to last sentence from 'never correct' to 'may have been incorrect'	The sentence states that it is **likely** that the diagnosis was never correct, which we believe to be true.
13	SH	British Thoracic Society	2	3.1 c	The document notes the evidence of possible misdiagnosis in up to 30% of people and this could be linked to comorbidities such as obesity or GORD (gastro-oesophageal reflux disease). It may be useful to include a section noting the possible need for investigation of other comorbidities in the assessment of disease especially since the main outcomes include assessment of health related quality of life which can be influenced by these comorbidities.	Thank you. We will make reference to the possible need for investigation of other conditions as you suggest, but we will not be able to cover these in any detail given the large number of potential differential diagnoses and co-morbid conditions. The focus of the Guideline will be those steps which might help make a positive diagnosis of

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						asthma..
14	SH	Novartis Pharmaceuticals UK Ltd	2	3.1 c	The issue of over-diagnosis is highlighted but we comment that conversely, studies also indicate an under/misdiagnosis in a significant group of patients.	Thank you, noted.
15	SH	Aerocrine Ltd	1	3.1 c	The main reason for misdiagnosis of asthma is probably the lack of use of objective measurements/tests. The test procedure must be quick and easy to use and interpret to be feasible in the primary/community care setting. Even spirometry may be difficult to perform and interpret correctly, at least within primary care. FeNO measurement is easy and practical and may be used instead of more complicated tests, such as mannitol provocation test. (Sverrild 2013)	Thank you
16	SH	Aerocrine Ltd	3	3.1 d	• FeNO is a sensitive marker of exposure to allergens and chemical sensitizers (Ihre 2006, Bodini 2007, Vahlkvist 2006, Boyle 2012). • Persistently high FeNO levels, in spite of ICS treatment, seem to indicate excessive allergen exposure in highly sensitized individuals (Buchvald 2003, Syk 2009, Szefler 2008).	Thank you
17	SH	British Thoracic Society	3	3.1 d	It should be noted that markers of airway inflammation and hyper-responsiveness change in response to treatment although exploration of the data would be useful especially in guiding those centres that are developing a service.	Thank you. We agree, and will try to allow for the effect of treatment on the measures considered in the guideline.
18	SH	Aerocrine Ltd	2	3.1 e	• An additional bullet point is suggested to be added here about the importance of achieving asthma control in patients already diagnosed as it is well known that poor asthma control has a negative impact on patient health and quality of life, healthcare utilization and costs. • Current treatment guidelines from for instance BTS/Sign emphasize the importance of continuous treatment of the underlying airway inflammation for achieving control of asthma • Later sections describe the use of FeNO o in identifying the patients who would benefit from anti-inflammatory treatment ((3.2 c), 3.2 d) 4.3.1 e)) o in identifying patients with poor control and at risk for impairment (3.2 d) o in guiding treatment, leading to improved asthma control (4.3.1 k).	Thank you. We agree that the Introduction says less about monitoring than diagnosis, and have added a paragraph.
19	SH	Faculty of Sports and Exercise Medicine	3	3.2	Carefully monitored therapeutic trials of N=1 may have a role in confirming or refuting a diagnosis.	Thank you

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20	SH	NAPP Pharmaceuticals	3	3.2	We suggest that the current practice section within the guideline should provide specific information on some of the areas which are going to be discussed. For example which measures of airway inflammation are going to be used to measure control?	The measures we will consider are indicated in paragraphs 4.3.1g, 4.3.1j, and 4.3.1k. We cannot pre-empt the guideline and say at this stage which will be recommended.
21	SH	Royal College of Paediatrics and Child Health	12	3.2 a	Recognising that viruses are also a trigger for asthma should also be discussed. - Chest. 2010 August; 138(2 Suppl): 4S–10S.The Relationship of Airway Hyperresponsiveness and Airway Inflammation. Airway Hyperresponsiveness in Asthma: Its Measurement and Clinical Significance. William W. Busse, MD - American Review of Respiratory Disease. 1976 Feb;113 (2):131-9. Mechanisms of bronchial hyperactivity in normal subjects after upper airway respiratory tract infection. Empey DW, Laitinen LA, Jacobs L, Gold WM, Nadel JA.	Thank you
22	SH	British Society for Allergy and Clinical Immunology (BSACI	1	3.2 a	Symptoms listed as intermittent or variable; should also include chest tightness	Thank you, this is not an exhaustive list
23	SH	Guy's & St. Thomas's NHS Foundation Trust	1	3.2 a	Symptoms should be listed as intermittent or variable; should also include chest tightness	Thank you, this is not an exhaustive list
24	SH	London Respiratory Team	2	3.2 a	The diagnostic process requires an on-going assessment with health professional and patient working together throughout the investigative process before a final diagnosis is made	Thank you
25	SH	Royal College of Paediatrics and Child Health	11	3.2 a	The symptoms of sputum production and chest pain should also be mentioned.	Thank you, this is not an exhaustive list
26	SH	Pharmaxis Pharmaceuticals Ltd	1	3.2 c "Testing for Airway inflammation… …uncertainty about both sensitivity and specificity of FeNO, particularly whether it can distinguish general atopy from asthma".	Please consider reordering the tests described in Section 3.2 based on their typical usage in clinical practice. The tests described in section 3.2e (e.g. blood and skin tests, exercise testing; measures of airway reactivity) would be more commonly used in routine practice over those described in 3.2c.	Thank you
27	SH	Guy's & St. Thomas's NHS	2	3.2 c	Be more specific about sputum eosinophil counts: absolute counts are accurate but percentages depend on the proportions of other cells;	Thank you

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		Foundation Trust			important to distinguish these when appraising evidence	
28	SH	Severe Asthma National Network	2	3.2 c	FeNO and Sputum eosinophil counts are not routinely measured in primary care and are mainly measures used in highly specialised centres therefore not equitable access.	Thank you. We will consider which test should be done rather than where they will take place.
29	SH	Aerocrine Ltd	4	3.2 c	• FeNO is a highly sensitive marker for Th2 cytokine-driven inflammation in the bronchial mucosa (Corren 2011, Alving & Malinovschi 2010). A persistently high FeNO (> two weeks ruling out rhinovirus infections, no change in treatment) is highly specific for this type of inflammation. • FeNO and sputum eosinophil count may dissociate due to the fact that eosinophils are activated systemically, and this activation is not targeted by inhaled corticosteroids (Alving & Malinovschi 2010). Hence, FeNO is a more accurate marker of the local inflammation present in asthmatic airways than sputum eosinophils (Cowan 2010). • FeNO can be raised in asymptomatic subjects, signalling for important, however subclinical, inflammation, since raised FeNO indicates elevated risk of developing respiratory symptoms and even clinical asthma within 3-4 years (Olin 2010, Bastain 2011, Malinovschi 2012). • FeNO has been shown to be superior to conventional tests as an assessment tool in diagnosing patients with symptoms suggestive of asthma (Smith 2004, Sivan 2009, Cordeiro 2011). • An upcoming study clearly demonstrates the diagnostic usefulness of FeNO in identifying corticosteroid-responsive inflammation and in confirming/excluding an asthma diagnosis (Price, 2013).	Thank you
30	SH	Birmingham Children's Hospital	3	3.2 C	Lots of debate re FeNO being used only in specialised centres and also whether use of FeNO is actually evidenced based	Thank you. We will consider which test should be done rather than where they will take place. We will review the evidence base for FeNO
31	SH	National Paediatric Respiratory & Allergy Nurses Group *(NPRANG)*	3	3.2 C	Lots of debate re FeNO being used only in specialised centres and also whether use of FeNO is actually evidenced based	Thank you. We will consider which test should be done rather than where they will take place. We will review the evidence base for FeNO
32	SH	Aerocrine Ltd	5	3.2 d	• FeNO has been shown to predict future risk and impairment (Zeiger 2011, van Veen 2008, Contoli 2010). • Guiding asthma treatment using FeNO measurements significantly reduce exacerbation rates in both adults and children (Mahr 2013,	Thank you

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					Mahr et al Peds Paper 2013 AAP.PDF Donohue Jain Respir Med 2013 (in press).p Donohue 2013, Syk 2013). • FeNO has also been shown to predict corticosteroid responsiveness (Smith 2005, Berry 2007) and to identify patients with poor treatment adherence (Koster 2011, McNicholl 2012).	
33	SH	British Society for Allergy and Clinical Immunology (BSACI	3	3.2 d	Measures of airways inflammation are often affected by disease therapy as well as severity.	Thank you
34	SH	Guy's & St. Thomas's NHS Foundation Trust	3	3.2 d	Measures of airways inflammation can in theory be used to monitor asthma control, but there are no universally accepted standards and their outputs are often affected by disease therapy as well as severity.	Thank you
35	SH	Royal College of Nursing	5	3.2 d	There is limited research to support this statement in children and further research is recommended. The availability of testing airway inflammation in children is limited at present and not available in some secondary and tertiary care centres.	Thank you. We will consider which test should be done rather than where they will take place.
36	SH	Pharmaxis Pharmaceuticals Ltd	2	3.2 e *"Other diagnostic strategies include blood or skin tests to detect allergic reactions to environmental influences, exercise tests to detect evidence of bronchoconstriction, and measures of airway hyper-reactivity, such as histamine/ methacholine PC20 and mannitol*	In addition to "accuracy", please also consider other forms of value to the NHS: **Standardisation in administration:** • Consistency in specified or approved protocols within hospitals and across hospital systems [SIGN 101, 2012] • Repeatability of results between visits to ensure a consistency in diagnosis, and in monitoring asthma-progression and/or treatment control within a centre. • Reproducibility of results between medical facilities to ensure a consistency in diagnosis and in monitoring asthma-progression and/or treatment control for joined-up patient-centric care. **Quality:** • Consistency in formulation (e.g. between different suppliers of methacholine / histamine / blood or skin test allergens/ mannitol) • Differences in methods used in preparing solutions (e.g. histamine /	Thank you

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				challenge. However, it is debatable which test or measure or combination of them is the most effective to accurately diagnose asthma"	methacholine) that require titration in hospital pharmacies, due to their limited-shelf life. • Differences in methods used in assessing the degree of AHR from bronchoconstrictor stimuli [SIGN 101, 2012] • Potential risks associated with human error in preparing solutions. **Simplicity in administration** • Thus, enabling non-hospital based medical facilities to conduct diagnosis and / or monitoring of asthma progression and/or treatment control. • Convenience; disposability, infection control/ sterilisation. **Evidence base:** • Mannitol has been evaluated and approved by the MHRA as a licensed test for AHR [Mannitol SmPC]. • The precision manufacturing of respirable dry-powder mannitol enables an accurate, reproducible and standardised assessment of AHR, which is important to ensure consistency in diagnosis as well as evaluating progression and/or treatment control during routine monitoring. • Mannitol has been shown to be have an equivalent sensitivity and specificity to methacholine in identifying exercise-induced bronchoconstriction, a clinician diagnosis of asthma [Anderson et al 2009]. However, unlike methacholine, the simple diagnostic kit enables the assessment to be undertaken without extensive laboratory or exercise equipment and by non-hospital medical facilities such as GP offices and outpatient clinics. • Mannitol has been demonstrated to optimise titrating of inhaled corticosteroid treatment in the control of asthma symptoms (Lipworth et al. 2012), and therefore enables an objective assessment in the monitoring of patients to inform decision-making in optimising treatment protocols (please see point 4 below).	
37	SH	Aerocrine Ltd	6	3.2 e	• Exercise and bronchial provocation tests (e g mannitol) are basically used as surrogate tests to estimate the underlying inflammation and the need for corticosteroid treatment. In this respect, FeNO is a much more accurate as well as a more easy and practical test to be used. • FeNO has been shown to predict both exercise-induced bronchoconstriction (Feitosa 2012, Grzelewski 2012) and	Thank you

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					hyperresponsiveness to mannitol (Sverrild 2013).	
38	SH	Severe Asthma National Network	3	3.2 e	Should read skin prick tests	Thank you, the text has been changed accordingly
39	SH	British Society for Allergy and Clinical Immunology (BSACI	4	3.2 e	Skin and blood tests for allergen-specific IgE demonstrate sensitisation, and should always be interpreted in relation to clinical history	Thank you
40	SH	Guy's & St. Thomas's NHS Foundation Trust	4	3.2 e	Skin and blood tests for allergen-specific IgE demonstrate sensitisation, not clinical "reactions" as implied; "to accurately diagnose" should read "accurately to diagnose".	Thank you
41	SH	Guy's & St. Thomas's NHS Foundation Trust	5	4	The management of diagnosed asthma is straightforward if performed properly, and with special attention to the efficient delivery of appropriate therapy	Thank you
42	SH	Primary care respiratory society	1	4	We strongly recommend that the section on the clinical need for the guideline situates this work with respect to the widely used BTS/SIGN asthma guideline, which has been developed by a NICE-accredited process. Lack of reference to these is a strange omission. It is imperative that the scope should acknowledge the existence of this guideline and explain how it hopes to add value and avoid potential confusion in the health care community should the recommendations differ from those in the BTS/SIGN guideline. It is perfectly reasonable to wish to develop further guidance on asthma diagnosis and monitoring but the reason for doing so should be made more explicit. It would be detrimental to asthma care if the strictures of the NICE guideline development process were to deliver a piece of guidance with no regard to the existing guidance, and no pragmatic approach to ensuring that there are no significant discrepancies. We would be reassured if NICE would clearly state that they see it as part of the development process to roadtest any draft recommendations in primary care, in order to confirm that the guidance is an improvement on and does not conflict with the BTS/SIGN guideline. And to liaise with BTS/SIGN about ensuring consistency of messaging to the NHS.	Thank you. The decision for NICE to produce a clinical guideline on asthma was made by the Department of Health. While NICE has a fairly comprehensive library of clinical guidelines, it appears odd for a topic of significant impact like asthma to be missing from this list. It is an opportunity for guidance to be produced using NICE's methodological processes, including health economics which the SIGN/BTS guideline does not include. NICE recognises the perceived overlap/duplication in work that producing a NICE guideline on asthma may generate and has liaised with SIGN about priority areas for this new guideline. The draft guideline will be issued to all stakeholders for consultation in due course and we will welcome comments at that stage from all, including stakeholders working in primary care.
43	SH	Neonatal and Paediatric Pharmacists Group (NPPG)	1	4 and specifically 4.3.2 and 4.4	Our comments are as follows: We are disappointed that the scope of the guideline does not include management of asthma. We appreciate that the reasons for proposing this are covered in the introduction to section 4. However there are NICE Technology Appraisals for only SOME of the	Thank you. Further NICE guidance on asthma will be considered in future alongside other priorities.

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					available therapies for asthma. We consider that this Guideline could be an opportunity for NICE to develop a fully inclusive guideline to cover all aspects of asthma from diagnosis and monitoring to management. We also note that one of the outcomes which will be considered (4.4) is the need for some medications such as oral corticosteroids and short-acting beta-agonists. It is therefore surely important to look at how these drugs are used in management of the disease. We consider that the exclusion of management of asthma from the Guideline will significantly reduce its usefulness in practice. We would urge that this exclusion is reconsidered or that a definite decision is made to follow up with guidance on management of asthma.	
44	SH	Royal College of Paediatrics and Child Health	2	4.1	Whilst it is recognised the issue of wheeze in infants represents a difficult issue, it would be desirable to see this group (and the various unique issues surrounding diagnosis and monitoring) included in the guideline.	Thank you. Expert advice received is that it is difficult to make a positive diagnosis of asthma in infants and certainly not without access to tests (which are beyond the reach of most UK practitioners). We completely agree that it would be desirable to offer recommendations but we don't think that clear guidance is possible in this age group.
45	SH	Novartis Pharmaceuticals UK Ltd	3	4.1.1	"Specific consideration will be given to subgroups based on age, broadly divided into younger children, older children, and older people (aged over 75 years)." This does not identify the standard adult population (aged 18-75 years) as a subgroup of interest and we thought it worth clarifying that this population is within scope. We also suggest that the age ranges included within "younger children" and "older children" should be specified.	Thank you. This means that adult patients between the ages of 16 and 75 are the default and this section only gives mention to other subgroups of specific interest. Specific consideration will be given to any age group where evidence exists and when separate diagnostic or monitoring strategies should be followed.
46	SH	British Thoracic Society	4	4.1.1	It may be beneficial to distinguish between those patients with symptoms but not treatment (ie pre-diagnosis), and those already on treatment (monitoring).	Thank you. This is the intent of section 4.1.1a. We have added the word 'suspected' asthma to this section.
47	SH	College of Emergency Medicine	1	4.1.1	Our comments are as follows: The groups that will be covered should include patients (including children) who present for the first time to an acute healthcare setting (e.g. an emergency department) with symptoms that might be asthma (e.g. SOB, wheeze).	Thank you. These patients are not excluded.
48	SH	Boehringer Ingelheim	2	4.1.1 a	The term "asthma" describes a diverse range of conditions, including acute asthma, exercise induced asthma, occupational asthma, allergic asthma, etc. Could the definition be more specific in including these types of asthma?	Thank you. We don't think this division is helpful, people can, for example, have allergic asthma and exercise induced asthma.
49	SH	Royal College of	6	4.1.1 b	Is the age subgroup for children defined as:	Thank you. This section means that adult

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		Nursing			Younger children – pre school Older children – school age? It would be helpful to clarify here.	patients between the ages of 16 and up wards are the default. This section only gives mention to other subgroups of specific interest. Specific consideration will be given to any age group where evidence exists and when separate diagnostic or monitoring strategies should be followed
50	SH	British Society for Allergy and Clinical Immunology (BSACI	6	4.1.1 b	Should also include adults	Thank you. This means that adult patients between the ages of 16 and 75 are the default and this section only gives mention to other subgroups of specific interest. Specific consideration will be given to any age group where evidence exists and when separate diagnostic or monitoring strategies should be followed.
51	SH	Guy's & St. Thomas's NHS Foundation Trust	6	4.1.1 b	Should also include adults surely	Thank you. This means that adult patients between the ages of 16 and 75 are the default and this section only gives mention to other subgroups of specific interest. Specific consideration will be given to any age group where evidence exists and when separate diagnostic or monitoring strategies should be followed.
52	SH	Intensive Care Society	1	4.1.1 b	The hospitalised asthmatic patient, at risk of deterioration, should be included	Thank you. These people are not excluded.
53	SH	Boehringer Ingelheim	3	4.1.1.b	The age cut off point for asthma has been chosen at 75 years. We would suggest lowering this to 60 / 65 years as the evidence base to make recommendations over the age of 75 years may be very limited.	Thank you. We have not specified an upper cut off.
54	SH	Birmingham Children's Hospital	4	4.1.2	Glad the subdividing ages but better if 0 – 2 as per BTS guidelines	Thank you. We will say what the evidence allows. However, we do not wish to give the impression that we will be dealing with the complex tests (ad research tools) in very young children. For example there are sophisticated techniques for trying to measure airway resistance in the very young – these are beyond the guideline remit.
55	SH	National Paediatric Respiratory &	4	4.1.2	Keep the sub division of the ages to correlate with the BTS, ie. 2-5, >5yrs and not to include children <2yrs	Thank you. We will say what the evidence allows. However, we do not wish to give the

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		Allergy Nurses Group *(NPRANG)*				impression that we will be dealing with the complex tests (ad research tools) in very young children. For example there are sophisticated techniques for trying to measure airway resistance in the very young – these are beyond the guideline remit.
56	SH	British Thoracic Society	5	4.1.2	The guideline excludes infants under 1y and we query the reason for this specific value rather than some other age value (2y, 3y, 5y or, as in QOF, 8y)?	Thank you. We will say what the evidence allows. However, we do not wish to give the impression that we will be dealing with the complex tests (ad research tools) in very young children. For example there are sophisticated techniques for trying to measure airway resistance in the very young – these are beyond the guideline remit.
57	SH	Severe Asthma National Network	4	4.1.2 a	Follow the BTS/SIGN guidelines and set age at 2 years and under	Thank you. We will say what the evidence allows. However, we do not wish to give the impression that we will be dealing with the complex tests (ad research tools) in very young children. For example there are sophisticated techniques for trying to measure airway resistance in the very young – these are beyond the guideline remit.
58	SH	Primary care respiratory society	2	4.1.2 a	We recognise that this was much discussed at the scoping meeting – and agree with the final decision to exclude infants under 12 months.	Thank you. We will say what the evidence allows. However, we do not wish to give the impression that we will be dealing with the complex tests (ad research tools) in very young children. For example there are sophisticated techniques for trying to measure airway resistance in the very young – these are beyond the guideline remit.
59	SH	NAPP Pharmaceuticals	4	4.2	For the healthcare setting covered we also suggest that this guideline would be relevant to tertiary care centres. It may be important at a tertiary care level to consider or rule out a diagnosis of asthma due to the possibility of misdiagnosis (which has been raised in 3.1c).	Thank you. We disagree with including tertiary care as this is a different population and encompasses a totally different set of investigations. The way in which this group is diagnosed and monitored is very different. 'Severe and difficult to control asthma' is a clearly defined and separate sub group distinct from the wider asthma population and the investigations involved in the

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						diagnosis and monitoring of this population are outside the scope of this guidance. The people referred to tertiary care with severe and difficult asthma to control asthma are the majority of people who have not responded to their treatment. We have added the term 'severe and difficult to control asthma' to section 4.3.2. 'Clinical issues that will not be covered' This guideline is for asthmatics in primary and secondary care. We focused upon diagnosis because of the large 'over diagnosis' problem that has been raised by stakeholders. This relates predominately to primary care.
60	SH	Asthma UK	2	4.2	The draft scope covers only primary, secondary and community care settings. It would be helpful to include tertiary care in addition to these, since this is where some of the most costly and invasive asthma treatments are given. Although there are other documents relating to tertiary settings (including the NICE technology appraisal on omalizumab and NHS England's service specification for severe asthma services), a NICE guideline would be a helpful addition and could even further strengthen future iterations of this and other service specification documents.	Thank you. We disagree with including tertiary care as this is a different population and encompasses a totally different set of investigations. The way in which this group is diagnosed and monitored is very different. 'Severe and difficult to control asthma' is a clearly defined and separate sub group distinct from the wider asthma population and the investigations involved in the diagnosis and monitoring of this population are outside the scope of this guidance. The people referred to tertiary care with severe and difficult asthma to control asthma are the majority of people who have not responded to their treatment. We have added the term 'severe and difficult to control asthma' to section 4.3.2. 'Clinical

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						issues that will not be covered' This guideline is for asthmatics in primary and secondary care. We focused upon diagnosis because of the large 'over diagnosis' problem that has been raised by stakeholders. This relates predominately to primary care.
61	SH	Novartis Pharmaceuticals UK Ltd	4	4.2	The healthcare settings within scope are described as "Primary, secondary and community care settings in which NHS-funded care is provided". We note that this has been amended since the draft version of the scope (circulated in advance of the stakeholder workshop held on 18th March 2013). The previous document referred to "Primary, secondary and tertiary care settings". We would like clarification on the reason why tertiary care settings appear to have been removed from the scope, especially in the context of specialised commissioning which focuses on the differential diagnosis of difficult asthma. We would suggest that the links between the Guideline on Diagnosis and Monitoring of Asthma and the proposed service specification for "Specialised Respiratory Services - Severe difficult to control asthma" are made explicit.	Thank you. We disagree with including tertiary care as this is a different population and encompasses a totally different set of investigations. The way in which this group is diagnosed and monitored is very different. 'Severe and difficult to control asthma' is a clearly defined and separate sub group distinct from the wider asthma population and the investigations involved in the diagnosis and monitoring of this population are outside the scope of this guidance. The people referred to tertiary care with severe and difficult asthma to control asthma are the majority of people who have not responded to their treatment. We have added the term 'severe and difficult to control asthma' to section 4.3.2. 'Clinical issues that will not be covered' This guideline is for asthmatics in primary and secondary care. We focused upon diagnosis because of the large 'over diagnosis' problem that has been raised by stakeholders. This relates predominately to primary care.
62	SH	Resuscitation	1	4.2 a	No specific mention is made of ambulance services. Whilst these may be	Thank you. The diagnosis of asthma is very

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		Council			included under primary care or community care, given the frequency of calls to the emergency medical services for this group of patients, specific mention of EMS would be appropriate here.	rarely made by the ambulance service nor is chronic asthma control monitored in this setting (monitoring here does not pertain to monitoring during an acute attack).
63	SH	Aerocrine Ltd	7	4.2 a	Only spirometry, FeNO and allergy tests are feasible in the primary/community care setting.	Thank you
64	SH	Pharmaxis Pharmaceuticals Ltd	3	4.2 a "Healthcare settings: Primary, secondary and community care settings in which NHS-funded care is provided"	Please consider the value of interventions and technologies that improve efficiencies within the asthma care pathway and relieve the burden on hospital systems: • Diagnosis of asthma is often made in a primary care setting. • Mannitol has been shown to offer equivalence in identifying exercise-induced bronchoconstriction to methacholine [Anderson et al 2009]. • Mannitol has the advantage of being able to be performed in a primary care setting, with basic resuscitation equipment and a spirometer. • The use of mannitol in primary care setting potentially offers overall healthcare and hospital system efficiencies, preserving hospital medical resources for patients that may require referral for further investigation at secondary or tertiary care facilities.	Thank you
65	SH	Primary care respiratory society	3	4.2 a	The wording here has changed since the scoping meeting. It appears that tertiary care has been excluded specifically. Is it worth clarifying that this is the case (if it is)?	Thank you. We disagree with including tertiary care as this is a different population and encompasses a totally different set of investigations. The way in which this group is diagnosed and monitored is very different. 'Severe and difficult to control asthma' is a clearly defined and separate sub group distinct from the wider asthma population and the investigations involved in the diagnosis and monitoring of this population are outside the scope of this guidance. The people referred to tertiary care with severe and difficult asthma to control asthma are the majority of people who have not responded to their treatment. We have added the term 'severe and difficult to control asthma' to section 4.3.2. 'Clinical

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						issues that will not be covered' This guideline is for asthmatics in primary and secondary care. We focused upon diagnosis because of the large 'over diagnosis' problem that has been raised by stakeholders. This relates predominately to primary care.
66	SH	Intensive Care Society	2	4.3	Monitoring of the hospitalised patient with severe asthma should be included	Thank you. This guideline will consider the routine monitoring of asthma control, not the routine management of acute asthma.
67	SH	Birmingham Children's Hospital	8	4.3 g	Not sure RCP3 used under 16s and also is it validated?	Thank you – we will consider the evidence base.
68	SH	Severe Asthma National Network	5	4.3.1	Add to the list exclusion of dysfunctional breathing / upper airway involvement	Thank you. We haven't included a list of all of the conditions which one might wish to exclude. This guideline will focus upon making a positive diagnosis of asthma.
69	SH	Royal College of Paediatrics and Child Health	5	4.3.1	Close monitoring of potential adverse events should be included e.g. growth suppression in childhood.	Thank you. This is an important point and well recognised in paediatric care and we will therefore not be looking at the literature to justify monitoring for growth suppression.
70	SH	British Society for Allergy and Clinical Immunology (BSACI	10	4.3.1	In pre-school children, the prescription of an inhaled bronchodilator or an inhaled corticosteroid can be regarded as a therapeutic trial and part of the diagnostic work up. In other patient, the response to a new asthma medication must be objectively and dispassionately assessed given that not all are effective in all patients and reported symptoms may relate to diseases other than asthma.	Thank you. We agree with your comment and the objective response to treatment will be added to the outcome measures. Objective response to treatment will be added to the outcome measures in section 4.4 of the scope.
71	SH	Royal College of Paediatrics and Child Health	3	4.3.1	It is important that the guideline emphasises the importance of considering alternative diagnoses (and their confirmatory tests) e.g. vocal cord visualisation in VCD.	Thank you. We haven't included a list of all of the conditions which one might wish to exclude. This guideline will focus upon making a positive diagnosis of asthma.
72	SH	Royal College of Paediatrics and Child Health	6	4.3.1	Monitoring of carer/patient satisfaction with quality of care should be included.	Thank you. We will not be looking at a separate question on patient satisfaction. However if there is data on patient / carer satisfaction with different diagnostic or monitoring strategies we will consider this

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						outcome measure although we doubt that much will be available or reported in the literature. We acknowledge that there may be some outcome data available for telemonitoring.
73	SH	College of Emergency Medicine	3	4.3.1	Our comments are as follows: Agree that the value of specific signs and symptoms, personal and family history of atopy and occupational history should be established as part of the guideline. The guideline should result in the production of standard tools for history taking and examination of patients presenting for the first time with symptoms that might be asthma.	Thank you
74	SH	College of Emergency Medicine	2	4.3.1	Our comments are as follows: The guideline should cover the question – Can (or should) asthma ever be formally diagnosed following a single presentation to a healthcare setting (e.g. GP or ED)? Or should it only be diagnosed formally after a period of monitoring / investigation and review by the patients GP or specialist?	Thank you for these suggestions, the GDG will agree the detailed questions and protocols for review.
75	SH	College of Emergency Medicine	4	4.3.1	Our comments are as follows: The guideline should cover what to do (in order to progress the diagnostic process) after the treatment of an initial presentation with symptoms that might be asthma. What would be expected of an emergency department (or GP or out-of-hours provider) in terms of history, examination and investigations? What would be expected in terms of onward referral for further assessment and investigation following the first presentation with symptoms that might be asthma?	Thank you for these suggestions, the GDG will agree the detailed questions and protocols for review.
76	SH	Asthma UK	3	4.3.1	Risk assessment The scope does not currently cover risk assessment to identify which people with asthma may be at increased risk of an asthma attack and could benefit from more intensive monitoring and closer management. This emerging approach is reflected in the 2011 revision to the BTS/SIGN asthma guidelines, which recommends that those with poor lung function and a history of exacerbations should be more closely monitored. This is an area of debate in asthma management at present so further publications on the subject are likely to emerge during the period before NICE completes its literature review. If people at risk of adverse outcomes could be more accurately identified and more appropriately treated and supported, it could lead to substantial improvements in care for the people who need the most help, as well as a reduction in unnecessary treatment for those who do not need it because they are at lower risk. Asthma UK would therefore be keen to see this included in the scope for NICE's guideline.	Thank you. We acknowledge that this is an emerging field and that these are patients that will need more frequent monitoring. We will make recommendations about the frequency of monitoring where evidence exists.
77	SH	Asthma UK	4	4.3.1	Self-monitoring Although the monitoring section of the scope refers to "patient-reported	Thank you. We agree however actions plans are more about self-management than

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					symptoms" it is important to see self-monitoring as a component of patient education and self-management rather than merely as a way of clinicians collecting more data. We would therefore distinguish patient-reported symptoms collected through clinician-administered questioning such as the RCP three questions or tools like the Asthma Control Test from patients' own self-monitoring (with independent medicine adjustment) using symptom diaries and action plans. The latter should be included in the scope, since patient education for independent self-monitoring (and management) has been shown to make a big difference to asthma outcomes. However, it needs to be done as part of a comprehensive programme in order to be effective.	monitoring alone and therefore outside our remit.
78	SH	British Society for Allergy and Clinical Immunology (BSACI	9	4.3.1	Skin tests should be carried out not only for "common aero-allergens" but also any allergens suspected from the clinical history or occupation as relevant eg. Pets, wheat flour, Aspergillus etc	Thank you. Common aero-allergens include pets and moulds. Testing for occupational allergens is outside the scope.
79	SH	Faculty of Sports and Exercise Medicine	4	4.3.1	The issue of recurrent cough which is often taken to be a feature of early asthma needs to be addressed.	Thank you, cough is included in 4.3.1 a.
80	SH	Cochrane Airways Group	2	4.3.1	The diagnostic test accuracy of symptoms, signs, history and diagnostic tests will be population dependent. In secondary care there may be a much higher prevalence of other respiratory pathology (that may cause false positive test results). It is important that diagnostic test performance in different settings is considered separately and not combined into a single average result. For example children with wheeze in hospital are a different population from children with wheeze who present in the community.	Thank you, we agree.
81	SH	Royal College of Paediatrics and Child Health	4	4.3.1	The guideline should include guidelines for referral to secondary/tertiary care if symptoms suggest an alternative diagnosis or diagnostic testing is required.	Thank you. We will consider which test will be done rather than where they will take place.
82	SH	Cochrane Airways Group	1	4.3.1	What will be used as the **gold standard** for the diagnosis of asthma in pre-school children, older children and adults (in order to assess the performance of the diagnostic tests)?	Thank you, this is a good question. When the GDG debate the clinical questions and protocols they will carefully consider the gold standard comparators. We are unable to pre-empt the GDG debate.
83	SH	Birmingham Children's Hospital	5	4.3.1 a	? need to mention diagnostic doubt – potential "flags" that might question diagnosis might need to be mentioned	Thank you. This guideline will focus upon making a positive diagnosis of asthma.
84	SH	National Paediatric Respiratory & Allergy Nurses	5	4.3.1 a	? need to mention diagnostic doubt – potential "flags" that might question diagnosis might need to be mentioned	Thank you. This guideline will focus upon making a positive diagnosis of asthma.

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		Group *(NPRANG)*				
85	SH	Royal College of Nursing	8	4.3.1 a	Consider also including signs and symptoms in response to allergic triggers	Thank you
86	SH	Resuscitation Council	2	4.3.1 a	It would be helpful to address the value and limitation of symptoms in distinguishing asthma from COPD. Also the value and limitation of clinical signs, such as wheeze on auscultation in confirming the diagnosis, and markers of severity.	Thank you. Section 4.3.1.a. covers this and we will also cross refer to the NICE COPD guideline (CG 101).
87	SH	British Society for Allergy and Clinical Immunology (BSACI	7	4.3.1 a	Should include chest tightness and day, as well as night symptoms	Thank you, we have edited the scope wording in section 4.3.1.a. to read *'For example. Wheezing, cough, breathlessness and other respiratory symptoms including diurnal variation and variation with season'*.
88	SH	Guy's & St. Thomas's NHS Foundation Trust	7	4.3.1 a	Should include chest tightness and day, as well as night symptoms	Thank you, we have edited the scope wording in section 4.3.1.a. to read *'For example. Wheezing, cough, breathlessness and other respiratory symptoms including diurnal variation and variation with season'*.
89	SH	NAPP Pharmaceuticals	5	4.3.1 a	The list of symptoms for asthma does not currently include chest tightness. We suggest including this within the list.	Thank you, this is not an exhaustive list.
90	SH	London Respiratory Team	3	4.3.1 a	There is huge value of a smoking history or environmental exposure to tobacco smoke in making a diagnosis of asthma	Thank you. This is of more importance in making a COPD diagnosis and this guideline will focus on making a positive diagnosis of asthma.
91	SH	NAPP Pharmaceuticals	6	4.3.1 b	The list of risk factors within this section does not include additional risk factors such as obesity, respiratory tract infections, other co-morbidities, tobacco smoke and other environmental factors. We suggest that these should be included as they may be important in considering a diagnosis of asthma.	Thank you. We agree that there are many features of a comprehensive clinical history but we will need to limit the literature search to the key elements.
92	SH	Primary care respiratory society	4	4.3.1 c	Again, this was much discussed at the scoping meeting. We agree that the guideline does not need to cover detailed specialist testing to identify occupational causes, but it SHOULD reinforce the need for clinicians – particularly in primary care - to be suspicious about potential workplace causes in adult onset asthma	Thank you we agree.
93	SH	Aerocrine Ltd	8	4.3.1 d	See 3.2 e)	Thank you
94	SH	Resuscitation Council	3	4.3.1 d	We would like to see specific inclusion of the use of serial peak flow measurements (i.e. peak flow charts) to record diurnal variation in PEF and	Thank you, peak flow variability is included.

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					identify "morning dips", which may be the main clue to diagnosis of asthma in some cases. I think that this simple and inexpensive tool is often overlooked.	
95	SH	London Respiratory Team	4	4.3.1 d	We would recommend use of BMI/waist circumference routinely in assessment to consider other causes of breathlessness and avoidance of inappropriate diagnosis	Thank you, this guideline will focus on making a positive diagnosis of asthma.
96	SH	Guy's & St. Thomas's NHS Foundation Trust	8	4.3.1 e	As before when referring to blood and sputum eosinophil "counts" important to distinguish between absolute numbers and percentages	Thank you
97	SH	NAPP Pharmaceuticals	7	4.3.1 e	In addition to the test listed, we suggest including the sputum test for eosinophil/neutrophil which may help to rule in/out asthma phenotypes.	Thank you. Monitoring of inflammatory cell phenotypes in sputum is a test that occurs in tertiary care and will not be covered within this guidance.
98	SH	Aerocrine Ltd	9	4.3.1 e	• Peripheral blood eosinophil count and FeNO cannot be used interchangeably. Rather, they provide independent and additive information (Malinovschi 2012, ERS abstract) *see also 3.2c* • Many studies demonstrate the usefulness of FeNO in assessing airway inflammation in patients with respiratory symptoms. Important to note is that FeNO both can identify and exclude the ICS-responsive airway inflammation, thus determining if a patient will response to ICS therapy or not (Berry 2007, Smith 2004, Smith 2005, Perez-de-Llano 2012, Price 2013).	Thank you
99	SH	AstraZeneca UK Ltd	4	4.3.1 e	We agree with the inclusion of biomarkers of airway inflammation and look forward to the assessment of value of these objective tests	Thank you
100	SH	Roche Products Ltd	2	4.3.1 e	We would welcome a broader statement to allow inclusion of the potential use of biomarkers and phenotyping; the heterogeneity of asthma means that not all patients respond to the same treatments and some patients remain symptomatic despite current standard of care. Potential exists, therefore, to characterize asthma into different phenotypes, where each phenotype is defined by distinctive pathologic or molecular characteristics that may be associated with a minimally invasive marker, or biomarker. Such biomarkers would be valuable tools for diagnosis, staging and monitoring of disease severity and for predicting and monitoring response to therapy without waiting for extreme clinical endpoints or invasive investigations.	Thank you, the use of these biomarkers for routine management has not been fully assessed.
101	SH	British Society for Allergy and Clinical	8	4.3.1 e	When referring to blood and sputum eosinophil "counts" important to distinguish between absolute numbers and percentages	Thank you

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		Immunology (BSACI				
102	SH	Royal College of Nursing	9	4.3.1 e	Why has measurement of sputum eosinophils not been included?	Thank you. Monitoring of inflammatory cell phenotypes in sputum is a test that occurs in tertiary care and will not be covered within this guidance.
103	SH	Aerocrine Ltd	10	4.3.1 f	See 3.2 e)	Thank you
104	SH	Roche Products Ltd	3	4.3.1 g	In addition to the questionnaires mentioned, we would welcome the inclusion of the Asthma Quality of Life Questionnaire (AQLQ) which is validated and widely used in randomised clinical trials and has been mapped to EQ-5D.	Thank you. Section 4.3.1.g says 'such as' and this is not an exhaustive list.
105	SH	Royal College of Nursing	7	4.3.1 g	Interested to note the inclusion of the use of tele-healthcare as a route for assessment.	Thank you
106	SH	Pharmaxis Pharmaceuticals Ltd	4	4.3.1 g **Monitoring** *Lung function* "j) Assessment of asthma control using tests such as measures of pulmonary function (for example spirometry) and measures of airway reactivity."	• Mannitol enables an objective assessment in the monitoring of patients, to inform and supplement decision-making when considering step-changes to treatment protocols. • Mannitol has been studied as an intervention to allow physicians to monitor control and titrate corticosteroid usage in stable asthma patients, according to patient response to mannitol challenges (Lipworth et al 2012). • In this study, the use of mannitol challenges to determine steroid titration compared a Control strategy of BTS-determined best practice for steroid titration, demonstrated: **mannitol reduced mild exacerbations significantly versus a control group**. • These results indicate that mannitol offers value to clinician decision-makers in rationalising and optimising the use of available treatments to inform stepping up/down of medicines to control asthma symptoms.	Thank you
107	SH	Severe Asthma National Network	6	4.3.1 g	RCP3 questions >16yrs not valid for children.	Thank you
108	SH	NAPP Pharmaceuticals	8	4.3.1 g	There are a number of different tests for assessing asthma which are listed within this section. We suggest including further information on training and the appropriateness of such tests for each of the healthcare settings e.g. which ones are best utilised in primary care, community, secondary care etc	Thank you. Healthcare professionals should be trained and technically competent to conduct the tests. We will not be addressing this. In relation to 'healthcare setting' - we will deal with which tests work regardless of the setting.

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109	SH	London Respiratory Team	5	4.3.1 g	Use of anxiety and depression scores can be useful in holistic assessment	Thank you we are monitoring control of asthma.
110	SH	Novartis Pharmaceuticals UK Ltd	5	4.3.1 g	We query why AQLQ has not been included.	Thank you. Section 4.3.1.g says 'such as' and this is not an exhaustive list.
111	SH	NAPP Pharmaceuticals	9	4.3.1 h	For monitoring asthma there is the possibility of telehealthcare. When incorporating this within the guideline we suggest including the evidence base for this with guidance for when monitoring in this manner would be appropriate, as a 2010 Cochrane review stated that 'telehealthcare interventions are unlikely to result in clinically relevant improvements in health outcomes in those with relatively mild asthma, but they may have a role in those with more severe disease who are at high risk of hospital admission.	Thank you. We cannot pre-empt the evidence base.
112	SH	Primary care respiratory society	5	4.3.1 h	Should telehealth be under patient reported symptoms only, or also under lung function ?	Thank you we added the sub headings to help with clarify but can see that they have complicated things. The sub headings are helpful in 'diagnosis' but we will delete the sub headings from the monitoring section of the scope as follows; 'patient reported symptoms'; 'lung function' and 'airways inflammation'.
113	SH	Cochrane Airways Group	3	4.3.1 h	Tele-heathcare tends to be part of a package of care in trials and is difficult to assess by itself.	Thank you, noted.
114	SH	London Respiratory Team	6	4.3.1 h	We consider that further work is required to assess the value of tele-health as a means of assessing and monitoring asthma before recommendation	Thank you we cannot pre-empt the evidence.
115	SH	Cochrane Airways Group	4	4.3.1 i	Adherence and inhaler technique are separate issues and should not be combined into one monitoring category	Thank you we agree that these should be separate points.
116	SH	Birmingham Children's Hospital	6	4.3.1 i	How are we monitor adherence may need to be mentioned	Thank you this will hopefully fall out of the evidence base.
117	SH	AstraZeneca UK Ltd	2	4.3.1 i	Monitoring –we are pleased to see adherence to be monitored alongside inhaler technique as this was discussed at the scoping meeting	Thank you
118	SH	London Respiratory Team	7	4.3.1 i	Please consider including inhaler devices in the scope of guidance – as the current NICE TAG guidance on inhalers is very old and some new evidence has been published since. Consider noting whether we should be moving away from CFC-free inhalers. We would also like to see mention of the use of peak flow meters and patient self- management plans in the monitoring section	Thanks you. Self-management plans and inhaler devices are about management rather than monitoring. With regard to peak flow meters we have

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						added this to 4.3.1. j.
119	SH	Birmingham Children's Hospital	7	4.3.1 i	Pleased that inhaler technique mentioned	Thank you
120	SH	Aerocrine Ltd	11	4.3.1 i	• Treatment adherence can effectively be monitored with FeNO measurements (Koster 2011, McNicholl 2012). • FeNO is dose-dependently reduced by inhaled corticosteroids within 14 days with better dose separation than sputum and blood eosinophil count, serum ECP and mannitol reactivity (Nolte 2013, Matsunaga 2013, Anderson 2012). • This supports the view that FeNO can be used to monitor also inhalation technique as well as corticosteroid deposition in the airways dependent of type of inhaler and/or drug formulation (Matsunaga 2013, Zietkowski 2006, Nolte 2013, Nicolini 2010).	Thank you
121	SH	NAPP Pharmaceuticals	10	4.3.1 i	Within the monitoring section it lists that adherence and technique should be monitored. Within the guideline itself it will be important to provide further information on how this will be achieved e.g. what will the review period be, how technique will be assessed.	Thank you we agree that these should be separate points.
122	SH	Primary care respiratory society	6	4.3.1 j	This should explicitly mention peak flow monitoring since this is much more widely used than spirometry in monitoring.	Thank you. We have added peak flow meters to 4.3.1.j
123	SH	Severe Asthma National Network	7	4.3.1 j	What are the measures of airway reactivity they need to be stated	Thank you but at this stage (within the scope) we do not specify these. The GDG will debate at the question and protocol stage.
124	SH	Cochrane Airways Group	5	4.3.1 k	Although machines are available to measure FeNO in primary care, there is no clear consensus about what thresholds should be used to monitor therapy, nor what changes in asthma treatment should be made. For example, an existing trial on this topic needed to have a safety net to prevent repeated increases in inhaled corticosteroids in participants whose FeNO remained high.	Thank you we agree the positioning is problematic but there is a lot of stakeholder interest in it and it is entirely appropriate for inclusion within the guideline.
125	SH	Aerocrine Ltd	12	4.3.1 k	• FeNO guided asthma treatment improves asthma control and significantly reduces exacerbation rates in both children and adults (Powell 2011, Mahr 2013, Donohue 2013, Syk 2013). • FeNO has been shown to predict future risk and impairment (Zeiger 2011, van Veen 2008, Contoli 2010).	Thank you
126	SH	Royal College of Nursing	10	4.3.1 k	Why has measurement of sputum eosinophils not been included?	Thank you. Monitoring of inflammatory cell phenotypes in sputum is a test that occurs in tertiary care and will not be covered within this guidance.

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127	SH	College of Emergency Medicine	5	4.3.2	Our comments are as follows: The management of asthma (including that of acute exacerbations of asthma) should be the topic of NICE guidance in the future. Whilst most of the acute management is straightforward and is the topic of guidance from elsewhere e.g. the British Thoracic Society, the evidence for the use of emerging treatments in the acute setting e.g. magnesium sulphate could be reviewed and made part of such guidance.	Thank you. We have passed your suggested topic for 'acute exacerbations of asthma' on to NICE for consideration.
128	SH	Resuscitation Council	4	4.3.2a	Incorrect wording here. **"Management"** of asthma includes all aspects of clinical assessment, investigation, diagnosis and treatment. We think what is meant here is that **treatment** of asthma will not be covered by the guideline.	Thank you we agree and have edited 4.3.2. a) accordingly.
129	SH	British Thoracic Society	6	4.3.4.4	We note that the proposed guideline will not look at treatment (ie management of asthma) but would point out that the evaluation of success (4.4) is mainly linked to efficacy of appropriate treatment. Further detail should be included on how the diagnostic process will be evaluated and how this will result in appropriate treatment. We suggest that challenge testing should cover direct / indirect testing and also consider the methodology i.e. deep inhalation vs tidal breathing methods.	Thank you. Re 1st paragraph – we agree and this guideline will focus upon making a positive diagnosis of asthma. Re 2nd paragraph – we disagree; we are unable to undertake detailed analyses of challenge testing.
130	SH	Faculty of Sports and Exercise Medicine	6	4.4	For asthma presenting in childhood what is the likelihood of persistence or resolution later in childhood or in the transition from childhood to adulthood?	Thank you but this is beyond our remit.
131	SH	Royal College of Paediatrics and Child Health	7	4.4	Outcomes should include the frequency of adverse events.	Thank you. The GDG will debate the specifics of the relevant outcomes (in relation to the benefits and harms) where relevant.
132	SH	NAPP Pharmaceuticals	11	4.4	The main outcomes section includes parameters for measuring outcomes. Within the guideline it will be important to include recommendations for how these will be measured. For example for measuring health related QoL which tool will be used within each healthcare setting? For example the AQLQ may be appropriate for secondary/tertiary care while the mini AQLQ may be considered for primary care.	All the methods will be assessed in terms of effectiveness, cost effectiveness and practicality.
133	SH	Intensive Care Society	3	4.4	The need for critical care should be included	Thank you – the GDG will debate the relevance of the outcomes – however we don't believe that admission to ITU is likely to feature as an outcome in papers of diagnosis

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						and monitoring.
134	SH	AstraZeneca UK Ltd	3	4.4	We are concerned that the outcomes to be measured (accuracy of diagnostic tests, frequency of asthma attacks, need for oral corticosteroids and short-acting beta-agonists, frequency of unscheduled emergency treatments, health-related quality of life and time off school/work) are also measures relevant to the management of asthma which is outside the scope of this guidance. We believe there is a possibility that monitoring of asthma without considering management may give false outcomes for any cost effectiveness analysis of monitoring conducted within the guideline. What reassurances can the GDG provide to mitigate this risk?	Thank you, the issue of downstream effects is routinely considered in all NICE cost effectiveness analyses, as it will be in this guideline. It is impossible to give further details without knowing which questions will be prioritised for new cost effectiveness analysis.
135	SH	Primary care respiratory society	8	4.4	We note that there is no reference to asthma deaths as an outcome. As we do not fully understand the meaning and use of the section 'Outcomes' it is hard to know whether this should be here or not. It was discussed at the scoping meeting. It is important as an outcome, not because of the number of people who die from asthma, but because of the large number of deaths believed to be avoidable.	Thank you. This section identifies the 'outcomes' that are likely to be of most importance across the literature pertinent to this guideline. The GDG will finalise the outcomes per question per protocol
136	SH	Primary care respiratory society	7	4.4	We think the heading 'Outcomes' needs some explanation. What are these outcomes being measured in respect of? Outcomes of implementation of the guidance or what?	Thank you. This section identifies the 'outcomes' that are likely to be of most importance across the literature pertinent to this guideline. The GDG will finalise the outcomes per question per protocol
137	SH	Asthma UK	5	4.4	With the exception of the proposed outcome on the accuracy of diagnostic tests, the outcomes listed in section 4.4 are not directly linked to the diagnosis and monitoring tools being assessed. Frequency of asthma attacks, need for steroids, emergency treatment, health related quality of life, and time off school or work are all outcomes that matter to people with asthma, but are linked to the management of asthma that follows an accurate diagnosis. If these outcomes are to be covered, management may need to be indirectly included in assessments of effectiveness if the guideline is not to cover this issue.	Thank you. This section identifies the 'outcomes' that are likely to be of most importance across the literature pertinent to this guideline. The GDG will finalise the outcomes per question per protocol.
138	SH	Aerocrine Ltd	13	4.4 a	• It must be asked: accuracy of what? If we want to estimate corticosteroid-sensitive airway inflammation, FeNO is probably the most accurate test available today and should be the reference test and not the index test (see Sverrild JACI 2010, Taylor 2012).	Thank you. The details of the review questions and protocols will be agreed by the GDG

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						We have added 'responses to treatment' to the outcome measures.
139	SH	Pharmaxis Pharmaceuticals Ltd	5	4.4 a **Main Outcomes** *Accuracy of diagnostic tests*	Please consider points highlighted in No. 2. • Standardisation (repeatability / reproducibility of assessment over the patients life-time) • Quality in formulation • Simplicity in administration	Thank you
140	SH	Cochrane Airways Group	6	4.4 a	The positive and negative predictive values of diagnostic tests in the appropriate environment (such as primary care) may be more important than test sensitivity and specificity. We need to know which tests are useful to rule in and rule out asthma. This also needs separate assessment by age-group. Pre-school children have a different set of competing diagnosis for wheezing in comparison to working adults with wheeze.	Thank you. We will bear you comment in mind but the GDG will agree the most robust guide for reporting.
141	SH	Aerocrine Ltd	14	4.4 b	• See already mentioned studies demonstrating that FeNO-guided treatment reduces the rate of asthma exacerbations both in children and adults (Mahr 2013, Donohue 2013, Syk 2013)	Thank you
142	SH	Aerocrine Ltd	15	4.4 c	• FeNO-guided treatment has been shown to reduce the need for SABA dispensings (Zeiger 2011)	Thank you
143	SH	Pharmaxis Pharmaceuticals Ltd	6	4.4 c **Main Outcomes** *Need for oral corticosteroids and short-acting beta-agonists*	Please also consider inhaled corticosteroids and/or other medicines that reflect a step-change in treatment to control asthma symptoms.	Thank you
144	SH	Royal College of Nursing	11	4.4 d	Frequency of unscheduled emergency treatments *and visits/admissions*	Thank you. We have edited the wording to 'unscheduled healthcare utilisations'.
145	SH	College of Emergency Medicine	6	4.4 d	Our comments are as follows: Attendance at an emergency department data for patients with exacerbation of asthma, as well as the outcome of those attendances (e.g. admission to hospital, discharge from ED or death from asthma in ED) should be an outcome measure.	Thank you. Death as a reported outcome is unlikely to feature in papers pertaining to diagnosis or monitoring. We will edit the wording to 'unscheduled healthcare utilisations'.
146	SH	College of Emergency Medicine	9	4.4 d	Our comments are as follows: The guideline should cover how data collected about individuals attending emergency departments with an exacerbation of asthma can be used in terms of whole populations. E.g. data on the number	Thank you this is outside the remit

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					of such presentations per population group served. This might help target resources / advice on specific populations including patients registered with specific GP surgeries, or those in groups based on, for example, race, gender or disability.	
147	SH	College of Emergency Medicine	7	4.4 d	Our comments are as follows: The guideline should cover what demographic and clinical data should be collected when patients with known asthma attend emergency departments with an exacerbation, and how this should be communicated to primary care. The guideline should cover what demographic data related to issues of equality (if any) should be gathered by emergency departments.	Thank you this is outside the remit
148	SH	College of Emergency Medicine	8	4.4 d	Our comments are as follows: The guideline should seek consensus on how this data should be used for individual patients e.g. should all patients who are treated in an ED for an exacerbation of asthma have a GP review of their treatment / management? If so, after how long? Should emergency departments have direct access to appropriate review clinics (either in primary or secondary care) for patients attending with exacerbations of asthma? Should there be a threshold (in terms of number or frequency of ED attendances) above which a specific management review pathway is initiated? If so what would that pathway be?	Thank you this is outside the remit
149	SH	Pharmaxis Pharmaceuticals Ltd	7	4.4 d **Main Outcomes** *Frequency of unscheduled emergency treatments*	Please consider all forms of medical resource utilisation. For examples, non-hospitalised / non-emergency exacerbations may still require an early medical intervention and therefore a consumption of unscheduled resource use.	Thank you this is outside the remit
150	SH	Severe Asthma National Network	8	4.4 d	Treatments replace with reviews.	Thank you this is outside the remit
151	SH	Resuscitation Council	5	4.4 d	We wonder if the frequency of emergency treatment should be subdivided into presentations in primary care, use of emergency ambulances and ED admissions. The severity of attacks doesn't feature as an outcome measure but may be difficult to record accurately.	Thank you. We have edited the wording to 'unscheduled healthcare utilisations'.
152	SH	Primary care respiratory society	9	4.4 f	We agree that logging time off work and school is an important indicator of degree of control of people's asthma. This will require a data collection system to be set up as we believe these data are not routinely collected.	Thank you. This guideline is focused upon secondary research (not primary).
153	SH	Aerocrine Ltd	16	4.5	• A recent primary care study demonstrates that asthma management including FeNO improves asthma outcomes while reducing the overall cost of asthma care (Lester, 2012)	Thank you

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					• Using FeNO in primary care could mean cost-savings from improved diagnostic accuracy and a better guided asthma therapy (Price 2013) • An economic assessment of FeNO testing in the UK highlighted that asthma diagnosis using FeNO measurement cost less per patient as compared with standard diagnostic tests and that asthma management using FeNO measurement instead of lung function testing resulted in further annual cost-savings and quality-adjusted life-years gained for patients with mild to severe and moderate to severe asthma. Asthma diagnosis based on FeNO measurement with NIOX MINO alone is potentially less costly and more accurate than standard diagnostic methods (Price 2009).	
154	SH	British Thoracic Society	7	4.5	The economic analysis of diagnostic processes will potentially be of value in establishing the cost-benefit of different testing processes.	Thank you
155	SH	Roche Products Ltd	4	5.1	In Feb 2013, NICE published the Quality Standard for Asthma (QS25) which covers the entire disease pathway and refers to the British Thoracic Society / SIGN guideline for Asthma. We would welcome the alignment of the new NICE clinical guideline to QS25 as appropriate, as well as NICE endorsement of the BTS-SIGN guideline for asthma management so that clinical guidance is available across the patient pathway.	Thank you. The Quality Standard will align to the guideline following publication.
156	SH	Royal College of Paediatrics and Child Health	9	5.2	Measurement of inhaled Nitric Oxide in asthma – NICE guideline – publication expected in 2014. This could be included as part of this guideline.	Thank you. We are aware of this work (please see Section 5.2 of our Scope) and the Guideline Development Group will incorporate its findings.
157	SH	Roche Products Ltd	5	5.2	The guidance for Omalizumab for the treatment of severe persistent allergic asthma has now been published and should be moved to section 5.1.	Thank you
158	SH	Asthma UK	1	General	A NICE guideline on asthma is a welcome development, and Asthma UK looks forward to its publication and implementation, particularly as NICE will be reviewing cost-effectiveness as well as clinical effectiveness. The guideline has the potential to aid improvements in how asthma is assessed. However, NICE should work closely with the group responsible for developing the British Thoracic Society/Scottish Intercollegiate Guidelines Network asthma guideline in order to ensure that its guideline complements their comprehensive publication. In terms of the outcomes it is proposed the guideline should cover, it is difficult to see how the effectiveness of diagnostic tests and monitoring tools	1st paragraph – thank you 2nd paragraph – thank you 3rd paragraph – Thank you, the issue of downstream effects is routinely considered in all NICE cost effectiveness analyses, as it will be in this guideline. It is impossible to give further details without knowing which questions will be prioritised for new cost effectiveness analysis.

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					can be demonstrated independently beyond their accuracy. Wider clinical outcomes such as the frequency of asthma attacks are linked to the management of asthma that follows an accurate diagnosis, and management may need to be indirectly included in assessments of effectiveness if the guideline is not to cover this issue.	
159	SH	Birmingham Children's Hospital	9	General	Any recommendations on minimum frequency of review in primary and secondary care	Thank you we cannot pre-empt what the guideline will recommend.
160	SH	National Paediatric Respiratory & Allergy Nurses Group *(NPRANG)*	6	General	Any recommendations on minimum frequency of review in primary and secondary care	Thank you we cannot pre-empt what the guideline will recommend.
161	SH	NAPP Pharmaceuticals	1	General	As a general comment, we would like to suggest that this guideline should be linked in some way to the management of asthma. Diagnosis, monitoring and management of asthma are all intrinsically linked and all are both important and often undermanaged. Therefore we suggest linking to the BTS/SIGN guidelines.	Thank you. Further NICE guidance on asthma will be considered in future alongside other priorities. The decision for NICE to produce a clinical guideline on asthma was made by the Department of Health. While NICE has a fairly comprehensive library of clinical guidelines, it appears odd for a topic of significant impact like asthma to be missing from this list. It is an opportunity for guidance to be produced using NICE's methodological processes, including health economics which the SIGN/BTS guideline does not include. NICE recognises the perceived overlap/duplication in work that producing a NICE guideline on asthma may generate and has liaised with SIGN about priority areas for this new guideline.
162	SH	AstraZeneca UK Ltd	1	General	AstraZeneca UK Ltd would like to thank NICE for the opportunity to comment on the draft scope for the Asthma: diagnosis and monitoring of asthma in adults, children and young people NICE clinical guideline	Thank you
163	SH	Royal College of Paediatrics and	13	General	BTS/SIGN guidelines already address many of the areas that this proposal from NICE intends to cover.	Thank you. The decision for NICE to produce a clinical guideline on asthma was made by the

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		Child Health				Department of Health. While NICE has a fairly comprehensive library of clinical guidelines, it appears odd for a topic of significant impact like asthma to be missing from this list. It is an opportunity for guidance to be produced using NICE's methodological processes, including health economics which the SIGN/BTS guideline does not include. NICE recognises the perceived overlap/duplication in work that producing a NICE guideline on asthma may generate and has liaised with SIGN about priority areas for this new guideline.
164	SH	Royal College of Paediatrics and Child Health	15	General	Children under the age of 5 years cannot perform lung function tests reliably. Asthma is therefore a clinical diagnosis.	Thank you
165	SH	Birmingham Children's Hospital	1	General	Do we need this document as we work very closely from the BTS/SIGN guidelines which are evidenced based	Thank you
166	SH	Birmingham Children's Hospital	10	General	Does not mention PEFR specifically in monitoring although does so in diagnosis but we presume NICE will look at usefulness of PEFR in all ages in diagnosis and monitoring	Thank you. We have added peak flow to monitoring section of the scope.
167	SH	National Paediatric Respiratory & Allergy Nurses Group *(NPRANG)*	7	General	Does not mention PEFR specifically in monitoring although does so in diagnosis but we presume NICE will look at usefulness of PEFR in all ages in diagnosis and monitoring	Thank you. We have added peak flow to monitoring section of the scope.
168	SH	Severe Asthma National Network	9	General	Establishment of smoking status is not mentioned in the diagnostic section	Thank you. This is of more importance in making a COPD diagnosis and this guideline will focus on making a positive diagnosis of asthma.
169	SH	GlaxoSmithKline	1	General	GSK has no comments on the draft scope. We are pleased with the addition of and focus on patient reported outcomes. The initial draft scoping meeting was productive and the outputs appear to have been captured in this consultative document	Thank you
170	SH	Group of Occupational Respiratory Disease Specialists	3	General	1. In terms of the draft scope for the NICE review, it has been suggested that the focus should be on case finding. The view of the GORDS group is that the evidence-based review should consider the following aspects:	Thank you. The GDG will consider these points and make a final agreement on the focus of these questions.

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		(GORDS)			a. What proportion of the occupational asthma predicted by epidemiological studies is not currently being identified as cases in the UK? (i.e. how many cases are currently being missed?) b. What is the best method for finding cases of occupational asthma in primary and secondary care? (i.e. when and how should it be considered amongst adults with asthma) c. What is the predictive value of a patient's occupation in making a diagnosis of asthma (i.e. does working in certain high risk job significantly increase the risk of asthma, and by how much?) d. What are the benefits of early case recognition in terms of asthma severity, use of medication, maintained employment, working days lost, and total societal costs.	
171	SH	National Paediatric Respiratory & Allergy Nurses Group *(NPRANG)*	1	General	Is this clinical guideline really needed as we already have and use the evidenced based BTS/SIGN guidelines which have an excellent chapter on the diagnosis of asthma.	Thank you. The decision for NICE to produce a clinical guideline on asthma was made by the Department of Health. While NICE has a fairly comprehensive library of clinical guidelines, it appears odd for a topic of significant impact like asthma to be missing from this list. It is an opportunity for guidance to be produced using NICE's methodological processes, including health economics which the SIGN/BTS guideline does not include. NICE recognises the perceived overlap/duplication in work that producing a NICE guideline on asthma may generate and has liaised with SIGN about priority areas for this new guideline.
172	SH	Royal College of Paediatrics and Child Health	16	General	It is inappropriate in most children to do any invasive tests such as bronchoscopy and biopsy, or methacholine challenges. Exercise testing is occasionally useful in children.	Thank you
173	SH	Royal College of Paediatrics and Child Health	10	General	It may be of use mentioning the need to diagnose other conditions that lead to increased airway hyper-responsiveness e.g. rhinitis, as the recognition and treatment of these would improve the symptoms of asthma. - Arch Dis Child 2011;96:i1014 doi:10.1136/adc.2011.213462. The 'unified airway': the RCPCH care pathway for children with asthma and/or rhinitis Gillian Vance, et al	Thank you. This guideline will focus upon making a positive diagnosis of asthma.

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					- Thorax 2009;64:999-1004. Upper airway · 1: Allergic rhinitis and asthma: united disease through epithelial cells. A Bourdin, D Gras, I Vachier, P Chanez - CHEST February 1999; vol.115 no.2 550-556. Rhinosinusitis and Asthma. Epiphenomenon or Causal Association. Fernando M.de Benedicits, Andrew Bush - Primary Care Respiratory Journal 2012;21(2):222-228. Poor asthma control?-then look up the nose. The importance of co-morbid rhinitis in patients with asthma. Glenis Scadding, Samantha Walker.	
174	SH	Royal College of Paediatrics and Child Health	17	General	One cannot help feeling that this proposal is driven by trying to save money, rather than trying to improve quality of care for those with asthma.	Thank you
175	SH	Medicines and Healthcare Products Regulatory Agency	1	General	Since this clinical guideline will focus on diagnosis and monitoring (specifically excluding management) of asthma, we will **not** comment on the scope.	Thank you
176	SH	Royal College of Paediatrics and Child Health	14	General	Tests which may be appropriate in adults are often inappropriate in children, with the possible exception of skin prick tests for atopy, and genetic tests in the relatively distant future.	Thank you
177	SH	Department of Health	1	General	Thank you for the opportunity to comment on the draft scope for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you

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178	SH	Group of Occupational Respiratory Disease Specialists (GORDS)	1	General	The draft scope for the NICE asthma diagnosis and monitoring guideline was discussed by the GORDS members on 26/4/13. The GORDS group would like to make the following comments: 1. We welcome the inclusion of occupational asthma within the scope of this review, and feel this condition warrants special attention in the guideline. There is good evidence that occupational asthma is currently under-diagnosed in the UK, that long delays occur at each step of the patient journey, and that late diagnosis adversely affects prognosis [1,2]. Existing evidence-based UK guidance and NICE Quality Standards[1-4] advocate considering the diagnosis in all adult with asthmatic symptoms. Early referral to a clinician with a specialist interest in the condition, with access to the full range of diagnostic tests [5] is likely to offer the best patient outcomes balancing future health and employment [1,2,6]. If diagnosed early, and further exposures can be avoided, there is an opportunity for asthma to be effectively "cured", avoiding a lifetime of prescribed medications and healthcare visits [1,6]. The GORDS group believe it is important that all national guidance provides the same clear and consistent message, in order to promote best practice in primary and secondary care. It would also be helpful to signpost the more specialised guidance, by referencing it in the NICE document.	The guideline is mainly intended to improve the diagnosis of asthma irrespective of a specific cause.
179	SH	Birmingham Children's Hospital	2	General	The need/ not need of chest Xray not mentioned	Thank you, CXR may be useful for other conditions but not for the diagnosis of asthma.
180	SH	National Paediatric Respiratory & Allergy Nurses Group *(NPRANG)*	2	General	The need/ not need of CXR not mentioned	Thank you, CXR may be useful for other conditions but not for the diagnosis of asthma.
181	SH	Royal College of Nursing	1	General	The Royal College of Nursing welcomes proposals to develop this guideline. It is timely. The draft scope seems comprehensive.	Thank you
182	SH	Royal College of Paediatrics and Child Health	1	General	The scope is excellent and timely	Thank you

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183	SH	Scottish Intercollegiate Guidelines Network (SIGN	1	General	The SIGN/BTS British Guideline on the Management of Asthma, which is applicable to the whole of the UK, currently includes sections on the diagnosis and monitoring of asthma. These sections, along with a number of others, are currently being updated as part of the regular biennial review of the guideline and publication of the revised guideline is expected in the summer of 2014. The Steering Committee for the SIGN/BTS asthma guideline is concerned that publication of a NICE guideline on the diagnosis and management of asthma could lead to there being conflicting recommendations on these topics in two separate pieces of national guidance. For the benefit of healthcare practitioners and patients alike, this is something we would wish to avoid.	Thank you. We certainly wish to avoid confusion and we hope that this will not happen given that the guidelines will consider the same evidence. The NICE guideline also considers health economics.
184	SH	UKCPA-Respiratory Group	1	General	The UKCPA-Respiratory Group welcome the development of this guideline by NICE. We have no comments regarding the scope outlined.	Thank you
185	SH	Severe Asthma National Network	1	General	There is a wide variance in practice across the UK, SANN feels this guideline will help reduce the variations in diagnosis and monitoring.	Thank you
186	SH	Royal College of Paediatrics and Child Health	18	General	There is emerging evidence that as prophylactic asthma prescriptions for children have risen, GP consultations for asthma and hospital admission rates have started to fall.	Thank you
187	SH	Novartis Pharmaceuticals UK Ltd	6	General	We consider that guidance on when to refer from primary care to secondary care and on which criteria to refer is part of the diagnosis process and that it would therefore be useful to include this within the scope of the Clinical Guideline.	Thank you. We will look at which test work rather than where the test is done.
188	SH	Birmingham Children's Hospital	11	General	We presume NICE will clarify the requires components of Asthma Annual review as mentioned in the NICE Quality standards (as per monitoring section of this)	Thank you. We are unable to pre-empt the recommendations.
189	SH	National Paediatric Respiratory & Allergy Nurses Group *(NPRANG)*	8	General	We presume NICE will clarify the requires components of Asthma Annual review as mentioned in the NICE Quality standards (as per monitoring section of this)	Thank you. We are unable to pre-empt the recommendations.
190	SH	Royal College of Paediatrics and Child Health	8	General	We think an obstacle will be determining the diagnostic accuracy of the value of tests for the diagnosis of asthma – given that asthma is not clearly defined and 'response to anti-asthma therapy' is an important feature. In many ways what we want to find out is whether the patients respiratory symptoms are 'steroid' responsive or not. One issue we believe results in asthma over-diagnosis is the use of "trials of	Thank you. We have edited and added response to treatment under section 4.4.

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					asthma therapy". These are often NOT clearly defined and are not objectively carried out. After such a trial it is not infrequent that the child/parent or patient replies that the medication has worked a 'bit'. Formalising what a diagnostic trial of anti-asthma therapy is and how it is tested would be worthwhile.	
191	SH	British Thoracic Society	1	General	We welcome that NICE recognises the importance of asthma - but query why guidance is required given the NICE accredited guideline produced by SIGN/BTS. We are aware that SIGN, our partners in producing the British Guideline on the management of Asthma, are making a similar observation in its response.	Thank you. The decision for NICE to produce a clinical guideline on asthma was made by the Department of Health. While NICE has a fairly comprehensive library of clinical guidelines, it appears odd for a topic of significant impact like asthma to be missing from this list. It is an opportunity for guidance to be produced using NICE's methodological processes, including health economics which the SIGN/BTS guideline does not include. NICE recognises the perceived overlap/duplication in work that producing a NICE guideline on asthma may generate and has liaised with SIGN about priority areas for this new guideline.
	SH	Aerocrine Ltd	17	Reference List to items 1-16 above	**REFERENCE LIST:** Alving, K. and A. Malinovschi, **Basic aspects of exhaled nitric oxide.** Eur Respir Monograph, 2010. 49: p. 1-31. Anderson, W.J., P.M. Short, P.A. Williamson, and B.J. Lipworth, **Inhaled corticosteroid dose response using domiciliary exhaled nitric oxide in persistent asthma: the fenotype trial.** Chest, 2012. 142(6): p. 1553-61. Bastain, T.M., T. Islam, K.T. Berhane, R.S. McConnell, E.B. Rappaport, M.T. Salam, W.S. Linn, E.L. Avol, Y. Zhang, and F.D. Gilliland, **Exhaled nitric oxide, susceptibility and new-onset asthma in the Children's Health Study.** Eur Respir J, 2011. 37(3): p. 523-31. Bodini, A., D. Peroni, A. Loiacono, S. Costella, R. Pigozzi, E. Baraldi, A.L. Boner, and G.L. Piacentini, **Exhaled nitric oxide daily evaluation is effective in monitoring exposure to relevant allergens in asthmatic children.** Chest, 2007. 132(5): p. 1520-5.	Thank you

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					Berry, M., A. Morgan, D.E. Shaw, D. Parker, R. Green, C. Brightling, P. Bradding, A.J. Wardlaw, and I.D. Pavord, **Pathological features and inhaled corticosteroid response of eosinophilic and non-eosinophilic asthma.** Thorax, 2007. 62(12): p. 1043-9. Boyle, R.J., C. Pedroletti, M. Wickman, L. Bjermer, E. Valovirta, R. Dahl, A. Von Berg, O. Zetterstrom, J.O. Warner, and A.S. Group, **Nocturnal temperature controlled laminar airflow for treating atopic asthma: a randomised controlled trial.** Thorax, 2012. 67(3): p. 215-21. Buchvald, F., H. Eiberg, and H. Bisgaard, **Heterogeneity of FeNO response to inhaled steroid in asthmatic children.** Clin Exp Allergy, 2003. 33(12): p. 1735-40. Contoli, M., S. Baraldo, B. Marku, P. Casolari, J.A. Marwick, G. Turato, M. Romagnoli, G. Caramori, M. Saetta, L.M. Fabbri, and A. Papi, **Fixed airflow obstruction due to asthma or chronic obstructive pulmonary disease: 5-year follow-up.** J Allergy Clin Immunol, 2010. 125(4): p. 830-7. Cordeiro, D., A. Rudolphus, E. Snoey, and G.J. Braunstahl, **Utility of nitric oxide for the diagnosis of asthma in an allergy clinic population.** Allergy Asthma Proc, 2011. 32(2): p. 119-26. Corren, J., R.F. Lemanske, N.A. Hanania, P.E. Korenblat, M.V. Parsey, J.R. Arron, J.M. Harris, H. Scheerens, L.C. Wu, Z. Su, S. Mosesova, M.D. Eisner, S.P. Bohen, and J.G. Matthews, **Lebrikizumab Treatment in Adults with Asthma.** N Engl J Med, 2011. 365(12): p. 1088-98. Cowan, D.C., J.O. Cowan, R. Palmay, A. Williamson, and D.R. Taylor, **Effects of steroid therapy on inflammatory cell subtypes in asthma.** Thorax, 2010. 65(5): p. 384-90. Donohue, J.F. and N. Jain, **Exhaled nitric oxide to predict corticosteroid responsiveness and reduce asthma exacerbation rates.** Respiratory medicine, 2013. *In press* Feitosa, L.A., A. Dornelas de Andrade, C.M. Reinaux, and M.C. Britto,	

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					Diagnostic accuracy of exhaled nitric oxide in exercise-induced bronchospasm: Systematic review. Rev Port Pneumol, 2012. 18(4): p. 198-204. Grzelewski, T., A. Grzelewska, P. Majak, W. Stelmach, A. Kowalska, R. Stelmach, A. Janas, and I. Stelmach, **Fractional exhaled nitric oxide (FeNO) may predict exercise-induced bronchoconstriction (EIB) in schoolchildren with atopic asthma.** Nitric Oxide, 2012. 27(2): p. 82-87. Ihre, E., P. Gyllfors, L.E. Gustafsson, M. Kumlin, and B. Dahlen, **Early rise in exhaled nitric oxide and mast cell activation in repeated low-dose allergen challenge.** Eur Respir J, 2006. 27(6): p. 1152-9. Koster, E.S., J.A. Raaijmakers, S.J. Vijverberg, and A.H. Maitland-van der Zee, **Inhaled corticosteroid adherence in paediatric patients: the PACMAN cohort study.** Pharmacoepidemiol Drug Saf, 2011. 20(10): p. 1064-72. Lester, D., A. Mohammad, P.I. Hernandez, E.E. Leach, and E.A. Walker, **An investigation of asthma care best practices in a community health center.** J Health Care Poor Underserved, 2012. 23(3 Suppl): p. 255-64. Mahr, T.A., J. Malka, and J.D. Spahn, **Inflammometry in pediatric asthma: A review of fractional exhaled nitric oxide in clinical practice.** Allergy Asthma Proc, 2013 *in press* (published online) Malinovschi, A., K. Alving, P. Kalm-Stephens, C. Janson, and L. Nordvall, **Increased exhaled nitric oxide predicts new-onset rhinitis and persistent rhinitis in adolescents without allergic symptoms.** Clin Exp Allergy, 2012. 42(3): p. 433-40. Malinovschi, A., J. Fonseca, T. Jacinto, K. Alving, C. Janson, **Additive role of exhaled NO and blood eosinophil count to predict wheezing in a random population sample,** ERS abstract 2012 Matsunaga, K., H. Kawabata, T. Hirano, H. Sugiura, Y. Minakata, and M. Ichinose, **Difference in time-course of improvement in asthma control measures between budesonide and budesonide/formoterol.** Pulm Pharmacol Ther, 2013. 26(2): p. 189-94.	

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					McNicholl, D.M., M. Stevenson, L.P. McGarvey, and L.G. Heaney, **The Utility of Fractional Exhaled Nitric Oxide Suppression in the Identification of Nonadherence in Difficult Asthma.** American Journal of Respiratory and Critical Care Medicine, 2012. 186(11): p. 1102-1108. Nicolini, G., A. Chetta, A. Simonazzi, P. Tzani, M. Aiello, and D. Olivieri, **Both bronchial and alveolar exhaled nitric oxide are reduced with extrafine beclomethasone dipropionate in asthma.** Allergy Asthma Proc, 2010. 31(5): p. 85-90. Nolte, H., I. Pavord, V. Backer, S. Spector, T. Shekar, D. Gates, P. Nair, and F. Hargreave, **Dose-dependent anti-inflammatory effect of inhaled mometasone furoate/formoterol in subjects with asthma.** Respir Med, 2013. 107(5): p. 656-64. Olin, A.C., A. Rosengren, D.S. Thelle, L. Lissner, and K. Toren, **Increased fraction of exhaled nitric oxide predicts new-onset wheeze in a general population.** Am J Respir Crit Care Med, 2010. 181(4): p. 324-7. Perez-de-Llano, L.A., F. Carballada, O. Castro Anon, M. Pizarro, R. Golpe, A. Baloira, M. Vazquez Caruncho, and M. Boquete, **Exhaled nitric oxide predicts control in patients with difficult-to-treat asthma.** Eur Respir J, 2010. 35(6): p. 1221-7. Powell, H., V.E. Murphy, D.R. Taylor, M.J. Hensley, K. McCaffery, W. Giles, V.L. Clifton, and P.G. Gibson, **Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial.** Lancet, 2011. 378(9795): p. 983-90. Price, D, Berg J, Lindgren P. **An economic evaluation of NIOX MINO airway inflammation monitor in the United Kingdom**. Allergy 2009; 64(3): 431-438 Price, D., D. Ryan, P Dorinsky, A Burden, J von Ziegenweidt, S Gould, D Freeman, K Gruffyd-Jones, A Copland, C Godley, A Chisholm, M Thomas, **Fractional exhaled nitric oxide (FeNO) in real-life asthma diagnosis and management pathways: current and proposed use,** *submitted*	

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					oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomised controlled trial. Lancet, 2008. 372(9643): p. 1065-72. Taylor, D.R., **Biomarkers of inflammation in asthma: a clinical perspective.** Semin Respir Crit Care Med, 2012. 33(6): p. 620-9. Vahlkvist, S., M. Sinding, K. Skamstrup, and H. Bisgaard, **Daily home measurements of exhaled nitric oxide in asthmatic children during natural birch pollen exposure.** J Allergy Clin Immunol, 2006. 117(6): p. 1272-6. van Veen, I.H., A. Ten Brinke, P.J. Sterk, J.K. Sont, S.A. Gauw, K.F. Rabe, and E.H. Bel, **Exhaled nitric oxide predicts lung function decline in difficult-to-treat asthma.** Eur Respir J, 2008. 32(2): p. 344-9. Zeiger, R.S., M. Schatz, F. Zhang, W.W. Crawford, M.S. Kaplan, R.M. Roth, and W. Chen, **Elevated exhaled nitric oxide is a clinical indicator of future uncontrolled asthma in asthmatic patients on inhaled corticosteroids.** J Allergy Clin Immunol, 2011. 128(2): p. 412-4. Zietkowski, Z., A. Bodzenta-Lukaszyk, M.M. Tomasiak, W. Szymanski, and R. Skiepko, **Effect of ciclesonide and fluticasone on exhaled nitric oxide in patients with mild allergic asthma.** Respir Med, 2006. 100(9): p. 1651-6.	
	SH	Group of Occupational Respiratory Disease Specialists (GORDS)	4	References relating to GORD items 1-3	1. Nicholson PJ, Cullinan P, Burge PS & Boyle C. Occupational asthma: Prevention, identification & management: Systematic review & recommendations. British Occupational Health Research Foundation. London. 2010. 2. Fishwick D, Barber CM, Bradshaw LM, Harris-Roberts J, Francis M, Naylor S, Ayres J, Burge PS, Corne JM, Cullinan P, Frank TL, Hendrick D, Hoyle J, Jaakkola M, Newman-Taylor A, Nicholson P, Niven R, Pickering A, Rawbone R, Stenton C, Warburton CJ, Curran AD; British Thoracic Society Standards of Care Subcommittee Guidelines on Occupational Asthma. Standards of care for occupational asthma. Thorax 2008 Mar;63(3):240-50. 3. BTS/SIGN Asthma Guideline: 2012. 4. Barber CM, Naylor S, Bradshaw L, Francis M, Harris-Roberts J,	Thank you

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					Rawbone R, Curran A, Fishwick D; British Thoracic Society Research Committee. Facilities for investigating occupational asthma in UK non-specialist respiratory departments. Occup Med (Lond) 2008 Jan;58(1):71-3. 5. Barber CM, Naylor S, Bradshaw LM, Francis M, Harris-Roberts J, Rawbone R, Curran AD, Fishwick D; British Thoracic Society Research Committee. Approaches to the diagnosis and management of occupational asthma amongst UK respiratory physicians. Respir Med 2007 Sep;101(9):1903-8. 6. Baur X, Sigsgaard T, Aasen TB, Burge PS, Heederik D, Henneberger P, Maestrelli P, Rooyackers J, Schlunssen V, Vandenplas O and Wilken D on behalf of the ERS Task Force on the Management of Work-related Asthma. Guidelines for the management of work-related asthma. Eur Respir J 2012; 39: 529–45. 7. De Bono J, Hudsmith L. Occupational asthma: a community based study. Occup Med (Lond) 1999;49:217-9. 8. Barber CM, Frank T, Walsh K, Burton C, Bradshaw L, Fishwick D. Knowledge and utilisation of occupational asthma guidelines in primary care. Prim Care Respir J. 2010 Sep;19(3):274-80. 9. Walters G, McGrath E, Ayres JG. Audit of the recording of occupational asthma in primary care. Occ Med 2012;62:570-73	
	SH	Pharmaxis Pharmaceuticals Ltd	8	References to relating to Pharmaxis points 1-7	**References**  SIGN_101 [British Guideline on the mana  Anderson-2009-RespRes-v10-Mannitol-Chit  Lipworth_2012_Ches v141 p607-15 [STAI (provided for convenience): Anderson et al (2009) Resp. Res. 10:4 SIGN 101(2012) British Guideline on the management of asthma Lipworth et al (2012) The STAMINA study. Chest v141 p607-15 SmPC: Summary of Product Characteristics: www.medicines.org.uk/emc/medicine/25105/SPC [last accessed 8 May 2013]	Thank you

These organisations were approached but did not respond:

AAH Pharmaceuticals
Acupuncture Association of Chartered Physiotherapists
ADDEPT
Aintree University Hospital NHS Foundation Trust
ALK-Abelló
Allergy Alliance
Allergy UK
Allocate Software PLC
Amgen UK
Arrhythmia Alliance
Assocation of NHS Occupational Physicians
Association of Anaesthetists of Great Britain and Ireland
Association of Chartered Physiotherapists in Respiratory Care
Association of Paediatric Chartered Physiotherapists
Association of Paediatric Emergency Medicine
Association of Respiratory Nurse Specialists
Barnsley Hospital NHS Foundation Trust
Black and Ethnic Minority Diabetes Association
Black Country Partnership Foundation Trust
Boston Scientific
Brahms UK Limited-Thermo Fisher Scientific
British Acupuncture Council
British Cardiovascular Society
British Infection Association
British Lung Foundation
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Psychological Society
BUPA Foundation
Calderdale and Huddersfield NHS Trust
Calderstones Partnerships NHS Foundation Trust
Cambridge University Hospitals NHS Foundation Trust
Capsulation PPS
Capsulation PPS

Care Quality Commission (CQC)
Chartered Society of Physiotherapy
Children & Young Peoples Allergy Network Scotland
Children England
Children's Commissioner for Wales
Clarity Informatics Ltd
Croydon Health Services NHS Trust
Cygnet Hospital Harrow
Department of Health, Social Services and Public Safety - Northern Ireland
Dorset Primary Care Trust
East and North Hertfordshire NHS Trust
Education for Health
Expert Patients Programme CIC
Faculty of Intensive Care Medicine
Fair Play for Children
Five Boroughs Partnership NHS Trust
Foundation Trust Network
Hammersmith and Fulham Primary Care Trust
Harrow Local Involvement Network
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Hindu Council UK
Hockley Medical Practice
Humber NHS Foundation Trust
Independent Children's Homes Association
Independent Healthcare Advisory Services
Inner North West London PCTs
Institute of Biomedical Science
Integrity Care Services Ltd.
Joint Committee on Immunology & Allergy
Kent Community Health NHS Trust
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Limbless Association
Liverpool Community Health
London Ambulance Service NHS Trust
London Clinic
Luton and Dunstable Hospital NHS Trust
Manchester Metropolitan University

Merck Sharp & Dohme UK Ltd
Ministry of Defence
National Childbirth Trust
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Institute for Health Research Health Technology Assessment Programme
National Institute for Health Research
National Patient Safety Agency
National Treatment Agency for Substance Misuse
NHS Connecting for Health
NHS County Durham and Darlington
NHS Direct
NHS England
NHS Halton CCG
NHS Lanarkshire
NHS Plus
NHS Richmond
NHS Sheffield
NICE technical lead
NORTH EAST LONDON FOUNDATION TRUST
Northern Ireland Chest Heart and Stroke
Nottingham City Council
Orion Pharma
Oxford Health NHS Foundation Trust
Parkwood Healthcare
Pharmaceutical Services Negotiating Committee
Pharmametrics GmbH
Public Health Wales NHS Trust
Royal Berkshire NHS Foundation Trust
Royal Brompton Hospital & Harefield NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners in Wales

Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition
Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine
Sandoz Ltd
Sanofi
SCHOOL AND PUBLIC HEALTH NURSES ASSOCIATION
Sheffield Childrens Hospital
Sheffield Hallam University
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence
South East Coast Ambulance Service
South East Coast Ambulance Service NHS foundation Trust
South London & Maudsley NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
South Western Ambulance Service NHS Foundation Trust
Southport and Ormskirk Hospital NHS Trust
Spectranetics Corporation
St John Ambulance
St Mary's Hospital
Teva UK
Thames Ambulance Service Ltd
The Chartered Institute of Environmental Health
The Intensive Care Society
Torbay and Southern Devon Health and Care NHS Trus
Translucency Ltd.
Trinity-Chiesi Pharmaceuticals
UK National Screening Committee
Unite - the Union
University Hospitals Birmingham
Vygon
Walsall Hospitals NHS Trust
Walsall Local Involvement Network
Welsh Government
Western Cheshire Primary Care Trust
Western Sussex Hospitals NHS Trust

Westminster Local Involvement Network
Wirral University Teaching Hospital NHS Foundation Trust
Worcestershire Health and Care NHS Trust
York Hospitals NHS Foundation Trust