National Institute for Health and Care Excellence

Cystic fibrosis
Scope Consultation Table
20 November 2014 – 18 December 2014

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
Alder Hey Children's NHS Foundation Trust	1	General	Role of Home IV therapies and setting up of homecare packages and training packages for parents/patients with CF to learn how to self-administer antibiotics at home Evaluation of evidence: more beneficial than hospital antibiotics, more risk?	Thank you for your comment. The committee will consider this during the protocol development for delivery of care.
Alder Hey Children's NHS Foundation Trust	2	General	Port-care in patients that need long term IV access. Best strategies to unblock/look after ports	Thank you for your comment. The management of central venous catheters is a complex matter and applies to the use of such devices in a range of settings in addition to antibiotic administration. The guideline will therefore not address this aspect of management. Please also note that the intravenous fluids therapy in children guideline is in development and will be published in October 2015. For further details see: http://www.nice.org.uk/guidance/indevelopment/gid-cgwave0655
Alder Hey Children's NHS Foundation Trust	3	General	Risk of multiple antibiotic allergies for CF patients. Availability and efficacy of de-sensitising methods (link with allergy departments)	Thank you for your comment. This is covered under the key area of antimicrobial management of pulmonary disease
Alder Hey Children's NHS Foundation Trust	4	General	Vaccination recommendations for CF patients. Influenza vaccination, boosters of pneumococcal vaccinations?	Thank you for your comment. Please refer to the Joint Committee on Vaccination and Immunisation (JCVI) for advice on immunisation.
Alder Hey Children's NHS Foundation Trust	5	General	Where do latest therapies fit in? Omalizumab for ABPA and Ivacaftor.	Thank you for your comment. The guideline scope will include certain immunomodulatory

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			Funding and commissioning of expensive therapies, and review of the CF tariff taking those into consideration	drugs, including corticosteroids and azythromycin. The committee will consider at protocol development whether other agents should also be included. NICE may consider assessing ivacaftor and lumacaftor through the technology appraisal process. Please check our proposed technology appraisals page on the website here.
Alder Hey Children's NHS Foundation Trust	6	General	When talking about bronchoscopy as a diagnostic method, include best evidence in terms of antibiotic cover pre- and post bronchoscopy. If using aminoglycosides ?wait one day post surgery or on same day. Duration of antibiotic treatment post-bronchoscopy	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. This was not prioritised as topic for consideration in this guideline because it was not perceived to be an area with uncertainty or variation in clinical practice. The guideline does not cover all aspects of CF management as this is a very large topic area.
Alder Hey Children's NHS Foundation Trust	7	General	Treatment of GORD in CF, specially since Domperidone was re-classified by the MHRA in 2014	Thank you for your comment. The treatment of GORD in CF is covered in the Gastro-oesophageal reflux in children and young people guideline and Dyspepsia and gastro-oesophageal reflux disease (CG184) published guideline. https://www.nice.org.uk/guidance/cg184
Alder Hey Children's NHS Foundation Trust	8	General	Sodium chloride supplementation: restrict it to warmer months or use around the year?	Thank you for your comment. The scope now includes a key area on nutritional management and the committee will consider at protocol development whether to include sodium chloride supplementation.
Alder Hey Children's NHS Foundation Trust	9	General	Antifungal prophylaxis whilst on iv antibiotics. Evidence for or against routine	Thank you for your comment. Rather than restricting the evidence to antibiotic therapy, the

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			prophylaxis with oral agent. Also monitoring for patients on long term itraconazole; important of level monitoring and most evidence based target range	key area on chest disease has now been widened to address antimicrobial agents, thus potentially including antifungal agents. This will be looked at in more detail at protocol development stage.
Alder Hey Children's NHS Foundation Trust	10	General	**Examining models of care is rather a complicated task. Is the NICE methodology well placed for this task?**	Thank you for your comment. The guideline will follow the NICE Interim methods guide for developing service guidance alongside the Guidelines Manual (2014) which set out the methods that underpin the development of NICE guidance. NICE Guideline Manual (2014): https://www.nice.org.uk/article/pmg20/chapter/1%20Introduction%20and%20overview NICE Interim methods guide: https://www.nice.org.uk/article/pmg8/chapter/1%20Introduction
Alder Hey Children's NHS Foundation Trust	11	General	**Palivizumab (passive immunisation against RSV) for infants with CF is a contentious intervention that requires evaluation. It is painful and costly and there is no proven benefit.**	Thank for your comment. Please refer to the Joint Committee on Vaccination and Immunisation (JCVI) for advice on immunisation**. http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_120395.pdf**
Alder Hey Children's NHS Foundation Trust	12	General	**Ivacaftor and other mutation specific therapies must be evaluated. I am aware of the QALYs ceiling adopted by NICE, but that can't be a reason for not evaluating a therapy that is the most costly in England. It has massive implications for the future of CF care in the UK.**	NICE may consider assessing ivacaftor and lumacaftor through the technology appraisal process. Please check our proposed technology appraisals page on the website here.
Association of chartered physiotherapists in	1	1.1	Section 1.1 states that those who have had an organ transplant will be covered however in section 1.3 point 8 in areas that	Thank you for your comment. The guideline will not be addressing decisions on or methods for transplantation; however, the committee group

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Cystic Fibrosis		and 1.3	will not be covered, transplantation appears. This appears confusing and contradictory.	will consider those who have received an organ transplant when making recommendations in topic areas which are included in the scope. We have clarified section 1.3 to reflect this.
Association of chartered physiotherapists in Cystic Fibrosis	2	1.3 (point 6)	Our greatest concern is around the wording of and limitation of the guideline to 'chest physiotherapy'. Regarding wording, 'Chest physiotherapy' is generally recognised solely as postural drainage and manual techniques and so using this term rather than airway clearance techniques may lead to confusion and inappropriate limitation of the guideline to techniques which are no longer widely used in the management of people with Cystic Fibrosis. More importantly, current service specifications and guidance regarding cystic fibrosis management recognise that the airway clearance aspect of physiotherapy is a small aspect of the effective physiotherapy management of Cystic Fibrosis. We have concerns that a document which covers management of Cystic Fibrosis and yet limits the physiotherapy management solely to airway clearance will negatively impact on the full and holistic treatment of people with Cystic Fibrosis. We particularly recognise the strong impact that NICE guidance has on future planning and provision of services and so have concerns that the omission of important areas of physiotherapy management will have a	Thank you for your comment. We have now revised the question on chest physiotherapy. The scoping group considered that 'airway clearing techniques' are part of chest physiotherapy. The priority techniques to be addressed under chest physiotherapy will be considered by the committee during the protocol development for the evidence review. Please also note that an additional question on exercise and Cystic Fibrosis has been added.

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			significant impact on the care we are able to provide in the future. Following the rollout of newborn screening, some people with CF may be managed effectively with more emphasis on interventions such as active play, exercise, inhalation therapy, etc than on airway clearance. Again the concern is that by limiting this scope to airway clearance techniques, then the overall guidance around effective management for individual presentations of Cystic Fibrosis will be limited. We suggest that this section is worded 'Physiotherapy management' and is inclusive of other important aspects such as activity/exercise, musculoskeletal, continence, sinus management, inhaled medication delivery, etc.	
Association of chartered physiotherapists in Cystic Fibrosis	3	1.5 (point 3)	In keeping with the comments above, we have issues with the wording of this question where 'chest physiotherapy' may be interpreted as postural drainage and manual techniques in isolation. We are also concerned about the limits of a single question regarding physiotherapy management. We hope that NICE will consider the above comments and look at more than one question around physiotherapy management to include: • The acceptance of and effectiveness of different airway	Thank you for your comment. We have now revised the question on chest physiotherapy. Inclusion of airway clearance will be considered by the committee during the protocol development for the evidence review.

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			clearance techniques • The acceptance of and effectiveness of exercise • The acceptance of and effectiveness of musculoskeletal interventions • The acceptance of and effectiveness of continence interventions	
Association of chartered physiotherapists in Cystic Fibrosis	4	1.6	Including adherence and patient satisfaction in this outcomes section would enhance it. Cystic fibrosis is managed with multiple treatments and the ability to adhere to a treatment is vital. It is known from current literature that adherence is variable depending on the treatment and so an understanding of adherence levels to a particular treatment compared with another is useful. Regarding patient satisfaction, there is a high level of self management required from people with CF. This means that patient satisfaction with a treatment is of great importance. People's engagement with a particular treatment may vary according to their satisfaction with it. Overall there is little point in knowing that a treatment has positive effects on the current list of included outcomes if there is no indication whether the patient will actually take it or be happy with it.	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. Assessment of adherence to prescribed therapies has not been prioritised for inclusion in this guideline scope. Please note that this guideline will cross-refer to the medicines adherence guideline (CG76) and also the upcoming guideline on medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015). Please note that patient and carer satisfaction has been added as an outcome in this guideline scope.
Association of	5	General	**Exercise** – we have concerns that this	Thank you for your comment. We have now

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chartered physiotherapists in Cystic Fibrosis			aspect of management, which is considered central to the management of CF, has so little visibility in the scope. Exercise testing and provision is a focus within current UK, European, American, Australian and other worldwide CF guidance. It's omission from this guideline is therefore surprising and concerning. We would like to see exercise identified within the physiotherapy section in section 1.3 and also as a key question.	included a new key area on the role of exercise in maintaining health in patients with cystic fibrosis.
Association of chartered physiotherapists in Cystic Fibrosis	6	General	**Infection control** – Given current issues within Cystic fibrosis management, we feel that the inclusion of infection control as a key area should be considered. A question of "How can services be organised to minimise the risk of cross-infection?" has been included in the scope however the topic doesn't appear to have been given the priority as a key area that it deserves.	Thank you for your comment. The key area of models for delivery of care and MDT teams will also look at how services can be organised to minimise cross-infection. Please see section 1.5 of the scope on key issues and questions.
Association of chartered physiotherapists in Cystic Fibrosis	7	General	**End stage management including oxygen/NIV** – End stage management does not appear either as an excluded area or as a key area. Management associated with this phase is also absent and so treatments such as oxygen therapy and NIV are not covered.	Thank you for your comment. The end of life care in children and young people and care of the dying adult guidelines in development will be cross-referred to in the Cystic fibrosis guideline. The guideline will address the clinical care of patients through all phases of their life. However, the broader aspects of end of life care in adults will not be specifically addressed in this guideline.
Association of chartered physiotherapists in Cystic Fibrosis	8	General	Overall we have concerns that this scope remains large enough so as to have the potential to only give very short summaries on complex topics. There is also the issue that, despite being so large, there are still worrying omissions and limitations such as the inclusion only of airway clearance as a	Thank you for your comment. We have now revised the question on chest physiotherapy. Inclusion of airway clearance will be considered by the committee during the protocol development for the evidence review.

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			representation of the physiotherapy management of Cystic Fibrosis. We know that potentially commissioners, clinicians and people with CF will look to this guideline as a structure of what to offer/expect within the management of Cystic Fibrosis and are therefore concerned that the above issues/omissions have the potential to negatively impact on the future care offered to people with Cystic Fibrosis.	
British Paediatric Respiratory Society	1	General	Overall the scope as outlined is good but as formulated it is likely to largely reproduce existing guidelines as orchestrated through the CF Trust (albeit that these have used less well structured methodology). The context of this guideline should be within the evidence that there has been little improvement in outcomes amongst CF patients in recent years and thus focus on those areas of CF care where there is room for improvement using existing therapies. The guideline seems to be heavily focused on monitoring as opposed to delivering optimal care. I have suggested specific issues below:	Thank you for your comment. Additional key areas have been added, whilst other key areas have been revised in light of stakeholder consultation. Please see responses to your specific issues.
British Paediatric Respiratory Society	2	1.5.4	Monitoring of nutritional status should be expanded to include guidelines on strategies to optimise nutritional outcomes in CF. Poor nutrition is probably the most important continuing unmet need in CF. This needs far greater emphasis in any new guideline	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the effectiveness of nutritional interventions in CF.

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British Paediatric Respiratory Society	3	1.5.4	There is no mention of micronutrients. The guideline needs to make clear recommendations about the use of all micronutrients in age appropriate doses.	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the effectiveness of nutritional interventions in CF.
British Paediatric Respiratory Society	4	1.5.5	There needs to be a recommendation for the use of insulin and not just how to monitor for CFRD	Thank you for your comment. Specialist management of CFRD is recognised as a complex area. Although guidance exists on the management of other forms of diabetes CFRD is in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence to highlight the need for specialist involvement in their care.
British Paediatric Respiratory Society	5	1.5.8	There needs to be a recommendation for the treatment approach to evidence of reduced bone mineral density. Most centres are now monitoring for this complication in accordance with recommendations but there is wide variation in practice in relation to subsequent treatment.	Thank you for your comment. The specialist management of cystic-fibrosis-related bone disease will not be covered in this guideline. The committee will develop recommendations in terms of the role of exercise in maintaining health and in terms of surveillance for reduced bone mineral density.
British Paediatric Respiratory Society	6	1.5.9	Poor adherence to prescribed therapies needs to be addressed more consistently as part of good clinical practice in CF. This guideline might usefully provide recommendations on strategies to assess and address this as part of routine care.	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. Assessment of adherence to prescribed therapies has not been prioritised for inclusion in this guideline scope. Please note that this guideline will cross-refer to the medicines adherence guideline (CG76) and also the upcoming guideline on medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015).
British Paediatric	7	General	Should have an infant/neonatal specific	Thank you for your comment. We have had to

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Respiratory Society			section to include meconium ileus, nutrition with a stoma, diagnosis (including antenatal diagnosis)?	prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. This was not prioritised as topic for consideration in this guideline because it was not perceived to be an area with uncertainty or variation in clinical practice. The guideline does not cover all aspects of CF management as this is a very large topic area.
British Paediatric Respiratory Society	8	General	The CFSPID terminology and group would need a section rather than 'non-classical' CF.	Thank you for your comment. We consider that the sections on key figures and current practice is sufficiently detailed.
British Paediatric Respiratory Society	9	1.3	With monitoring and physio, exercise testing and management plans should be included.	Thank you for your comment. A new key area on the role of exercise in maintaining health has been added to the scope and will look at the effectiveness of programmes of exercise in the management of cystic fibrosis.
British Paediatric Respiratory Society	10	1.5	Psychological problems - eating disorders should also be considered (esp in teenage girls)	Thank you for your comment. The committee will prioritise the key psychological and behavioural problems to address during the development of the evidence review protocol for this question.
British Paediatric Respiratory Society	11	1.5	what is effective transition, rather than just what is important for families, should be mentioned.	Thank you for your comment. General issues pertaining to transition will be addressed in the NICE Transition from children's to adult services guideline in development and will be cross-referred to in the Cystic fibrosis guideline. Issues pertaining to transition that are specific to children and young people with cystic fibrosis will be addressed in the Cystic fibrosis guideline.
British Paediatric Respiratory Society	12	2.1.7	Should also include comments about Burkholderia Cepacia and Atypical Mycobacterium. Also about the importance of Pseudomonas Aeruginosa eradication	Thank you for your comment. We have included these bacteria as examples and have amended the scope to reflect this.

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			protocols.	
British Paediatric Respiratory Society	13	2.2.2	a comment needs to be made that the outpatient clinics need to be segregated according to the microbiologist results from the respiratory secretions of the patients.	Thank you for your comment. The issue of cross-infection is addressed in section 2.2.5.
British Paediatric Respiratory Society	14	General	A number of comments were received regarding cross-infection and the hope that the guideline would provide practical, feasible advice regarding segregation etc	Thank you for your comment. The evidence reviews will consider strategies for respiratory pathogen monitoring.
British Paediatric Respiratory Society	15	General	A number of commentators have suggested that if an area needs to be removed, then the age related prevalence of nasal polyps and rectal prolapse would seem to be low priority	Thank you for your comment. This key area has been revised in light of stakeholder consultation and the complications to be considered as part of assessment will be prioritised in collaboration with the committee during the development of the protocol for the evidence review.
British Paediatric Respiratory Society	16	General	All commentators agreed this was a mammoth task with a very wide scope – some commented that the scope did seem wider than has previously been attempted by a NICE GDG	Thank you for your comment. The scope has now been revised in light of stakeholder consultation.
British Thoracic Society	1	General	Section: Who the guideline is for. In Cystic Fibrosis patients and parents are usually heavily involved in the formation of guidelines, and will wish to be fully involved in the process and on the guideline development group.	Thank you for your comment. We acknowledge the importance of including patients and carers in the guideline development process. The committee will include two lay members. One of these will be an individual with cystic fibrosis and the other a parent or carer of people with cystic fibrosis.
British Thoracic Society	2	1.1	We agree with the 'groups to be covered'; particularly important are the increasing number of patients who are post-lung transplant, who still have cystic fibrosis with associated malabsorption, bowel, liver, sinus problems and CF-related diabetes	Thank you for your comment.
British Thoracic	3	1.3	It is important to consider the burden and	Thank you for your comment. The committee will

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Society		10-15	benefit that can be imposed on patients by surveillance for multiple potential complications, and whether the traditional 'annual review' process with quite extensive investigations and potentially protracted consultations with many different disciplines, is still the most appropriate method.	consider benefits and harms with regard to both clinical and cost-effectiveness for all topics included in the scope including surveillance for complications.
British Thoracic Society	4	1.5	Consider a recommendation on full gene sequencing by genetic laboratories to identify both mutations in patients with suspected cystic fibrosis to confirm a diagnosis with full gene-type, and also in patients with non-classic CF or bronchiectasis to help reduce the number of equivocal cases	Thank you for your comment. Gene sequencing has not been prioritised as topic for consideration in this guideline because it was not perceived to be an area with uncertainty or variation in clinical practice. The guideline does not cover all aspects of CF management as this is a very large topic area.
British Thoracic Society	5	1.5. 2	Consider including allergic bronchopulmonary aspergillosis in the list of complications	Thank you for your comment. This key area has been revised in light of stakeholder consultation and the complications to be considered as part of assessment will be prioritised in collaboration with the committee during the development of the protocol for the evidence review.
British Thoracic Society	6	1.5.10	Include 'outreach care' in the list of models of care, whereby the specialist CF team travel to do outreach clinics nearer to the patient's home. This is separate from network care or shared care, as it allows the specialist CF team to deliver full specialist care. This is emerging as a useful model of care for adult patients where shared care is not appropriate	Thank you for your comment. The examples provided in models for delivery of care are not an exhaustive list and these will be prioritised with committee when developing the evidence review protocols.
Cystic Fibrosis Nurses Association	1	General	There is a section regarding screening of CFRD but not the management of CFRD. Would it be prudent to have an additional working group to look at all aspects of	Thank you for your comment. Specialist management of CFRD is recognised as a complex area. Although guidance exists on the management of other forms of diabetes CFRD is

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			CFRD as this is the largest co-morbidity of Cystic Fibrosis	in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence regarding the need for specialist involvement in their care.
Cystic Fibrosis Nurses Association	2	1.6	This should include people on home IV antibiotics as well as number of admissions .Many people are unable to be admitted to hospital for therapies and choose home care due to family , work and college commitments .This part of the scope excludes / affects socio-economic satus	Thank you for your comment. This is covered under the models of delivery of care and during protocol development the role of home intravenous antibiotics will be considered.
Cystic Fibrosis Nurses Association	3	2.1.6	People with 50% lung function are not always able to lead normal lives as is stated here. Many people require a huge burden of treatment which interferes with normal life , ability to work etc.. This could affect equality of opportunity and socio-economic status.	Thank you for your comment. We have stated that "a FEV1 of 50% and above will enable people to live relatively normal lives"; this is in line with the Cystic Fibrosis Registry Annual Data Report 2013 (p. 9; http://www.cysticfibrosis.org.uk/media/598478/annual-data-report%20-summary-2013-jul14.pdf). The committee will consider burden of treatment as related to quality of life and satisfaction outcomes.
Cystic Fibrosis Nurses Association	4	2.1.5	You refer to 'cases' rather than 'people'	Thank you for your comment. We have amended the scope to correct this.
Cystic Fibrosis Nurses Association	5	2.1.6	Should there be mention of time to exacerbation as this is also a key indicator /outcomes in research as well as FEV 1	Thank you for your comment. Please note that the list of outcomes will be specified by the committee at protocol development and will vary for each evidence review.
Cystic Fibrosis Trust	1	1.3	The Trust would like to see the following included in the key areas to be covered, bronchodilators e.g. long-acting beta agonist (LABA) with long-acting muscarinic antagonist (LAMA) and aminophylline. Steroid treatments and oxygen therapy.	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. We consider that the use of bronchodilator therapy should take place when patients have bronchospasm, but there is

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				no specific role for its use in CF. We also consider that there are well setup services to supply the use of such oxygen therapy already in the NHS. This is not specific to CF, but is the same for any patient with respiratory failure. Both topics were not prioritised for consideration in this guideline because they are not perceived to be areas with uncertainty or variation in clinical practice. The guideline does not cover all aspects of CF management as this is a very large topic area. Please note that steroids will be looked at when reviewing the evidence on immunomodulatory agents.
Cystic Fibrosis Trust	2	1.5 part 10	With regard to the MDT we would like to see some acknowledgment of the working relationship between the MDT at CF Centres and the teams at the centres providing the specialist care I.E. the working relationship between CF MDTs and all the areas not covered in 1.3 MDTs	Thank you for your comment. The committee will consider the best set-up for multidisciplinary teams and models for delivery of care and develop recommendations accordingly.
Cystic Fibrosis Trust	3	1.3	Remove reference to meconium ileus.	Thank you for your comment. This has been revised.
Cystic Fibrosis Trust	4	General	Acknowledgment that CF is a multi-system disease	Thank you for your comment. We have clarified this in section 2.1.1.
Cystic Fibrosis Trust	5	2.1.5	Everyone should know there genotype, CF Trust able fund this via CF Centres for any adult who does not know.	Thank you for your comment. Gene sequencing has not been prioritised as topic for consideration in this guideline because it was not perceived to be an area with uncertainty or variation in clinical practice. The guideline does not cover all aspects of CF management as this is a very large topic area.
Diabetes UK	1	1.3	The prevalence of cystic-fibrosis-related diabetes is high, and prevalence increases	Thank you for your comment. Specialist management of CFRD is recognised as a

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			with increasing age. We know that cystic-fibrosis-related diabetes has an impact on body weight, survival and lung function – all of which are listed as main outcomes of the guidelines. Therefore, we would recommend that, in addition to 'surveillance of cystic-fibrosis-related diabetes' (CFRD) the following be added to the key areas that will be covered by this guideline: - Screening for CFRD (to include information on the frequency of this; when screening should start; how often screening should be undertaken) - The glucose (or HbA1c) values that should be used to diagnose CFRD - How glucose should be managed in CFRD (this should include information on appropriate treatment, when insulin should be started, what the appropriate glucose targets should be for CFRD and how nutritional therapies should be adapted for people with CFRD). - The screening and management of micro and macro vascular complications for people with CFRD, particularly where this differs from the wider population.	complex area. Although guidance exists on the management of other forms of diabetes CFRD is in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence regarding the need for specialist involvement in their care.
Digital Assessment Service, NHS Choices	1	General	The Digital Assessment Service welcome the guidance and have no comments as part of the consultation	Thank you for your comment.
Gilead Sciences	1	1.3.4	Section: Antibiotic management The 2013/14 NHS standard contract for	Thank you for your comment. The committee will address this at protocol development for this

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			cystic fibrosis states "the service will deliver the aims of improving life expectancy and quality of life for adults/children with CF by providing high quality proactive and preventative treatment and care to optimize lung function and nutritional status". With this in mind Gilead requests that the proposed guidelines refer to all three inhaled antibiotics used in the treatment of cystic fibrosis. This includes Colistimethate, Tobramycin and Aztreonam lysine inhalation (Cayston®). Aztreonam lysine is licensed for the suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged six years and older. The NHSCB CF Clinical Commissioning policy 2013 has recommended that Aztreonam Lysine (Cayston ®) be routinely funded for treatment of *Pseudomonas aeruginosa* infection in patients meeting the specialised commissioning criteria.	evidence review. Furthermore, the committee will make recommendations regarding the different antimicrobials represented in the evidence
Gilead Sciences	2	1.5.3	Section: What is the effectiveness of antibiotic treatment: To treat chronic pulmonary infection, including clinical exacerbations and colonisation? The clinical data for Aztreonam lysine (Cayston ®) has been reviewed by the clinical reference group for cystic fibrosis. Aztreonam lysine (Cayston®) has been recommended within license to mitigate progressive loss of lung function (defined as greater than 2% per year decline in FEV1 as % of predicted) or there is a	Thank you for your comment. The committee will make recommendations on the use of antimicrobial treatments for pulmonary infection as indicated in the scope. The specific details of which treatments will be reviewed will be agreed with the committee at protocol development.

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			continued need for IV therapy for exacerbations ie more than 2 per year despite therapy with an alternating regimen of tobramycin and colistin. (reference: Clinical commissioning policy statement: inhaled therapy for adults and children with cystic fibrosis NHSCB/A01/PS/a section 3.5.3)	
HQT Diagnostics	1	General	RCT showed improved clinical outcomes in Cystic Fibrosis when Vitamin D was increased. In a small sample, deaths were reduced 4X Suggest test Vitamin D levels and supplement to: 25(OH)D = 100-150nmol/L. Re-test after 3 months and evaluate symptoms Source: www.vitamindwiki.com/Cystic+Fibrosis	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the effectiveness of nutritional interventions in CF. The specific interventions to be prioritised will be agreed with the committee at protocol development.
HQT Diagnostics	2	General	Supplementation with omega-3 fatty acids may provide some benefit for people with Cystic Fibrosis, due to reduction in Omega-6 and reduction in Inflammation. Suggest test Fatty Acids and supplement to: Omega-3 Index: >8% Omega-6/3 Ratio: <3:1 Re-test after 3 months and evaluate symptoms Source: http://cfcenter.stanford.edu/education/ed_day/documents/AntiInflammatoryDietforCysticFibrosis.pptx	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the effectiveness of nutritional interventions in CF. The specific interventions to be prioritised will be agreed with the committee at protocol development.

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			www.hqt-diagnostics.com www.expertomega3.com/omega3-studies.asp	
HQT Diagnostics	3	General	Diet and exercise need to be considered to optimise bone health: http://cfcenter.stanford.edu/education/ed_day/documents/CFedday2012-Matel.pptx	Thank you for your comment. We have now included new key areas on the management of nutrition and the role of exercise in maintaining health. The specific interventions to be prioritised will be agreed with the committee at protocol development.
Neonatal and Paediatric Pharmacists Group (NPPG)	1	General	We would like to register our concern regarding the omission of an additional pharmacist on the Cystic Fibrosis guideline development group (one adult and one paediatric specialist), in line with the two members for each of the other key disciplines (with the other notable exception of psychology). The inclusion of a single pharmacist who may have limited experience at either end of the age spectrum which CF spans introduces a risk that the differences in treatment of adults and children may be overlooked and we feel that this should be addressed. Like clinicians, physiotherapists and dieticians, pharmacists working within CF are specialists in the treatment of either children or adults. There are unique challenges presented by the treatment of each patient population, to which the specialist pharmacist working in that area	Thank you for your comment. We agree and will be seeking to appoint 2 pharmacists (paediatric and adult) on the committee.

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			becomes an expert in dealing with. For examples, drug dosing, formulation and pharmacokinetics often differ between children and adults, further complicated in CF as pharmacokinetics in CF differ from the healthy populations. The challenges associated with finding a suitable formulation for a child are unique to paediatric medicine. On the other hand pharmacists working in adult CF medicine are experts in the drug treatment of later complications associated with CF, for example, end-stage disease and palliation, and increasingly additional complications associated with increased longevity such as renal disease and cardiovascular complications. Paediatric pharmacists may have little or no expertise in these areas – a function of (reassuringly) little exposure to these complications of CF. In addition, not all drugs are licensed for use in both children and adults. Alongside these differences are the inevitable barriers to adherence that will present differently in the child and adult populations, which the respective specialist pharmacist is well placed to tackle. Whilst there may not be precedence for mandating both adult and paediatric specialist pharmacists in NICE guideline development groups, we, on behalf of the UK Cystic Fibrosis Pharmacist Group and UK Neonatal and Paediatric Pharmacist Group, as registered stakeholders, feel that	

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			the inclusion of both a paediatric and adult pharmacist specialist in CF is essential to the success of the CF guideline development group. This is particularly important as the need for confidentiality limits a single pharmacist from consulting with an adult or paediatric specialist colleague. We therefore urge you to consider these points to ensure that expert pharmacist input is guaranteed in each area of the guidelines with regards to medicines, which will equally affect adults and children.	
Neonatal and Paediatric Pharmacists Group (NPPG)	2	General	We have no other comments on this scope.	Thank you for your comment.
NHS England	1	1.3	I would suggest that the palliative care of people with advanced cystic fibrosis should be included. Also, the management of family issues including bereavement might be worth including as the genetic nature of cystic fibrosis means that there may be more than one sibling illness/death, and the psychological impact thereof.	Thank you for your comment. The end of life care in children and young people and care of the dying adult guidelines in development will be cross-referred to in the Cystic fibrosis guideline. The guideline will address the clinical care of patients through all phases of their life. However, the broader aspects of end of life care in adults will not be specifically addressed in this guideline.
NHS England	2	1.6	Would days lost from education and/or employment be a suitable outcome to consider?	Thank you for your comment. The NICE methods manual stipulates that where the intervention under consideration is commissioned by the NHS and does not have a clear social care or public health focus then the "Reference Case" should focus on health outcomes in NHS settings. Therefore we would not normally consider these as priority outcomes within a guideline unless they served as a good proxy for a health outcome that would perhaps

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				not be reported. In making their recommendations the committee would be able to use any knowledge they had about the likely impact on days lost from education and/or employment as part of a supporting rationale where relevant.
Nordic Pharma	1	General	Thank you for the opportunity for commenting on the scope; we have no comments	Thank you for your comment.
PHARMAXIS PHARMACEUTICALS	1	1.1	Please define and/or provide guidance on the term: "non-classic CF"	Thank you for your comment. We consider this to be widely used terminology and is sufficiently clear.
PHARMAXIS PHARMACEUTICALS	2	1.3	Please include a review of "management with disease modifiers" such as ivacaftor, as is a relevant intervention currently integral to the management of CF within the UK NHS. Whilst the currently labelled indication reflects a small sub-population of CF patients with the G551D CFTR mutation (~6% in the UK), the effective size of the sub-population, within this orphan condition, is essentially no different to the rationing of other CF treatments that have acquired sub-population indications and/or reimbursement restrictions. CF carries a significant burden in all patients with the disease, so there is a universally high unmet need. The associated budget impact for ivacaftor presents a skew in budgetary allocation towards a few CF patients, with the potential for inequity and diversion of resources away from the majority of CF patients that do not have this mutation.	NICE may consider assessing ivacaftor and lumacaftor through the technology appraisal process. Please check our proposed technology appraisals page on the website here.

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			It is important that all interventions are valued fairly and in accordance with equality to enable rationale implementation of efficient and cost-effective interventions across the whole of CF services.	
PHARMAXIS PHARMACEUTICALS	3	1.3	Within point 14, or separately within this Section 1.3, please include a review of "education (e.g. disease, equipment maintenance, hygiene practices), adherence and compliance" to ensure optimised health outcomes from treatments. Non-compliance is an important issue Several studies indicate a 30–70% therapeutic adherence in CF , , , . Adherence worsens with age and disease severity . Managing and promoting adherence to treatment is an essential component of CF care2. Non-compliance in the treatment of patients with CF can lead to impairment to patient health in terms of inadequate disease control and reduced quality of life. In turn, these place additional pressure on healthcare systems since non-compliant patients may experience worsening of their condition and require more costly interventions. It is also simply wasteful of scarce NHS resources. CF patients have a strong desire to lead a normal life. Young people often wish to hide visible differences from their peers, which is difficult, as this is at odds with complicated therapeutic schedules , , . On average, patients take seven daily therapies and spend 75-100 minutes per day to complete	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. The management of adherence to prescribed therapies has not been prioritised for inclusion in this guideline scope. Please note that this guideline will cross-refer to the medicines adherence guideline (CG76) and also the upcoming guideline on medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015).

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			treatment tasks , . Nebulised medications in particular add to the treatment burden11. A study that compared self-reported adherence to rhDNase with computer based dispensing in adult patients with CF demonstrated a significant disparity between the pharmacy records and the patient self-reported adherence . While over 80% of patients continuing rhDNase stated that they took treatment for more than 20 days per month, only 24% of patients actually collected sufficient treatment to allow for more than 20 days therapy12. The life-long duration and complexity of CF therapies have been pointed out as being the main determinants of therapeutic adherence6. Furthermore, the fact that many pharmacological treatments are taken prophylactically may also be an important factor in patient compliance as patients do not feel the immediate benefit of the medication. This may also explain why 14.7% of patients only take their respiratory medications when they feel worse6. Patient education and programmes that help improve treatment adherence and compliance may therefore optimise patient benefits from treatment.	
PHARMAXIS PHARMACEUTICALS	4	1.5	As per point 2 above, please include an evaluation of the cost-effectiveness of ivacaftor	NICE may consider assessing ivacaftor and lumacaftor through the technology appraisal process. Please check our proposed technology appraisals page on the website here.
PHARMAXIS	5	1.5	Hypertonic saline (HS): Please see ERG	Thank you for your comment. The committee will

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PHARMACEUTICALS			discussions related to inhaled Mannitol TA266. It is important to note that HS is not licenced nor is it's use regulated by the EMA/MHRA. Whilst it is increasingly used in UK care, usage, in terms of dose (3-7%) and duration in practice appear highly variable. The absence of a standard for HS and that there is a limited and contradictory evidence-base supporting the efficacy and safety of HS, hinders the ability to conduct a direct or indirect comparison to other treatments. To enable its place in treatment to be fully evaluated, the evidence base from manufactures of "HS for use in CF" is needed, to be able to support its appropriate use within best supportive care.	make recommendations regarding the use of different dosages of hypertonic saline based on the best available clinical and economic evidence and will seek to reduce variation in practice in this area. Off-label use may be recommended if the clinical need cannot be met by a licensed product and there is sufficient evidence and/or experience of using the medicine to demonstrate its safety and efficacy to support this.
PHARMAXIS PHARMACEUTICALS	6	1.6	Please also consider Life Years Gained as well as HR-QoL In addition to looking at incremental cost/QALY we believe that it is relevant to assess the incremental costs per life year gained. Generic indicators of quality of life such as the SF-36 and instruments measuring utility scores have limited sensitivity in CF. One reason for this is that patients with CF have grown accustomed to their condition, and do not report a lower quality of life score compared to a general population control group . With the high starting scores reported in CF, ceiling effects give an underestimation of the true impact on patient perceived quality of life. As such their use in cost-effectiveness assessment is challenging. In	Thank you we appreciate there are challenges in the use of the QALY (NICE's preferred method in economic evaluation) in this population for the reasons you outline. However, there would also be limitations using the cost per life year gained as it does not facilitate a comparison with interventions in other areas which are competing for the same scarce/finite NHS resources. That said, we would be advised by the committee on the appropriateness of the QALY for any analysis undertaken and alternatives measures of cost-effectiveness are permissible. Also, if it is thought that the QALY doesn't sufficiently capture the benefits then it is always possible to do sensitivity analysis to assess the implications on the results of a higher health state utility.

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			the absence of an accurate HR-QoL measure, we propose the use of life-years gained instead. This measure reflects a basic need within healthcare: to prolong the lives of CF patients. Disease-specific instruments such as the cystic fibrosis Questionnaire (CFQ-R) inform clinical practice about the effect of disease progression and are a widely accepted and validated tool for use in patients with CF . It should, however, be cautionary noted that the CFQ-R was not designed to have optimal sensitivity to report patient perceived quality of life. Patients with CF grow up with the disease. They will not readily express needs they are not (yet) aware of (latent needs) because they have adapted to their condition. The development of the CFQ-R did not include the techniques used to elicit latent needs, so it is unlikely that all items reflecting the highest needs of patients were incorporated in the CFQ-R. Furthermore, it is important to recognise that this instrument was initially developed for studying antibiotic treatment, and the identification of symptoms that may precipitate a respiratory exacerbation. However, questions such as "Have you had to cough up mucus" and "Have you been coughing during the day" may be inappropriate to reflect improvements associated with mucoactive therapies such as rhDNase or mannitol, as this is a beneficial feature of therapy. Evaluating the impact of treatments over a	

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			life-long time horizon is appropriate for this condition.	
PHARMAXIS PHARMACEUTICALS	7	1.6	Please consider including FEV1% predicted and the relative change in lung function from a patient's baseline. Lung function (and change in lung function) is a relative metric to the patient's underlying medical condition and should be considered in the context of the patient's age, BMI, disease state etc. For example, given their smaller lung volume, a 100mL change in a child may be of greater consequence than in an adult. Similarly, changes should be considered relative to a starting lung function e.g. a 100mL change in a healthy patient may be less meaningful to one with severe lung deterioration. For this reason, the use of FEV1% predicted (of normal for the population) and the (average of) relative change from baseline for individual patient assessments (rather than an average cohort change) are more sensitive and informative when monitoring patient lung function over time.	Thank you for your comment. The committee will consider different measures of change in lung function as appropriate during the protocol development for each evidence review.
PHARMAXIS PHARMACEUTICALS	8	1.6	Please consider the need for objective measures of exacerbations when comparing interventions. We agree that respiratory symptom exacerbations have a high clinical, economic and QoL impact for patients, and are a driver of disease progression. Exacerbations associated with infections typically expedite the progression of lung disease in patients with CF. In addition, the frequency of exacerbations is a strong	Thank you for your comment. The scope currently includes rate of infections as an outcome measure, and the list provided is not intended to be exhaustive. Please note that the list of outcomes will be specified by the committee at protocol development and will vary for each evidence review.

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			predictor of morbidity and mortality . They also increase the risk of subsequent exacerbations. Accordingly, exacerbations are associated with increased hospitalisation and antibiotic use leading to overall increased treatment costs. It has also been shown that a major proportion of health care expenditure for CF is directly attributable to the treatment of pulmonary exacerbations . To enable a fair comparison between interventions, it is however important to consider the comparability and objectiveness used to measure exacerbations (e.g. Fuch's criteria) so that one is able to judge their relative impact on disease and healthcare resource utilisation.	
PHARMAXIS PHARMACEUTICALS	9	1.6	Please consider: Time to exacerbation as a relevant exacerbation endpoint. According to UK CF registry data, patients with CF experienced an average of 1-2 respiratory exacerbations requiring IV antibiotics, per year1. In practice, however, many of these exacerbation episodes disproportionately occur to the same patients, and many more non-hospitalised exacerbations (e.g. that may be treated in primary care facilities) would also be expected across the whole population. Given the orphan designated status of CF, for practical, ethical and economic reasons it is not feasible to power a study on the basis of exacerbation differences. In accordance with EMA guidance, studies of 26 or 52 week duration in CF are therefore	Thank you for your comment. The scope currently includes rate of infections as an outcome measure, and the list provided is not intended to be exhaustive. Please note that the list of outcomes will be specified by the committee at protocol development and will vary for each evidence review.

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			typically powered on the basis of lung function improvement. Differences in the number of exacerbations that are captured within these trials are therefore often an unpowered secondary endpoint. Given the infrequent nature of these spontaneous events, time to exacerbation provides an alternative meaningful metric sampled from the full population studied.	
Profile Pharma Ltd	1	1.5.10	Our comments are that we believe an additional question in this section could be as follows; how can adherence monitoring play a more important role in improving the management of Cystic Fibrosis, both in understanding health behaviours and optimising efficacy and cost effectiveness of treatments?	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. Adherence monitoring has not been prioritised for inclusion in this guideline scope. Please note that this guideline will cross-refer to the medicines adherence guideline (CG76) and also the upcoming guideline on medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015).
Profile Pharma Ltd	2	1.5.10	Our comments are that we believe an additional question in this section could be as follows; how can remote monitoring be utilised in the management of Cystic Fibrosis to provide data on biomarkers from the home, to the clinic, which will allow both earlier interventions to treat exacerbations and more individualised, efficient use of clinic time and resources?	Thank you for your comment. The issue of remote monitoring is captured within the review of models for delivery of care, which includes telemedicine.
Roche Products Limited	1	1.3	Roche believes NICE should consider the evolving evidence for interventions that promote patient adherence and improve	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness

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		and 1.6 and 2	clinical outcomes in cystic fibrosis (CF). The need to support patients and carers to improve medication adherence in CF is well recognised and we believe has care implications that are unique in comparison to other chronic illnesses. Poor treatment adherence in CF is common and rates of adherence to long-term pulmonary medications have been shown to be significant predictors of subsequent health-care use and costs (Quittner et al. Chest. 2014; 146(1):*142-151*). For patients and carers, adherence to CF therapy is time-consuming, inconvenient and may interfere with quality of life. Given the research linking adherence to lung health outcomes, including slower disease progression and improved survival, there is a growing need to measure and evaluate adherence in clinical care. As new medications are approved for CF, new methods to monitor adherence are being developed, assessed and subsequently	evidence will inform care. Adherence monitoring and improvement has not been prioritised for inclusion in this guideline scope. Please note that this guideline will cross-refer to the medicines adherence guideline (CG76) and also the upcoming guideline on medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015).

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			tailored by clinicians to each individual patient's needs (Eakin MN, Riekert KA. Curr Opin Pulm Med. 2013 Nov;19(6):*687-91*). Large ongoing studies include the phase 3, randomised iCARE study (ClinicalTrials.gov NCT01232478).	
Roche Products Limited	2	2	In addition to the identified NHS guidance, NHS England have issued a Clinical Commissioning Policy Statement NHSCB/A01/PS/a: Inhaled Therapy For Adults And Children With Cystic Fibrosis (2013) [available at: http://www.england.nhs.uk/wp-content/uploads/2013/04/a01-ps-a.pdf (accessed December 2014)	Thank you for your comment. The committee will make recommendations regarding the mode of drug delivery based on the routes represented in the evidence.
Royal Brompton Hospital	1	General	The breath of the guideline is vast and is in danger of trying to cover too much which may leave it with very superficial guidance	Thank you for your comment. The scope has now been revised in light of stakeholder comments.
Royal Brompton Hospital	2	1.3	Areas not covered: CFRD is a major complication and should be covered as should CF bone disease	Thank you for your comment. Specialist management of CFRD is recognised as a complex area. Although guidance exists on the management of other forms of diabetes CFRD is in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence regarding the need for

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				specialist involvement in their care. The committee will develop recommendations in terms of the role of exercise in maintaining health and in terms of surveillance for reduced bone mineral density.
Royal Brompton Hospital	3	1.1	Can there be more clarity about the term "non-classic CF"	Thank you for your comment. We consider this to be widely used terminology and is sufficiently clear.
Royal Brompton Hospital	4	1.2	Will this include Primary care and the expectations of prescribing?	Thank you for your comment. Primary care settings are included in the scope of this guideline.
Royal Brompton Hospital	5	1.5.2	Should this be 1 of the Key 10 questions when it is already available as published data from the National CF registry?	Thank you for your comment. The committee will seek to make recommendations for monitoring for these conditions based on the age-related prevalence. The National CF registry will be considered as a source of evidence when designing review protocols.
Royal Brompton Hospital	6	1.5.2	Should include treatment-related complications	Thank you for your comment. This will occur as part of each treatment modality reviewed as part of the guideline development.
Royal Brompton Hospital	7	1.5.3	Needs to include management using drugs that are not organ-specific, e.g anti-inflammatories (azithromycin) and mutation-specific therapies	Thank you for your comment. This has now been added to the scope. NICE may consider assessing ivacaftor and lumacaftor through the technology appraisal process. Please check our proposed technology appraisals page on the website here.
Royal Brompton Hospital	7	1.5.5	This could be extended to treatment not just monitoring	Thank you for your comment. Specialist management of CFRD is recognised as a complex area. Although guidance exists on the management of other forms of diabetes CFRD is in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence regarding the need for

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				specialist involvement in their care.
Royal Brompton Hospital	8	1.5.6 1.5.7	This should be broader than just asking if ultrasound scanning is enough, treatment of liver disease and use of urso should come under this heading. Using 2 of the key 10 questions for liver complications when you are only using 1 for the lung seems to have weighted things wrongly	Thank you for bringing this to our attention. We have moved the question on the use of ursodeoxycholic acid to the correct section. Numbers in section 1.5 refer to broad topic areas; there are five questions on monitoring and management of pulmonary issues and two on monitoring and management of liver disease.
Royal Brompton Hospital	9	General	Guideline Development Group: There is bias in the adult CF specialist physician representation: There is only a call for one Paediatric CF Specialist but 2 adult CF specialists are called for (3 if the chair is counted). Only 1 pharmacist is asked for – this specialty has both adult and paediatric sub-specialisation and having only 1 will risk an area not being covered sufficiently	Thank you for your comment. Please note that there was an error in the advert for committee membership as it should have read one adult CF specialist. We also agree with your point regarding pharmacists and will be seeking to appoint 2 pharmacists (paediatric and adult) on the committee.
Royal College of General Practitioners	1	1.3	Page 2: The following do not appear to have been considered: 1. Medicines management and co-ordination The GP is likely to be responsible for prescribing much of the routine therapy recommended by the Specialist CF Centre. There needs to clear communication about the medication recommended particularly when it may be unfamiliar to GPs or used out of product license. GPs should be expected to provide adequate amounts of medication – a minimum of one month at a time but ideally	This guideline will address the care of patients with CF in all settings NHS care is provided. The committee will consider the issues raised during the guideline development. The guideline will also include considerations on service delivery. Please refer to the Joint Committee on Vaccination and Immunisation (JCVI) for advice on immunisation. Genetic counselling has not been prioritised as topic for consideration in this guideline because it was not perceived to be an area with uncertainty or variation in clinical practice. The end of life care in children and young people and care of the dying adult guidelines in development will be cross-referred to in the Cystic fibrosis guideline. The guideline will

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			this would be longer for chronic medications. e.g. pancreatic enzymes, vitamins etc. The local pharmacies and hospital pharmacy will need to coordinate an ordering and delivery service. 2. Immunisations The GP practice need to ensure that patients are fully immunised and arrange for annual influenza immunisation every autumn. 3. Management of co-morbidites particularly non-CF health-related issues and mental health issues. 4. Management of fertility and pregnancy 5. Genetic counselling 6. The management of end of life issues. 7. Family Carers health and support	address the clinical care of patients through all phases of their life. However, the broader aspects of end of life care in adults will not be specifically addressed in this guideline. The specialist management of cystic-fibrosis-related fertility and pregnancy problems will not be covered in this guideline. The guideline does not cover all aspects of CF management as this is a very large topic area. A new key area on the provision of information and support for infants, children, young people, adults and their carers has not been added to the scope in light of stakeholder consultation.
Royal College of General Practitioners	2	1.6	Page 6 - Consider some patient and carer-based outcomes for instance, patient and carers satisfaction questionnaires such as the family and friends test. Number of days in hospital Number of health care contacts in a year to improve access to telephone and video support, one stop clinics and reduce	Thank you for your comment. We have included satisfaction as an outcome. Other outcomes will be agreed with the committee during the protocol development of the evidence reviews.

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			number of hospital clinic appointments	
Royal College of Nursing	1	General	There is a section regarding screening of CFRD but not the management of CFRD. We think it would be prudent to have an additional working group to look at all aspects of CFRD as this is the largest co-morbidity of Cystic Fibrosis	Thank you for your comment. Specialist management of CFRD is recognised as a complex area. Although guidance exists on the management of other forms of diabetes CFRD is in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence regarding the need for specialist involvement in their care.
Royal College of Nursing	2	1.6	We feel this should include people on home IV antibiotics as well as number of admissions .Many people are unable to be admitted to hospital for therapies and choose home care due to family, work and college commitments. This part of the scope excludes / affects socio-economic status	Thank you for your comment. This is covered under the models of delivery of care and during protocol development the role of home intravenous antibiotics will be considered.
Royal College of Nursing	3	2.1.6	People with 50% lung function are not always able to lead normal lives as is stated here. Many people require a huge burden of treatment which interferes with normal life, ability to work etc... This could affect equality of opportunity and socio-economic status. A 50% lung function is a significant morbidity; Cystic Fibrosis, other respiratory diseases such as Asthma, & COPD limitations limits the ability to perform in daily life which is expected in these conditions. With a 50% lung function (as well as intervention) - it seems unreasonable to expect that people with CF	Thank you for your comment. We have stated that "a FEV1 of 50% and above will enable people to live relatively normal lives"; this is in line with the Cystic Fibrosis Registry Annual Data Report 2013 (p. 9; http://www.cysticfibrosis.org.uk/media/598478/annual-data-report%20-summary-2013-jul14.pdf). The committee will consider burden of treatment as related to quality of life and satisfaction outcomes.

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			would be able to cope 'better' than those with other conditions, and not be affected by the intervention of therapy that is required at this point.	
Royal College of Nursing	4	2.2.1	We agree with all the teams listed - but would also expect school nursing service, health visitors & family to be included; the Cystic Fibrosis specialist service commissioning for adult services should also then include support for the family of those affected with Cystic Fibrosis (offered by school nursing, health visitors etc) - e.g. in Bristol, the Cystic Fibrosis specialist outreach team and nursing service support the family as well as the patient. We would expect this to be considered in commissioning of service provision.	Thank you for your comment. The national commissioning process does not recognise this, so we do not consider that it would be helpful to include it in the guideline.
Royal College of Paediatrics and Child Health	1	1.3	We believe this to be ambitious in its scope, and comprehensive guidelines are already agreed by the European CF Society and the CF Trust UK. Are all of these areas able to be covered at once by NICE?	Thank you or your comment. Please note that the scope has now been revised in light of stakeholder comments.
Royal College of Paediatrics and Child Health	2	1.3 10-13	There is variation across the country in the age at which screening is done for diabetes, liver disease and osteoporosis, and the tests which are used.	Thank you for your comment. The committee will seek to make recommendations to reduce variation in practice within these areas as they are included in the scope.
Royal College of Paediatrics and Child Health	3	1.4	Economic aspects should cross reference to NICE technology appraisal guidance on nebulised therapies and Clinical Commissioning policy for Ivacaftor.	NICE may consider assessing ivacaftor and lumacaftor through the technology appraisal process. Please check our proposed technology appraisals page on the website here.
Royal College of Paediatrics and Child Health	4	1.5	Clinical data on the status at diagnosis, and the prevalence of complications can be obtained from the UK Port CF database managed by the CF Trust.	Thank you for your comment. The committee will consider this source of evidence when designing review protocols.

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Royal College of Paediatrics and Child Health	5	1.5 3	Guidance on when it is appropriate to request CT scans in young children is needed. Lung clearance index is not widely available except in research studies and in London. Guidance on when to start rhDNase in children with CF would be welcome.	Thank you for your comment. The committee will make recommendations regarding the use of CT scans and rhDNase and will take into account health economic aspects when formulating recommendations that could have significant cost impacts, such as the introduction of new equipment for measuring lung clearance indices.
Royal College of Paediatrics and Child Health	6	1.5 6-7	Answers to these questions would be welcomed, but are not clear from the literature.	Thank you for your comment. In the absence of robust clinical evidence the committee may make consensus recommendations based on their clinical and personal experience and expert testimony, as outlined in the NICE guidelines manual.
Royal College of Paediatrics and Child Health	7	1.5 8	Dexa scans in young children may not be available in all areas, or normal values may not have been agreed.	Thank you for your comment. Clinical guidelines make recommendations for clinical and cost effective treatment. NICE clinical guidelines do not have a role in ensuring appropriate availability of services locally. NICE has an implementation team who support the dissemination of the guideline.
Royal College of Paediatrics and Child Health	8	1.5 10	Debates around delivery of centre v network care for children with CF have raged for decades in the UK, I think it is unlikely that NICE will be able to get a definitive answer to this question.	Thank you for your comment. In the absence of robust clinical evidence the committee may make consensus recommendations based on their clinical and personal experience and expert testimony, as outlined in the NICE guidelines manual.
Royal College of Paediatrics and Child Health	9	13	Section: Surveillance for reduced bone mineral density Evidence base for the current recommendation of frequency of bone density scans. Currently 'all children with CF from age 10 yrs and then every 2 to 3 years.'	Thank you for your comment. The committee will seek to make recommendations on the frequency and method of monitoring for reduced bone mineral density based on the best available clinical and cost-effectiveness evidence.

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			Our clinical experience of outcome data is that many have normal BMD in the paediatric age group, and a lesser frequency may be appropriate. Alternatively more selective criteria are required. We would welcome a review of the evidence underpinning recommendations.	
Royal College of Paediatrics and Child Health	10	1.5 8	Key issues and questions section, regarding bone disease point 8, p8, we would suggest the addition of the following question: • What is the optimum strategy for preventing vitamin D deficiency?	Thank you for your comment. This will be looked at as part of nutritional management and the treatment of pancreatic exocrine insufficiency. The specific interventions to be prioritised will be agreed with the committee at protocol development.
Royal College of Pathologists	1	1.3.4 1.5.3	Consider reviewing the use of the term "bacterial colonisation" as this concept is challenged by many CF specialists on the basis that persisting growth of bacteria from the airways is rarely benign. Perhaps "to prevent acquisition of respiratory pathogens" or similar may be more appropriate.	The guideline includes as a key area both the prevention of bacterial colonisation and the treatment of chronic infection.
Royal College of Pathologists	2	1.5.3	Consider a section setting out some minimum standards for the microbiology laboratory performing the tests e.g. CPA accreditation, experience in regularly processing CF samples and involvement of medical microbiologist with interest in CF. Laboratory methods could be considered further but we appreciate these may be beyond the scope of a clinical guideline.	Thank you for your comment. While we would agree it is important for staff working in microbiology laboratory to have the necessary level of knowledge and expertise it is outside of the remit of this guideline to specify the qualifications or competencies professionals should have.
Royal College of Pathologists	3	1.5.3	Specific pathogens should be considered and discussed separately with regard to effectiveness of antimicrobial treatment. These should include both "typical" and	Thank you for your comment. This will be covered under the antimicrobial section.

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			emerging CF pathogens, including fungi and non-tuberculous mycobacteria. The contentious issue of anti-staphylococcal prophylaxis in children could be reviewed here specifically, given the major differences in practice between the UK and the USA (and other countries).	
Royal College of Pathologists	4	1.5.3	The role for antimicrobial susceptibility testing of Pseudomonas aeruginosa in chronically infected patients to guide antibiotic selection. There is currently wide variation in laboratory and clinical practice.	Thank you for your comment. This will be covered under the antimicrobial section.
Royal College of Pathologists	5	1.5.3	Commenting on optimal mode of antibiotic delivery – to include dosing aspects e.g. continuous infusion of betalactams	Thank you for your comment. The committee will make recommendations regarding the mode of antibiotic delivery based on the routes represented in the evidence.
Royal College of Pathologists	6	1.5.10	Is the intention for the guideline to cover general infection control aspects rather than just service organisation? This would be welcomed given the lack of up to date UK CF infection control guidance.	Thank you for your comment. General infection control aspects are covered in NICE CG139 on infection prevention and control.
Royal College of Pathologists	7	2.2.1	Given the crucial impact of infection on morbidity, mortality and suitability for transplantation a clinical microbiologist (with expertise in CF microbiology) should be recognised as an important member of the MDT to advise on use of lab micro, optimising antibiotics and infection control.	Thank you for your comment. We have amended the scope to reflect this.
Royal College of Physicians	1	General	Please take this email as confirmation that the RCP wishes to endorse the response submitted by the British Thoracic Society to the above consultation	Thank you for your comment.
UK CF Dietitians' Interest Group	1	General	The scope includes management of the respiratory aspects of CF but not the nutritional aspects. As this is such a major	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the

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			part of overall CF management nutritional interventions including fat soluble vitamin supplementation and providing nutritional support should be included	effectiveness of nutritional interventions in CF. The specific interventions to be prioritised will be agreed with the committee at protocol development.
UK CF Dietitians' Interest Group	2	1.1	Bullet point should include Infants, children, young people and adults	Thank you for your comment. We have amended the scope to clarify that infants are included.
UK CF Dietitians' Interest Group	3	1.3	Also needs infants adding to children, young people and adults	Thank you for your comment. We have amended the scope to clarify that infants are included.
UK CF Dietitians' Interest Group	4	1.5	Also needs infants adding to children, young people and adults	Thank you for your comment. We have amended the scope to clarify that infants are included.
UK CF Dietitians' Interest Group	5	1.3	Should include nutritional management to ensure a normal nutritional status	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the effectiveness of nutritional interventions in CF. The specific interventions to be prioritised will be agreed with the committee at protocol development.
UK CF Dietitians' Interest Group	6	1.5.2	Should include meconium ileus	Thank you for your comment. Distal ileal obstruction syndrome (meconium ileus equivalent syndrome) will be considered by the committee when developing the protocol for the evidence review on complications of CF.
UK CF Dietitians' Interest Group	7	1.5.4	In addition to GI manifestations there should be a section on **nutritional managements** to include issues such as: 'What are the effective strategies to promote a normal nutritional status?' 'What is the effectiveness of oral nutritional supplements?' What is the effectiveness of enteral tube feeding?' 'What are the	Thank you for your comment. We have now included a new key area on management of nutrition and the committee will look at the effectiveness of nutritional interventions in CF. The specific interventions to be prioritised will be agreed with the committee at protocol development.

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			effective strategies to prevent fat soluble vitamin deficiencies?'	
UK CF Dietitians' Interest Group	8	1.6	Should include measurement of fat soluble vitamin levels	Thank you for your comment. This will be looked at as part of nutritional management and the treatment of pancreatic exocrine insufficiency. The specific interventions to be prioritised will be agreed with the committee at protocol development.
UK CF Dietitians' Interest Group	9	2.2.1	Specialist microbiologist needs adding	Thank you for your comment. We have amended the scope to reflect this.
UK Clinical Pharmacy Association – Respiratory Group	1	3.1 f	Other chronic lung infections can require the use of long-term antibiotic therapy (eg *M. abscessus*, *B, cepacia*).	Thank you for your comment. We have included these bacteria as examples and have amended the scope to reflect this.
UK Clinical Pharmacy Association – Respiratory Group	2	4.3.1 h	Not clear what is meant by the **delivery** of antibiotic therapy (ie the physical administration PO/Neb) or the delivery in terms of the service delivery.	Thank you for your comment. We will be addressing both modes of drug delivery and models of service delivery.
UK Clinical Pharmacy Association – Respiratory Group	3	4.3.1 o	To be complete the guideline needs to cover more than just methods of surveillance for CFRD. The management of the condition and even risk factors for development should also be considered.	Thank you for your comment. Specialist management of CFRD is recognised as a complex area. Although guidance exists on the management of other forms of diabetes CFRD is in many respects a different condition. Its management is not incorporated within this scope but advice can be given based on screening evidence regarding the need for specialist involvement in their care.
UK Clinical Pharmacy Association – Respiratory Group	4	4.3.1 r	To be complete the guideline needs to cover more than just surveillance of osteoporosis but should also include the treatment of the condition including the use of bisphosphonates	Thank you for your comment. Please note that a multiple technology assessment of the use of bisphosphonates for preventing osteoporotic fragility fractures will be published in November 2015 (including a partial update of NICE technology appraisal guidance 160 and 161).
UK Clinical Pharmacy Association –	5	4.3.1	Not sure where this should fall but the issue of adherence with treatment should be	Thank you for your comment. Please note that this guideline will cross-refer to medicines

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Respiratory Group		t and 4.3.2.h/i	considered as this is increasingly being recognised as being important in terms of outcomes and effective use of expensive therapies. The role of the MDT in supporting patients with adherence and the evidence to support use of specific interventions should be considered.	adherence guideline (CG76) and also medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015).
UK Clinical Pharmacy Association – Respiratory Group	6	4.4 f	For accuracy the rate of exacerbations (over a period of time) would be more useful than the outright number.	Thank you for your comment. The scope currently includes rate of infections as an outcome measure, and the list provided is not intended to be exhaustive. Please note that the list of outcomes will be specified by the committee at protocol development and will vary for each evidence review.
UK Clinical Pharmacy Association – Respiratory Group	7	4.4 d and 4.4.h	Maybe outside relevant scope but to assess these criteria it may be necessary to look at the effectiveness and clinical relevance of current practice in microbiological sputum sampling and culture.	Thank you for your comment. The committee will consider current practice when developing the protocols for the associated topic areas.
UK Clinical Pharmacy Association – Respiratory Group	8	4.5 c	Aspergillosis is not a bacterial colonisation. Having said that colonisation with aspergillus vs infection with aspergillus vs ABPA should be considered. In addition other major fungal disease should be considered (Candida, Exophilia?)	Thank you for your comment. Please note that aspergillosis will be covered under the antimicrobial key area. Allergic ABPA will be covered in the immunomodulatory key area of the scope.
UK Clinical Pharmacy Association – Respiratory Group	9	4.5 g	This sentence doesn't quite make sense: should read "including; rhDNAse (Pulmozyme®), sodium chloride (saline) for nebulisation – hypertonic (3%, 6% and 7%) or isotonic (0.9%) and inhaled mannitol (Bronchitol®)	Thank you for your comment. This section has been revised in light of stakeholder consultation.
UK Clinical Pharmacy Association – Respiratory Group	10	General	We note that several groups of professions have been invited to provide representation from both adult and paediatric specialities. It is disappointing that this is not the case	Thank you for your comment. We agree and will be seeking to appoint 2 pharmacists (paediatric and adult) on the committee.

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			for CF Pharmacists. Paediatric and adult CF care is very different particularly around the use of medication and pharmacists from either speciality will not be ideally placed to comment on recommendations involving the other speciality. In an ideal world a pharmacist from each speciality would be included in preparing this guideline.	
UK Cystic Fibrosis Pharmacist Group	1	General (GDG composition)	We suggest that the inclusion of a single pharmacist – who may have limited experience at either end of the age spectrum which a life-long condition such as CF spans – introduces a risk that the differences in treatment of adults and children (some of which are subtle) may be overlooked. Most pharmacists working within CF in the UK are specialists in the treatment of either children *or* adults. This should be addressed by including both an adult and a paediatric specialist CF pharmacist on the GDG as for clinicians, physiotherapists and dietitians.	Thank you for your comment. We agree and will be seeking to appoint 2 pharmacists (paediatric and adult) on the committee.
UK Cystic Fibrosis Pharmacist Group	2	1.5.10	We would suggest that consideration be given to home intravenous antibiotics under the heading 'delivery of care' to promote equality in access to this model of care, where appropriate, regardless of geographic location.	Thank you for your comment. This is covered under the models of delivery of care and during protocol development the role of home intravenous antibiotics will be considered.
UK Psychosocial Professionals in CF Group	1	1.3.14	Social workers are listed as essential part of CF team and social impacts of CF are well documented. We therefore suggest change from "Recognising psychological and behavioural problems" to "*Recognising psychological, behavioural and social problems"*	Thank you for your comment. We recognise that many different healthcare professionals work with people with CF. The guideline does not aim to cover all aspects of care that a person with CF will require. The scope describes those areas where specific review of evidence is considered to be useful for the NHS.

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UK Psychosocial Professionals in CF Group	2	1.5.9	Whilst interventions for specific psychological/behavioural problems are explicitly excluded from this guidance, the role of CF psychologists and social workers is much wider than just delivery of such interventions directly to people with CF. Much work is preventative eg work on adapting to a chronic illness, or with families, and through early intervention, or is delivered through a "stepped care model" involving the support of less formal psychological work by other members of the MDT. These approaches would not be covered in guidance on interventions for specific psychological disorders. We therefore suggest addition to section 1.5.9 of "*Interventions to prevent development of psychological or behavioural problems in people with CF"*	Thank you for your comment. We have prioritised the importance of health care professionals recognising psychological and behavioural problems in people with CF in this guideline. The remit for this guideline is to focus on diagnosis and management, and therefore, the prevention of psychological or behavioural problems in CF will not be covered.
UK Psychosocial Professionals in CF Group	3	1.5	The issue of effective/optimal self management of a condition as complex as CF does not seem to be covered. While separate guidance may exist on adherence to prescribed medication, it may be useful for this to be covered in the current guidance to some extent. Also good CF self management requires engagement in many other activities as well as taking medication. We therefore suggest an addition to the scope to include "*Promoting effective self management of CF"*	Thank you for your comment. We have had to prioritise what we cover in the guideline and have prioritised those areas where an assessment of the clinical and cost effectiveness evidence will inform care. Self management in CF has not been identified as a priority key area to address in this guideline scope. Please note that this guideline will cross-refer to medicines adherence guideline (CG76) and also medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes guideline (to be published March 2015).
UK Psychosocial Professionals in CF Group	4	General	There seems to be an omission in the area of "end of life care in CF", which is a large part of management of CF in adult care. While other guidance exists in this area,	Thank you for your comment. The end of life care in children and young people and care of the dying adult guidelines in development will be cross-referred to in the Cystic fibrosis guideline.

Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
			there are some CF specific issues that could be addressed in this guidance. Otherwise we suggest this topic should be explicitly excluded from the guidance.	The guideline will address the clinical care of patients through all phases of their life. However, the broader aspects of end of life care in adults will not be specifically addressed in this guideline.
UK Psychosocial Professionals in CF Group	5	General	There seems to be an omission in the area of "Management of pregnancy in CF" as opposed to "fertility problems" which is explicitly excluded. If pregnancy etc is not covered perhaps this should be explicitly excluded also.	Thank you for your comment. We have now amended the scope to reflect this.
UK Psychosocial Professionals in CF Group	6	2.2.1	Current standards of care for CF list "clinical psychologist" rather than "psychologist" as necessary members of an MDT.	Thank you for your comment. We have amended the scope to reflect this.