### Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

<table>
<thead>
<tr>
<th>Organisation name</th>
<th>Document</th>
<th>Page No</th>
<th>Line No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alder Hey Children's NHS Foundation Trust</td>
<td>Genera l</td>
<td>8.3</td>
<td></td>
<td>Excellent to have clear evidence of the incidence of impaired growth in children and young people with CF. This supports the on-going need for specialist dietitians to be involved in the MDT care of children and young people with CF</td>
</tr>
<tr>
<td>Alder Hey Children's NHS Foundation Trust</td>
<td>Genera l</td>
<td>8.7</td>
<td></td>
<td>Excellent to have detailed information on the emerging incidence of CFRD in children and young people with CF. This will help support the case for increasing services for this group</td>
</tr>
<tr>
<td>Alder Hey Children's NHS Foundation Trust</td>
<td>Genera l</td>
<td>10.1</td>
<td></td>
<td>This is an excellent description and summary of the evidence base for nutritional interventions in CF which should enable dietitians to improve nutritional outcome. It is particularly helpful to see enteral tube feeding supported as an intervention</td>
</tr>
<tr>
<td>Alder Hey Children's NHS Foundation Trust</td>
<td>Genera l</td>
<td>10.2</td>
<td></td>
<td>The evidence for specific advice on PERT dosing is very weak but could this be explored further. In my experience effective enzyme dosing to reduce fat malabsorption remains a relatively poorly delivered aspect of CF care</td>
</tr>
<tr>
<td>Alder Hey Children's NHS Foundation Trust</td>
<td>Genera l</td>
<td></td>
<td></td>
<td>Excellent on all aspects of nutritional care and will be extremely helpful evidence both in the nutritional management of children and young people with CF but also in supporting the case for dietetics as an integral part of CF care</td>
</tr>
<tr>
<td>Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF)</td>
<td>Full</td>
<td>172</td>
<td>16</td>
<td>Cost of providing the MDT at the specialist centre. The costs for physiotherapy are based on a Band 7 staff member. However, the Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis Third Edition April 2017 (Cystic Fibrosis Trust publication) state that a CF Specialist Centre must be led by a Principal CF Physiotherapy Practitioner (Band 8). Therefore, we think that the economics for staffing in this guideline should reflect the higher banding and be costed at band 8.</td>
</tr>
<tr>
<td>Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF)</td>
<td>Full</td>
<td>177</td>
<td>4</td>
<td>CF physiotherapists are also involved in upper airway management. They assess chronic sinus symptoms and teach sinus washouts and use of sinus nebulisation.</td>
</tr>
</tbody>
</table>

**Developer's response**

- Thank you for your comment.
- Thank you for your comment.
- Thank you for your comment.
- Thank you for your comment. PERT dosing is discussed in the section "Evidence to recommendations" in the full guideline. The committee acknowledged the evidence presented comparing different treatment dosages, but they agreed it was of limited use because it was rated as of very low quality. The committee agreed that evidence regarding the effectiveness of PERT dose in relation to resolution of malabsorption symptoms, improvement in weight and improvement in patient satisfaction or health-related quality of life was very limited and of very low quality or completely lacking. The committee noted that trials were of short duration and therefore it was not possible to assess whether prescribing high dose PERT treatment had an impact on weight. They also noted the dosages used are very low compared to those used in clinical practice. The committee acknowledged that the evidence suggested improved fat absorption with higher doses of pancreatic enzyme replacement therapy. However, dosage was likely to vary on an individual basis since the severity of pancreatic insufficiency was not uniform in people with cystic fibrosis. Optimal dose might differ depending on body size and dietary composition and intake. Infants and young children have a higher intake of fat proportionately than older children, young people and adults.

- Thank you for your comment. The costing tool has been updated to include one band 8 lead in the specialist centre. A footnote has also been added to the table your comment refers to. The committee acknowledged the evidence presented comparing different treatment dosages, but they agreed it was of limited use because it was rated as of very low quality. The committee agreed that evidence regarding the effectiveness of PERT dose in relation to resolution of malabsorption symptoms, improvement in weight and improvement in patient satisfaction or health-related quality of life was very limited and of very low quality or completely lacking. The committee noted that trials were of short duration and therefore it was not possible to assess whether prescribing high dose PERT treatment had an impact on weight. They also noted the dosages used are very low compared to those used in clinical practice. The committee acknowledged that the evidence suggested improved fat absorption with higher doses of pancreatic enzyme replacement therapy. However, dosage was likely to vary on an individual basis since the severity of pancreatic insufficiency was not uniform in people with cystic fibrosis. Optimal dose might differ depending on body size and dietary composition and intake. Infants and young children have a higher intake of fat proportionately than older children, young people and adults.

- Thank you for your comment. The committee agreed that evidence regarding the effectiveness of PERT with pancreatic insufficienty and that the dose should be adjusted for each person in order to minimise symptoms of malabsorption. This recommendation is consistent with clinical practice and aligned with the CF Trust Consensus recommendations (CF Trust, Nutritional Management of Cystic Fibrosis 2016).

- Thank you for your comment. Based on this, the committee agreed to recommend offering PERT to people with cystic fibrosis with pancreatic insufficienty and that the dose should be adjusted for each person in order to minimise symptoms of malabsorption. This recommendation is consistent with clinical practice and aligned with the CF Trust Consensus recommendations (CF Trust, Nutritional Management of Cystic Fibrosis 2016).

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<th>Full</th>
<th>231</th>
<th>21</th>
<th>UK CF Registry records prevalence of stress urinary incontinence (question 8.4 UKCF registry document in physiotherapy section) this in the recommendations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF)</td>
<td>Full</td>
<td>264</td>
<td>38</td>
<td>Warnock spell incorrectly</td>
</tr>
<tr>
<td>Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF)</td>
<td>Full</td>
<td>290</td>
<td>14 - 22</td>
<td>The guideline states that NIV is not widely used in clinical practice. However, it is becoming an established treatment option within the UK and is increasingly not limited to patients using NIV for nocturnal ventilation. The recommendation for use of NIV to support airway clearance techniques (iACT) does not appear to be supported by any published evidence. There is reference to a study (Young 2008) which evaluates the use of NIV for treatment of hypercapnia in which there is no reference to ACT as either a primary or secondary outcome measure. There are other studies which specifically look at this issue and they are included below. We would also refer you to the Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis Third Edition April 2017 (Cystic Fibrosis Trust publication) Moran F et al. Non-invasive ventilation for cystic fibrosis. Cochrane Database Syst Rev. 2013 Apr 30; 4:CD002769. doi: 10.1002/14651858.CD002769.pub4.Review. Pub Med PMID: 23633038. Holland, AE et al. Non-invasive ventilation assistachest physiotherapy in adults with acute exacerbations of cystic fibrosis. Thorax. Oct 2003; vol. 58, no. 10, p.880-884, 0040-6376. Thank you for your comment. For the prevalence review on complications of cystic fibrosis, one of the criteria for inclusion was sample size &gt; 250 (please see appendix D for review protocols). The following study was already mentioned in the excluded studies list (appendix H): Blackwell 2005 (Exclusion reason: Sample size &lt;251). The following studies have been assessed as ineligible for inclusion due to sample size &lt;251, however are not mentioned in the list of excluded studies, because sample size was clear from the abstract and therefore we did not check the full text: Cornciachia 2001, Nixon 2002, Moran 2003, Vella 2009, Kozreniewska-Eksterowicz 2014. The following studies were checked full text based on your comment and were added to the excluded studies list (appendix H): Burge 2011; Orr 2001; Prasad 2006; White 2000 (All these 4 studies were excluded with exclusion reason: sample size &lt;251); Nankivell 2010 (Exclusion reason: literature review); Gumney 2005 (Exclusion reason: Conference abstract. Sample size &lt;251). Notes have been added next to these studies’ references in appendix H indicating that they were identified by stakeholders at consultation. Apologies but it was unclear what &quot;Daniels, Morrison, Lewis 2016 120&quot; refers to. Please note that the flow diagram of clinical article selection in appendix F has now been updated for this review to take into account these additional excluded studies. Thank you for your comment.</td>
</tr>
</tbody>
</table>


Dewey TJ et al. Non-invasive ventilation used as an adjunct to airway clearance treatments improves lung function during an acute exacerbation of cystic fibrosis: a randomised trial. Journal of Physiotherapy. 01 July 2015; vol./is.: 613 (142-147), 18369653.

Stanford, G et al. Positive pressure – analysing the effect of the addition of non-invasive ventilation (NIV) to home airway clearance techniques (ACT) in adult cystic fibrosis (CF) patients. Physiotherapy Theory & Practice. 01 May 2015; vol./is.: 314(270-274), 09593985.

We feel that this section is not fully representative and therefore not entirely accurate. Regarding use of NIV to support ACT – it could be suggested that symptoms associated with reduced oxygen levels may be addressed with the application of controlled oxygen therapy to support ACT in the first instance with NIV therapy trial where indicated to address hypercapnia and hypventilation.

Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF)

Full 292 8

We agree that the vest should not be offered as a first line airway clearance technique but are concerned that the recommendation states that it should never been used. There are instances where it is beneficial and these have been laid out in the Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis Third Edition April 2017 (Cystic Fibrosis Trust publication)

- High Frequency Chest Wall Oscillation could be considered when adherence with other airway clearance techniques is problematic
- High Frequency Chest Wall Oscillation should be considered when patients are unable to carry out other airway clearance techniques for reasons such as autism, learning difficulties
- High Frequency Chest Wall Oscillation could be considered for use in conjunction with other airway clearance techniques eg. Active Cycle of Breathing Technique, PEP mask.

If the recommendation is published as it is currently written, it will limit physiotherapists' ability to offer appropriate treatment in some cases. We feel that it should be allowed in particular circumstances as outlined above.

British Infection Association

Full General

Haemophilus influenzae is spelled incorrectly with capital and italic forms incorrect throughout. Many other microorganisms (such as Pseudomonas) are interchangeably spelled with italics or not or small letters or capitals.

British Infection Association

Full General

As an organisation we support the principals of the full and draft guideline

British Infection Association

Genera l General

Microorganisms are spell incorrectly with capital and small letters in the incorrect locations and no italics in the draft document

British Thoracic Society

Full 231 21

UK CF Registry records prevalence of stress urinary incontinence (question 8.4 UKCF registry document in physiotherapy section)

British Thoracic Society

Full 231 26

Prevalence studies published:

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.
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<td>British Thoracic Society</td>
<td>Full</td>
<td>290</td>
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<td>Regarding use of NIV to support ACT – it could be suggested that symptoms associated with reduced oxygen levels may be addressed with the application of controlled oxygen therapy to support ACT in the first instance with NIV therapy trial where indicated to address hypercapnia and hypoventilation.</td>
</tr>
</tbody>
</table>

Thank you for your comment. The study by Young (2008) met the protocol criteria because it compared NIV to no intervention (room air). We extracted data from this study on the outcomes outlined in the review protocol for airway clearance (appendix D). As per review protocol in appendix D, the evidence review did not assess for inclusion any studies that evaluated NIV as an adjunct to other airway clearance techniques. It only included studies that compared NIV (on its own) to no intervention or to another airway clearance technique. Given that the evidence on NIV used as an adjunct to other airway clearance techniques was not assessed for inclusion in the review, the recommendation to think about using non-invasive ventilation to help with airway clearance techniques has now been replaced with a recommendation to consider NIV in people with cystic fibrosis who have moderate or severe lung disease and cannot clear their lungs using standard airway clearance techniques. The full guideline explains the reasoning of the committee in relation to this point in more detail.

Thank you for your comment. The recommendation to think about using non-invasive ventilation to help with airway clearance techniques has now been amended because, as per review protocol in appendix D, the evidence review did not assess for inclusion any studies that evaluated NIV as an adjunct to other airway clearance techniques. It only included studies that compared NIV (on its own) to no intervention or to another airway clearance technique. The recommendation has been amended to say consider NIV in people with cystic fibrosis who have moderate or severe lung disease and cannot clear their lungs using standard airway clearance techniques. The corresponding section in the full guideline has been amended to state that NIV unloads the respiratory muscles, therefore, it reduces the symptoms associated with respiratory muscle fatigue in moderate and severe lung disease such as reduced oxygen and breathlessness. The Committee also agreed that NIV can be beneficial as a short-term option in moderate disease, when people have difficulty clearing their airways using other clearance techniques, by unloading the respiratory muscles and reducing fatigue. The committee discussed your comment and noted that oxygen therapy alone while correcting oxygen levels will not unload the respiratory muscles and therefore allow better airway clearance and longer clearance sessions through the reduction of fatigue. The committee members noted that they would of course use oxygen for desaturation alone however, they would add NIV if patients were tiring or not achieving sufficient chest clearance with standard airway clearance techniques. The committee decided not to add this discussion on oxygen therapy to the full guideline because oxygen therapy was not included in the review protocol on airway clearance and was not included in the recommendations either.

Thank you for your comment. The protocol of the review on the prevalence of complications of cystic fibrosis did not prioritise these complications, therefore the evidence on the prevalence of these complications was not reviewed and no recommendations were made on this.

Thank you for your comment. The protocol of the review on the prevalence of complications of cystic fibrosis did not prioritise these complications, therefore the evidence on the prevalence of these complications was not reviewed and no recommendations were made on this. The however are not mentioned in the list of excluded studies list, because sample size was clear from the abstract and therefore we did not check the full text: Cornacchia 2001, Nixon 2002, Moran 2003, Vella 2009, Korzeniowska-Eksterowicz 2014. The following studies were checked full text based on your comment and were added to the excluded studies list (appendix H): Bugge 2011; Orr 2001; Prasad 2006; White 2000 (All these 4 studies were excluded with exclusion reason: sample size <251); Nankivell 2010 (Exclusion reason: Conference abstract). Sample size < 251. Notes have been added next to these studies’ references in appendix H indicating that they were identified by stakeholders. Apologies but it was unclear what “Daniels, Morrison, Lewis 2016 120” refers to. Please note that the flow diagram of clinical article selection in appendix F has now been updated for this review to take into account these additional excluded studies.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.
British Thoracic Society  Short 11  18  Section 1.5.3 Frequency of review should be as clinically indicated and although mentioned elsewhere is should be emphasise that this review does not need to in the hospital. Bringing babies back every week in the first month of life is not appropriate. Some may not be diagnosed until 2 months of age anyway. Some less stable patients when older may need to be seen every couple of weeks. If guidance needs to be made then the statement should say the frequency of review depends on the stability of the patient and anticipated need to make treatment changes.  

Thank you for your comment. The recommendation does not specify where the review should take place which allows options such as telemedicine to be considered. Based on their clinical experience and expertise, the committee agreed to recommend more frequent routine reviews after diagnosis and in early life. Following those initial years, the person’s condition is likely to become more predictable. To guide the audiences reading the recommendation, the committee gave some examples of review frequency for different age groups, with frequency decreasing with age. The ranges of frequencies provided in the recommendation are not mandatory, only examples, and should be tailored to the individual with cystic fibrosis. A greater description of the committee’s discussion on this area is provided in the full guideline section titled “evidence to recommendations”.

British Thoracic Society  Short 11  25  Adult CF patients are not reviewed every 3-6 months, but flexibly according to need. Also this is contradicted in P12 line 1.  

Thank you for your comment. The recommendation mentions an example of frequency of routine reviews for adults with cystic fibrosis every 3 to 6 months. As explained in the section “Evidence to recommendations”, frequency of routine reviews would vary based on individual needs, therefore “3 to 6 months” is given as an example rather than as a standard to be followed for all adults. Given that the recommendation states “For example”, it does not prevent more frequent or less frequent reviews and does not contradict any other routine review timetables in the guideline.

British Thoracic Society  Short 12  10-12  Cough swabs are not used in adult patients. This section is confusing as combines paediatric and adult management  

Thank you for your comment. The committee discussed your comment and agreed that cough swabs can be used in adult patients. The section combines paediatric and adult management because most of the recommendations were the same in the two populations, therefore having two different sections would have led to a lot of repetition.

British Thoracic Society  Short 12  1  Adult patient are reviewed according to need. In sicker patients, pregnancy, pre transplant this is more frequently than 3 monthly. This statement contradicts p11 line 25  

Thank you for your comment. The recommendation mentions an example of frequency of routine reviews for adults every 3 to 6 months. As explained in the section “Evidence to recommendations”, frequency of routine reviews would vary based on individual needs, therefore “3 to 6 months” is given as an example rather than as a standard to be followed for all adults. Given that the recommendation states “For example”, it does not prevent more frequent or less frequent reviews and does not contradict any other routine review timetables in the guideline.

British Thoracic Society  Short 12  1  It says pulmonary assessment every 3 months  

Thank you for your comment. The committee recommended routine reviews at least every 3 months for adults with cystic fibrosis with clinical evidence of lung disease. A separate recommendation relating to the general population of adults with cystic fibrosis mentions an example of frequency of 3 to 6 months. As explained in the section “Evidence to recommendations”, frequency of routine reviews would vary based on individual needs, therefore “3 to 6 months” is given as an example rather than as a standard to be followed for all adults. Given that the recommendation states “For example”, it does not prevent more frequent or less frequent reviews and does not contradict any other routine review timetables in the guideline.

British Thoracic Society  Short 12  11  Some centres use cough plates instead of cough swabs or NPAs  

Thank you for your comment. The committee discussed your comment and decided not to add cough plates to the recommendation because these are not widely used.

British Thoracic Society  Short 12  17  Currently no standardisation in the equipment used for LCI. So would need to have a comment about this and its use in measuring trends. LCI is a research tool, not generally available in CF centres.  

Thank you for your comment. In the full guideline it is noted that LCI is currently in its infancy in the UK, but could provide additional respiratory information to spirometry. As a result the committee made recommendations to consider the use of LCI for those clinics that have access to the equipment and ability to interpret the results. To enable stronger recommendations in the future, a research recommendation to assess if LCI is a useful and cost-effective tool for the routine assessment and monitoring of changes in pulmonary status in people with cystic fibrosis was prioritised by the committee.

British Thoracic Society  Short 13  23  LCI - again feasibility  

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British Thoracic Society  Short 13  24  In view of high radiation, the chest CT should only be done if the results are going to effect a change in treatment  

The committee acknowledged that a CT scan costs considerably more than a chest X-ray and involves greater exposure to radiation. However, they believed a CT scan would show subtle structural changes in the lungs that would not be evident from a chest X-ray, such as early bronchiectasis. As a result, a CT scan could allow early escalation of treatment to prevent further deterioration that could be more costly to treat. Furthermore, the committee noted that the accuracy of CT scans to predict pulmonary exacerbations was demonstrated in the study by Sanders 2015. For these reasons, the committee concluded they could justify the use of CT scans as a cost-effective use of NHS resources and made a recommendation to think about
<table>
<thead>
<tr>
<th>British Thoracic Society</th>
<th>Short</th>
<th>14</th>
<th>4-5</th>
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<tr>
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<th>14</th>
<th>6</th>
<th>Cough swabs not used in adults – again this is confusing as advice combined for Paediatric and adult patients</th>
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<td></td>
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<th>15</th>
<th>6</th>
<th>HP-CEMO may have a role in those with reasons for not being able to do airway clearance by some other means (eg we have a young person with Cerebral palsy and CF, those who are less active)</th>
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<td></td>
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<td>Thank you for your comment. We have amended the recommendation to consider the use of high frequency chest wall oscillation in exceptional clinical circumstances as determined by the specialist CF team and following the NHS England policy on Individual Funding Requests. The section on evidence to recommendations in the full guideline explains that the CF team would use the NHS definition of exceptional clinical circumstances.</td>
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<tr>
<th>British Thoracic Society</th>
<th>Short</th>
<th>15</th>
<th>11</th>
<th>This is very vague comment. Currently hDNase is being offered to many children over 5-6 years per licence who have no reported symptoms but who demonstrate a benefit in terms of lung function and reduction in exacerbations. This statement can be interpreted</th>
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<td></td>
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<td>Thank you for your comment. The recommendation has been amended to refer to clinical evidence of lung disease rather than respiratory symptoms or other evidence of lung disease. As explained in the full guideline under &quot;Consideration of clinical benefits and harms&quot;, the Committee discussed whether a mucoactive or mucolytic agent should be prescribed to everyone who has cystic fibrosis. However, taking into account the potential adverse effects, as well as the inconvenience and the cost of treatment, it was agreed not to recommend it to everyone; instead, the Committee agreed that it should be offered to people with cystic fibrosis who have clinical evidence of lung disease.</td>
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<th>16</th>
<th>8</th>
<th>This goes against the CF Start study which has just been set up to answer this question. This statement should be taken out or modified otherwise patients will not be able to be recruited to this important study</th>
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<tr>
<td></td>
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<td>Thank you for your comment. The committee discussed your comment and concluded to keep the recommendation to offer fluclaxolin as antibiotic prophylaxis against respiratory Staphylococcus aureus infection for children with cystic fibrosis (although some amendments were made in relation to age cut-offs). The rationale for this recommendation is given in the full guideline. The committee noted that the evidence showed that anti-staphylococcal prophylaxis with an antimicrobial agent (either fluclaxolin or cephalasin) led to a decreased number of children in whom S aureus was isolated. Despite the fact that the evidence did not show this was associated with clinical benefit, there being no improvement in lung function or reduction in exacerbations in children given prophylaxis compared with those who were not, the reduction in S aureus was, nevertheless, a critically important outcome. Overall, the evidence did not reveal the occurrence of adverse events with prophylaxis. The committee were concerned about the theoretical possibility that long-term antimicrobial prophylaxis for S aureus might be associated with an increased risk infection with P aeruginosa. Although the evidence did not demonstrate this, the committee noted that the quality of the evidence for this outcome ranged from very low to low. The committee observed that, given the widespread expert consensus that this risk is a concern, they agreed that it could be mitigated by recommending that fluclaxolin be used rather than cephalasin. The fact that cephalosporins are broad spectrum is postulated to be the reason why an increase in pseudomonas isolation may be seen, although this is not known with certainty. Recommending fluclaxolin rather than a cephalasin was in keeping with current practice. In contrast to current recommendations in the USA, the committee did not think there were grounds to advise the non-use of prophylaxis. This was based on the low cost of prophylaxis treatment and the potentially serious consequences of S aureus pulmonary infection that would outweigh the cost of prophylaxis.</td>
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<th>Short</th>
<th>16</th>
<th>7/8 and 14</th>
<th>By convention it should be Staphylococcus aureus (Capital small letter)</th>
</tr>
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<tr>
<td></td>
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<td></td>
<td>Thank you for your comment. We have ensured there is consistency when referring to Latin names of organisms to ensure they are compliant with NiCE Style Guide. They are italicised and start with a capital letter. The genus names then abbreviated after first use in the full guideline but not in the short guideline where recommendations can be read as stand-alone recommendations so it was not felt appropriate to use abbreviations.</td>
</tr>
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</table>

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<thead>
<tr>
<th>British Thoracic Society</th>
<th>Short</th>
<th>18</th>
<th>Gene ral</th>
<th>Pseudomonas aeruginosa? Note heading line 14 is correct and different from heading of Staphylococcus Aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thank you for your comment. We have corrected the heading for Staphylococcus aureus to appear as Staphylococcus aureus.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>British Thoracic Society</th>
<th>Short</th>
<th>19</th>
<th>23</th>
<th>We are unsure about evidence to support that.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thank you for your comment. The discussion in the full guideline explains that no evidence was found for the treatment of B cepacia complex, therefore recommendations were based on committee’s clinical expertise. The committee agreed that if a person develops a new infection with B cepacia complex, an attempt should be made to eradicate the infection with antibiotic therapy whether or not the person was unwell with the infection. The committee noted that it is important to treat new B cepacia complex infections effectively as chronic infection can cause a deterioration in lung function and, in some people, an overwhelming, and even fatal, infection called 'cepa...</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>19</td>
<td>27</td>
<td>This cannot mean that in a patient with no pseudomonas or staphylococcus but with B cepacia you would NOT use nebulised tobramycin. Would you leave a cepacia patient on no long term antibiotics? thank you for your comment. The recommendation has now been amended to recommend to be aware that there is no evidence to support using antibiotics to suppress chronic Burkholtzena cepacia complex infection in people with cystic fibrosis who have stable pulmonary status. The recommendation also states that the possible risks (for example, drug toxicity) of treating the infection should be discussed with the person and their family members or carers (as appropriate). The full guideline explains that no evidence was found for the treatment of B cepacia complex, therefore, recommendations were based on committee’s clinical expertise. The committee advised that the long-term use of drugs used to suppress B cepacia complex can have adverse effects associated with additional treatment costs and quality of life decrements. Consequently, the committee did not want to recommend the use of those drugs in people who are chronically infected and stable, adding that reducing their treatment burden may subsequently promote adherence to their existing regimens and outweigh the benefits of suppressive treatment. However, the committee agreed that people who are deteriorating should consider a trial of chronic suppressive treatment with an inhaled antibiotic. Thank you for your comment.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>19</td>
<td>18 and 20</td>
<td>Burkholderia cepacia is correct I think you should change all to Capital small letter eg Staphylococcus aureus thank you for your comment. We have ensured there is consistency when referring to Latin names of organisms to ensure they are compliant with NICE Style Guide. They are italicised and start with a capital letter. The genus names then abbreviated after first use in the full guideline but not in the short guideline where recommendations can be read as stand-alone recommendations so it was not felt appropriate to use abbreviations.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>20</td>
<td>12-13</td>
<td>H influenza or h influenza? thank you for your comment. We have ensured there is consistency when referring to Latin names of organisms to ensure they are compliant with NICE Style Guide. They are italicised and start with a capital letter. The genus names then abbreviated after first use in the full guideline but not in the short guideline where recommendations can be read as stand-alone recommendations so it was not felt appropriate to use abbreviations.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>20</td>
<td>13</td>
<td>Should this statement say do not treat if don’t have evidence of a pulmonary infection? thank you for your comment. The committee discussed your suggestion and decided to keep the recommendation unchanged. The full guideline explains that no evidence was found for the treatment of H influenza, therefore recommendations were based on committee’s clinical expertise. The committee agreed it is important to treat H influenza in order to prevent chronic infection with this pathogen. This is because although there might not be detectable evidence of disease due to it, the belief is that it will cause lung damage and so should be eradicated. They discussed 2 possible scenarios if a person develops an infection. If the person is clinically well (asymptomatic), the committee recommended giving an oral antibiotic agent. If the person is clinically unwell (for example, with cough or reduced lung function), they recommended the use of an oral or intravenous antibiotic treatment depending on the severity of the illness. These recommendations are consistent with clinical practice and with the CF Trust recommendations (CF Consensus document: antibiotic treatment for Cystic Fibrosis, 2009).</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>21</td>
<td>16</td>
<td>Is if “eradication” ”the correct term in NTM infection? thank you for your comment. The committee discussed your comment and noted that eradication would be the aim but not necessarily the result of non-tuberculous mycobacterial therapy. Therefore the recommendation has been amended to recommend to consider non-tuberculous mycobacterial therapy aimed at eradication.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>21</td>
<td>22</td>
<td>[and Full) The NTM section needs clarification regarding which NTM as being discussed. – M abscessus (and for me recently M chelonae) are special cases as they are absolute contraindications to transplant whereas others M gordonae and as far as I know M avium are not. There is also the question of segregation of these from the CF ward and clinics. The full document suggests that MAC and Abscessus are being discussed together in the NTM section and only these organisms are being considered. These NTM organisms need to be discussed separately, under different sub-sections – particularly M abscessus. thank you for your comment. The recommendations do not specify which non-tuberculous mycobacteria (NTM) are being discussed because they apply to all NTM. These recommendations on NTM have been amended in order not to recommend which antibiotics should be considered or the duration of therapy aimed at eradication. Instead, the committee made a recommendation to seek specialist microbiological advice on this. The committee decided not to make more detailed recommendations, which would require us to differentiate between different NTM, because no evidence was found on NTM. However the full guideline mentions that the committee discussed the fact that the approaches to treating M avium complex and M abscessus differ (the full guideline mentions these two and no other NTMs because these two were the ones prioritised in the review protocol). The full guideline also mentions that there is existing consensus guidance on the management of non-tuberculous mycobacteria in a publication by Fioto et al. (2016) titled “US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis” (http:// thorax. bmj. com/ content/ 71/ Supp t_ 1/ 11) With regards to segregation, the section of the guideline that focuses on preventing cross-infection includes multiple recommendations on cohorting and separating people individually. The committee did not make recommendations specific to non-tuberculous mycobacteria (NTM) in this section because no evidence was identified on NTM. However all recommendations in the cross-infection section except for those specific to Pseudomonas aeruginosa and Burkholderia cepacia complex should apply to all people with cystic fibrosis, including those with NTM. This has now been explained in the full guideline.</td>
</tr>
</tbody>
</table>

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7 of 39
<table>
<thead>
<tr>
<th>British Thoracic Society</th>
<th>Short</th>
<th>22</th>
<th>5</th>
<th>Is this referring to IgE or IgG?</th>
<th>Thank you for your comment. This recommendation has been modified to specify that elevated aspergillus serology refers to aspergillus-specific IgG and/or IgE.</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>22</td>
<td>19</td>
<td>Should monitor for NTM in those patients who are to start on long term azithromycin</td>
<td>Thank you for your comment. The committee agreed that no change to the recommendation was needed because NTM is measured at the annual assessment.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>23</td>
<td>1</td>
<td>Free water intake and salt advice?</td>
<td>Thank you for your comment. The committee agreed that advice on water and salt intake did not need to be added to the recommendation because this is an implicit aspect of nutritional management. However this was added to the &quot;Evidence to recommendations&quot; section in the full guideline.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>23</td>
<td>20</td>
<td>Children, young people and adults – why does document not refer to adults as well?</td>
<td>Thank you for your comment. We have amended the recommendation to state the test should be repeated if symptoms or signs suggesting malabsorption occur at any age.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>24</td>
<td>19</td>
<td>Abdominal Xay should also be considered at least in children</td>
<td>Thank you for your comment. The recommendation states to consider further imaging for example with an abdominal ultrasound scan or abdominal CT scan for people who have an acute onset of peri-umbilical abdominal pain but no other clinical or radiological features of distal intestinal obstruction syndrome. Radiological features would be detected through an X-ray. This is now specified in the previous recommendation, which has been modified to state to suspect distal intestinal obstruction syndrome in people with cystic fibrosis who have an acute onset of peri-umbilical or right lower quadrant abdominal pain and any of the following: a palpable mass in the right lower quadrant; faecal loading in the right lower quadrant on a plain abdominal X-ray, especially if associated with small intestine air-fluid levels; clinical features of partial or complete intestinal obstruction, such as vomiting (especially bilious) and abdominal distension.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>25</td>
<td>1</td>
<td>diatrizoate meglumine - use trade name as well - Gastrografin - not known by generic name – readers won’t know what you are talking about.</td>
<td>Thank you for your comment. The NICE manual states that any references to products should be made in general terms to avoid giving the impression that NICE endorses a particular brand. However in this case, the trade name has been used given that no other brands are available.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>25</td>
<td>5</td>
<td>Poly ethylene glycol + Klean Prep – the trade names need to be added as well, otherwise no one will understand what to use</td>
<td>Thank you for your comment. The NICE manual states that any references to products should be made in general terms to avoid giving the impression that NICE endorses a particular brand. However &quot;macrogols&quot; have been added to the recommendation to increase the readers understanding.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>25</td>
<td>7</td>
<td>What about colonoscopic washout with either Gastorafin or N acetyl cysteine – we would do this before surgery and have never operated on anyone for DIOS.</td>
<td>Thank you for your comment. The committee agreed that consultation with a surgeon may identify colonoscopic washout as an option before surgery, however the committee decided not to include this in the recommendations because colonoscopic washout was not included in the review protocol and therefore evidence on this was not reviewed. This discussion has now been added to the section &quot;Evidence to recommendations&quot; in the full guideline.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>25</td>
<td>7</td>
<td>Inta-Rectal treatment – colonic washouts not discussed - would consider prior to surgery prior to surgery</td>
<td>Thank you for your comment. The committee agreed that consultation with a surgeon may identify colonoscopic washout as an option before surgery, however the committee decided not to include this in the recommendations because colonoscopic washout was not included in the review protocol and therefore evidence on this was not reviewed. This discussion has now been added to the section &quot;Evidence to recommendations&quot; in the full guideline.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>25</td>
<td>18</td>
<td>Need to be more precise about abnormal liver function tests</td>
<td>Thank you for your comment. The committee discussed your suggestion and decided not to include a definition of abnormal liver function blood tests to allow for clinical judgement to decide what tests are abnormal.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>27</td>
<td>3</td>
<td>There are limited normative data for DXA scans for pre-pubertal children so difficult to interpret in children. Also no mention of the frequency</td>
<td>Thank you for your comment. The committee agreed that the recommendations on BMD should apply to children and adults, but noted that z-scores should be measured in children and t-scores in adults. In the full guideline section titled &quot;evidence to recommendations&quot; it states there is little value in routine monitoring, as children and young people get treated to help accrue bone mass in spite of the results of the test. The risk factors provided in the recommendation should be assessed during routine reviews to the clinic. In the full guideline section titled &quot;evidence to recommendations&quot; it is suggested that scans could be repeated on an annual basis if the BMD SDS score is less than -2.00. However, the committee did not state the frequency of bone scans in their recommendations as this would be individualised to the patient using clinical expertise.</td>
</tr>
<tr>
<td>British Thoracic Society</td>
<td>Short</td>
<td>29</td>
<td>4</td>
<td>No mention of NTM in terms of cross infection risks</td>
<td>Thank you for your comment. The recommendations specific to Pseudomonas aeruginosa and Burkholderia cepacia complex were based on the clinical and economic evidence identified. The committee did not make recommendations specific to non-tuberculous mycobacteria (NTM) because no evidence was identified to make recommendations in addition to those that were not</td>
</tr>
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</table>

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pathogen specific. All recommendations in this section except for those specific to Pseudomonas aeruginosa and Burkholderia cepacia complex should apply to all people with cystic fibrosis, including those with NTM. This has now been explained in the full guideline.

Thank you for your comment. The recommendation has been reworded for clarity and it now states to keep people with transmissible or chronic Pseudomonas aeruginosa or Burkholderia cepacia complex infection separate from people who do not have these infections, for example by using separate outpatient clinics.

Thank you for your comment. The recommendation has been amended to state intermittent isolation of Pseudomonas aeruginosa.

Thank you for your comment. This bullet has been amended to “the use of communal areas” to remove the suggestion that waiting areas are used by some clinics. Communal areas was used in the recommendation to cover areas such as cafes, gyms and restrooms.

Thank you for your comment. The committee agreed that a diagnosis based on clinical manifestations alone with normal test results could happen in some rare cases. The recommendation has now been modified to specify that this is rare.

Thank you for your comment. We have amended the definitions for pulmonary exacerbation and infection to make it clearer.

This statement is ambiguous. Should not make a diagnosis of CF with normal sweat test and normal gene results

Thank you for your comment. The committee agreed that all the members of the multi-disciplinary team should assess the person with cystic fibrosis at the annual review, including the specialist clinical psychologist and the specialist pharmacist. This is consistent with the CF Trust Standards of Care 2011. The committee discussed your comment that the annual review could be a very intense and prolonged process. The committee noted that some centres do a rolling annual review (with different assessments performed at different times over the year), while other centres group all annual review assessments together. The committee did not make recommendations on this, but, leaving the choice to individual centres. Moreover, the recommendations (which have now been amended) specify that specialist pharmacists should advise people with cystic fibrosis on their own. Moreover they are rare in children.

Thank you for your comment. Managing the risks of cross-infection has been added to the recommendation.

Thank you for your comment. The committee considered your suggestion but concluded that advice on drugs, alcohol, smoking and sexually transmitted disease would not need to be tailored specifically for people with cystic fibrosis, instead the advice would be very similar to that given to the general population. As a result these topics have not been added to the recommendation.

Thank you for your comment. The recommendations on antimicrobial treatments for each pathogen differ. Long-term antibiotic use was not considered to be effective for each pathogen under consideration.

Thank you for your comment. The Committee decided not to include nasal polyps because they are very common in people without cystic fibrosis therefore they would not prompt an assessment for cystic fibrosis on their own. Moreover they are rare in children.

Thank you for your comment. The recommendations on antimicrobial treatments for each pathogen differ. Long-term antibiotic use was not considered to be effective for each pathogen under consideration.

Thank you for your comment. The recommendation has now been modified to specify that this is rare.

This statement is ambiguous. Should not make a diagnosis of CF with normal sweat test and normal gene results

Thank you for your comment. We have amended the definitions for pulmonary exacerbation and infection to make it clearer.

Thank you for your comment. The guidelines recommend that “the person with suspected or diagnosed cystic fibrosis and their family members or carers (as appropriate) can understand.” The recommendations will not include translation issues because this is not specific to cystic fibrosis. The committee also included a recommendation which directs readers of this guideline to the NICE guideline CG138 "Patient experience in adult NHS services: improving the experience of care for people using adult NHS services". The CG138 guideline recommends: "Establish the most effective way of communicating with each patient and explore ways to improve communication. Examples include using pictures, symbols, large print, Braille, different languages, sign language or communications aids, or involving an interpreter, a patient advocate or family members."

Thank you for your comment. We have changed this from information in clear English to information that people with suspected or diagnosed cystic fibrosis and their family members or carers (as appropriate) can understand.

Thank you for your comment. The Committee decided not to include nasal polyps because they are very common in people without cystic fibrosis therefore they would not prompt an assessment for cystic fibrosis on their own. Moreover they are rare in children.

Thank you for your comment. The Committee decided not to include nasal polyps because they are very common in people without cystic fibrosis therefore they would not prompt an assessment for cystic fibrosis on their own. Moreover they are rare in children.

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smaller patient numbers than other studies included in the review.

We would also like to draw the committee’s attention to a recently-published paper, the CF-204 study, a randomised, placebo-controlled crossover study comparing 8 weeks of treated with inhaled mannitol with placebo in children aged 6-17 years. The authors report, with mannitol, an improvement of 3.42% in percent predicted FEV1 and a reduction in pulmonary exacerbations; a similar incidence of adverse events was observed between groups.


Chiesi Limited

Full

322

24-38

We disagree with the conclusion given that evidence of lowmoderate quality finds no clinically significant difference in lung function measured by FEV1 produced by inhaled mannitol.

The conclusions drawn by the authors in the publications of the cited clinical trials was that the mean difference in lung function between inhaled mannitol, and a comparator of low-dose mannitol as placebo, was clinically meaningful. Bilton et al, found, over 26 weeks, an improvement from baseline of vs 2.4% for placebo-treated patients vs 2.4% of mannitol-treated patients. In a very similar trial, Aitken et al, 2012, found an improvement of 8.22% for mannitol-treated patients and 4.47% for placebo-treated patients. Secondary endpoints in both trials, including change in percent predicted FEV1 (3.60% and 2.42%, compared to placebo), corroborate the finding.1,2


Chiesi Limited

Full

387

27

We are concerned that nebulised tobramycin has been included as a treatment for people are not suitable for nebulised tobramycin and is included in the recommendations.

If the search protocol had included terms for chronic treatment, an additional paper would have been identified: Mazurek H et al, Pediatr Pulmonol 2014, 49:1076-1089. Long-term efficacy and safety of aerosolized tobramycin 300mg/4mL in cystic fibrosis.

We suggest that the scope of the recommendations be reviewed to include an examination of the data on nebulised tobramycin in the management of chronic Pseudomonas aeruginosa.

Chiesi Limited

Full

450

3

We are concerned that nebulised tobramycin has been included as a single treatment, whereas two distinct preparations are available, 300mg/5mL (TOBI ®), and 300mg/4mL (Bramitob ®) with distinct safety and tolerability profiles.

We suggest that the two preparations be considered separately, both from a clinical and a health economic perspective.

Chiesi Limited

Full

458

18-19

We are concerned that nebulised tobramycin has been included as a treatment for people are clinically deteriorating due to chronic Pseudomonas aeruginosa despite regular inhaled colistimethate sodium. Without the consideration of the evidence given by Mazurek et al, 2014, which was excluded from the search results due to the protocol not seeking evidence for nebulised tobramycin in chronic Pseudomonas aeruginosa infection.

Chiesi Limited

Full

458

7-9

We suggest that the committee consider the use of nebulised tobramycin for patients not suitable for nebulised colistimethate sodium, when there is evidence of ongoing Pseudomonas aeruginosa infection without a requirement for sodium colistimethate sodium DPI (see also comment 1).

Chiesi Limited

Full

General

Sect on

In the management of chronic Pseudomonas aeruginosa, an example of good practices may be to use a test pack of tobramycin for the initial patient test so as to minimise the potential for batch prioritized for inclusion in the review. (Please see list of excluded studies in appendix H). The study by De Boeck was published in May 2017. The cut-off date for the search on mucoactive agents was 5 January 2017. Therefore this study was not assessed for inclusion. Relevant studies published after the cut-off search date will be included in future updates of this guideline.

The committee noted that mannitol is rarely used in clinical practice in children and young people. They were aware of issues of poor tolerability and difficulties with the inhaler device in children and young people. The committee agreed that mannitol may be an option for children and young people when rhDNase and hypertonic sodium chloride have failed or are not tolerated and so has now made a recommendation to this effect.

Thank you for your comment. The omission of nebulised tobramycin in the protocol was due to an oversight therefore the protocol has now been amended (Appendix D). The search strategy for this review (Appendix E) was not limited to the preparation of tobramycin.

The evidence review also includes the following studies where nebulised tobramycin is at least one of the interventions: NICE TA 276; Chuchalin 2007; Hodson 2002; Konstan 2011a; Lenor 2007; Murphy 2004; Ramsey 1993; Ramsey 1999; Flume 2016. Mazurek et al. 2014 compared two preparations of nebulised tobramycin (TOBI and Bramitob) but comparisons of preparations were not included in the protocol.

Thank you for your comment. The Committee agreed it was reasonable to assume equivalent efficacy across those preparations and comparisons of preparations were not included in the protocol (Appendix D). In the economic model, the cheapest preparation is considered in the base case to reflect the best price available to the NHS. However, there is an option in the model to apply the more expensive preparation. Moreover, given that NICE cannot be seen to endorse a particular brand the generic name is used.

Thank you for your comment. The omission of nebulised tobramycin in the protocol was due to an oversight therefore the protocol has now been amended. The search strategy for this review (Appendix E) was not limited to a specific preparation of tobramycin and also included nebulised tobramycin. The evidence review also includes the following studies where nebulised tobramycin is at least one of the interventions: NICE TA 276; Chuchalin 2007; Hodson 2002; Konstan 2011a; Lenor 2007; Murphy 2004; Ramsey 1993; Ramsey 1999; Flume 2016. Mazurek et al. 2014 compared two preparations of nebulised tobramycin (TOBI and Bramitob) but this comparison was not included in the protocol.

Thank you for your comment. The guideline must adopt existing TA recommendations. Recommendation 1.6.34 taken from TA 276 states nebulised colistimethate is the first line treatment and recommendation colistimethate sodium dry powder inhalation as the second line treatment. Recommendation 1.6.37 also taken from TA 276 states people should consider stopping treatment if there is no clinical benefit.

Thank you for your comment. We agree that waste should be minimised. However, the committee agreed that the reduction of pharmacy waste is not specific to cystic fibrosis and should be
9.4 The guideline highlights the importance of information and support but does not identify reliable and responsible sources. The Cystic Fibrosis Trust publishes comprehensive information resources for people with cystic fibrosis and their families and carers compiled with independent input from cystic fibrosis specialists and people with cystic fibrosis. In 2016-2017 we published information resources about starting primary and secondary school, end of life care and advanced care planning.

Cystic Fibrosis Trust

Appendices

Full

127

Gene

ral

For some aspects of cystic fibrosis management, NICE has already produced guidance. These pieces of guidance need to be included in the body of the full NICE guidelines to ensure that stakeholders can easily reference guidance on available care for people with cystic fibrosis.

Cystic Fibrosis Trust

We suggest replacing the current text:

"For people who are clinically deteriorating despite regular inhaled colistimethate sodium, consider nebulised aztreonam, nebulised tobramycin, or tobramycin DPI (see recommendation 1.6.36 on using tobramycin DPI).

With: For people where colistimethate sodium is contraindicated, not tolerated, has not produced an adequate clinical response, or who are clinically deteriorating consider nebulised aztreonam, nebulised tobramycin, or tobramycin DPI (see recommendation 1.6.36 on using tobramycin DPI)."

Thank you for your comment. The pathway that will be developed for the guideline will cross refer to relevant NICE documents such as Technology Appraisals and Clinical Guidelines. There is also a section in the full guideline titled "Related NICE guidance" which may highlight the guidance you are referring to.

Cystic Fibrosis Trust

Full

285-292

6-7

We do not believe the recommendation "do not offer high-frequency chest wall oscillation as an airway clearance technique for people with cystic fibrosis" should be included in the guideline. Whilst current evidence does not show high-frequency chest wall oscillation to be superior to manual physiotherapy, PEP mask, ACBT and AD no evidence for patient preference was found for this critical outcome (p.285).

Physical airway clearance therapy is time consuming, intrusive, requires a high level of expertise and is often uncomfortable for people with cystic fibrosis. As reported in the guidance increasing numbers of patients have paid for high-frequency chest wall oscillation privately, displaying strong patient preference. As identified by the Cochrane Review in March 2017 (http://www.cochrane.org/CD006842/CF_use-vibrating-devices-help-people-cystic-fibrosis-clear-their-airways-mucus)) more adequately-powered long-term randomised controlled trials are necessary and outcomes measured should include frequency of exacerbations, individual preference, adherence to therapy and general satisfaction with treatment. Increased adherence to therapy may then lead to improvements in other parameters, such as exercise tolerance and respiratory function.

Cystic Fibrosis Trust

Full

667

32

Reference to “in times of austerity” could be construed as politically-motivated and should be removed.

Thank you for your comment. This sentence has been amended to address your comment.

Cystic Fibrosis Trust

Full (Short)

14 (32)

13-15

(21-23)

The guideline states 'A FEV1 of 50% and above wi...('This is not supported by a source and provides an unhelpful oversimplification of the nature of the condition, which is recognised elsewhere in the document as a multi-system disorder. Gastro-intestinal issues, CF-related diabetes and high treatment burden are three examples (of many) that are common challenges for people with CF (regardless of lung function) and barriers to living 'relatively normal lives.' Whatever the motivation for the inclusion of this statement, we strongly suggest it is removed.

Thank you for your comment. The statement which included FEV1 values has been amended to state "FEV1 is a key predictor of life expectancy in people with cystic fibrosis, and optimising lung function is a major goal of care."

Cystic Fibrosis Trust

Full/Short

The Cystic Fibrosis Trust support national evidence-based recommendations on cystic fibrosis practice and welcome the NICE Guideline ‘Cystic fibrosis: diagnosis and management’. The NICE considered as standard practice across all disease areas. Instead of adding a recommendation, a short narrative regarding pharmacy waste reduction has been added to the full guideline.

Thank you for your comment.
**Cystic Fibrosis Trust**

<table>
<thead>
<tr>
<th>Full/Sh ort</th>
<th>General</th>
<th>Gene ral</th>
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<tbody>
<tr>
<td>The UK CF Registry is inconsistently referred to as the 'UK registry' (p.14), the 'CF UK registry' (p.32), 'CF registry' (p.32), the Cystic Fibrosis Registry (p.175), UK CF Trust registry (p.212, 219).</td>
<td></td>
<td></td>
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</tbody>
</table>

Thank you for your comment. We have amended all references to the UK CF registry to "UK CF Registry".

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<tr>
<th>Full/Sh ort</th>
<th>General</th>
<th>Gene ral</th>
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<td>The UK CF Registry is highlighted in the Guidance as a priority source. Over 99% of people with cystic fibrosis consent to their anonymised data being collected in the UK CF Registry, which utilises data for research, annual reporting, quality improvement, and as the evidence base for the cost of cystic fibrosis care, informing proportionate year-of-care tariff payments by NHS England. It is also relied upon by the European Medicines Agency to evaluate the safety and efficacy of therapies for post-marketing surveillance. The Guideline shows that the UK CF Registry contains evidence which is not found anywhere else and is vital to understanding and managing cystic fibrosis, to work towards ensuring everyone with cystic fibrosis can look forward to a long and healthy life.</td>
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Recognising the importance of maintaining, developing and investing in the UK CF Registry as a common asset for the purposes stated above is critical, both at an operational (e.g. data entry) and strategic level (e.g. UK CF Registry Steering Committee).

Thank you for your comment.

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<td>We welcome the research priorities set out in the guideline, which – in part – complement the research priorities which the Cystic Fibrosis Trust has identified in collaboration with the James Lind Alliance (JLA) Priority Setting Partnership (PSP) for cystic fibrosis. The James Lind Alliance Priority Setting Partnership in cystic fibrosis brought together over 500 people from across the world and includes an even split of medical staff and lay people. This is the first time such a collaborative and representative process has been undertaken in cystic fibrosis. The work continues with the National Institute for Health Research (NIHR), the Cystic Fibrosis Trust, the Cystic Fibrosis Foundation and the UK Research Councils supporting the research questions identified to be funded and taken forward by experienced and collaborative researchers.</td>
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Thank you for your comment and your support.

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<td>It is unclear why CFTR-modulating therapies are not referenced in these guidelines, other than in relation to adherence and related impacts on cost-effectiveness (p.665-667). The Cystic Fibrosis Trust requests an explanation for this decision. Furthermore, the Committee’s suggestion to ration disease-modifying therapies (p.667) has no place in NICE Guidelines and the line “…such contracts should only be offered to people with cystic fibrosis who are treatment compliant to ensure the benefits from treatment can outweigh the high cost of treatment” must be removed. Definitions of ‘treatment compliance’ are not offered and the ethical implications are not considered.</td>
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The sentence on disease-modifying therapies has been removed as suggested. The Committee did not think it was appropriate to define treatment compliance as the range of modifying therapies has been removed as suggested.

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<td>Regarding the support of social workers within the CF MDT, the use of the word ‘specialist’ is conspicuous by its absence. Whilst the Cystic Fibrosis Trust recognises that specialism within this discipline is harder to define than for clinical roles, we suggest that this adjective is included regarding social workers, as expertise in the impact of cystic fibrosis on an individual’s life can profoundly improve the outcomes delivered by social worker intervention. This is particularly important in relation to the positive impact that high-quality social worker support can have on the ability of clinical colleagues within the MDT to focus on their primary duties. Inexperience with cystic fibrosis or a lack of continuity in personnel support may impact negatively on delivery of primary clinical duties. Additionally, high-quality support may enable individuals to better engage with their clinical team and self-manage care at home – a critical element of cystic fibrosis care.</td>
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The Committee did not think it was appropriate to define treatment compliance as the range would be individualised to the patient and the intervention.

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<tr>
<td>The guidance states: “The specialist cystic fibrosis centre should take responsibility for ensuring transitions are successful.” It is unclear which service (paediatric or adult) should assume this responsibility. This should be clarified.</td>
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</table>

Thank you for your comment. It was not within the scope of this guideline to specify the specialism of cystic fibrosis social workers as this guideline only applies to NHS settings and social workers, while working within NHS settings, are not employed by the NHS. The recommendations have been amended to state that the specialist cystic fibrosis multidisciplinary team should either include, or have access to, social workers.

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<tr>
<td>Thank you for your opportunity to comment on the draft for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.</td>
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Thank you for your comment.
Related to comment 1, since the draft guideline fails to make any mention of CFTR modulators, as a minimum, it should be explicitly stated in section 3.5 that these are not within the remit of the guidelines. However, it would be preferable to include recommendations on the use of CFTR modulators within the guideline.

We are concerned at the precedent that might be set if NICE Clinical Guidelines do not routinely take into consideration recommendations in NHS England clinical commissioning policies. This concern comes from the omission of CFTR modulators from the draft guideline. There is no reference made anywhere in the documentation relating to the availability of CFTR modulators and their importance in the management of CF patients, or alternatively, any clarification that these were outside the remit of the guideline.

Mannitol use in children has not been reviewed. A phase 2, randomised, placebo-controlled crossover study has been published recently. This showed that inhaled mannitol was associated with significant improvements in lung function and sputum weight, irrespective of rhDNase (recombinant human deoxyribonuclease) use, age or disease severity. Inhaled mannitol was well tolerated and was associated with a reduced incidence of pulmonary exacerbation adverse events.

We would suggest that evidence that is also reviewed so that recommendations can be made regarding the use of mannitol in children as a mucocactive agent.

We welcome the recommendation that more research is needed on whether all children with meconium ileus should receive ursodeoxycholic acid to reduce the risk of liver disease.

We welcome the recommendation that a specialist pharmacist should be included in the multidisciplinary team.

The guidelines appear comprehensive and set out key outlines for services.

The shortened guidelines appear entirely appropriate and follow best evidence based practice.

The guidelines are helpful and will provide a strong case for ensuring good quality care and are largely in keeping with clinical UK practice.

The recommendations are not particularly contentious. The nature of the document which is also to be read by lay people means that much of it makes statements that are unlikely to change existing practice. There are also a number of ‘think about’ or ‘consider’ in the recommendations.

The abbreviation DIOS usually stands for distal intestinal obstruction syndrome rather than intestinal obstruction syndrome.

It would be helpful to include information in a range of languages or access to translation (page 5 line 5).

Thank you for your comment. CFTR modulators were not included in the scope as current clinical practice in this area was considered to be consistent and effective, relative to the other areas under consideration. We cannot add CFTR modulators as an exclusion from the scope in section 3.5 at this stage as the scope is defined and finalised prior to guideline development. For completeness, a recommendation referring to the NICE technology appraisal on lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation has been added.

Thank you for your comment. CFTR modulators were not included in the scope as current clinical practice in this area was considered to be consistent and effective, relative to the other areas under consideration. For completeness, a recommendation referring to the NICE technology appraisal on lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation has been added.

Thank you for your comment.

Thank you for your comment.

Thank you for your comment.

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The abbreviation DIOS usually stands for distal intestinal obstruction syndrome rather than intestinal obstruction syndrome.

It would be helpful to include information in a range of languages or access to translation (page 5 line 5).

Thank you for your comment. We have changed the wording of the recommendation from information in clear English to information that people with suspected or diagnosis cystic fibrosis and their family members or carers (as appropriate) can understand. The recommendations will not include translation issues because this is not specific to cystic fibrosis. The committee also...
NHS England General General

It would be prudent to specify what level of contact (day and night) is the minimum, as this is currently left to interpretation (page 7, line 17).

Thank you for your comment. The committee agreed that the recommendation did not need to be more specific about the level of contact people can expect as a minimum because each centre will have their own process for providing this. There should be existing clear processes in place for accessing out of hours at each clinic.

NHS England General General

MDT specifics – W.T.E guidance would be beneficial as could be as little as for example, half a day specialist nurse cover, if part of a wider role (page 7, line 28).

Thank you for your comment. The recommendation on routine review in every clinic has now been modified to mention that no evidence was found on LCI. In the same section it is noted that LCI is currently in its infancy in the UK, but could provide additional information in people with cystic fibrosis at each clinic. The Committee’s discussion on this area is provided in the full guideline section titled “evidence to recommendations”.

NHS England General General

Are there any alternatives if allergic to penicillin (page 16, line 8)?

Thank you for your comment. We have amended the recommendation to state that if children are allergic to penicillins, an alternative oral anti-staphylococcus aureus agent should be considered.

NHS England Short 1.1.1

It would be worthwhile making reference to the National Guideline on sweat testing as it is important that only units who do sufficient number of sweat tests (generally thought to be 50 a year) should be carrying out this test. Otherwise, it should be done in a CF Specialist Centre.

Thank you for your comment. The Committee did not make reference to this sweat test guideline in the recommendation because NICE recommendations can only endorse guidelines that follow NICE processes and have been approved by NICE. However, in the section “Evidence to recommendations” in the full guideline, a reference has been added to the Guidelines for the Performance of the Sweat Test for the Investigation of Cystic Fibrosis in the UK, 2nd Version, by RCPH.

NHS England Short 1.2.3

- It says that relevant information should be given in clear English. It makes no mention of those in whom English is not their first language and there are a proportion of CF patients from Europe and Asian for whom English is not the first language. Mention should therefore be made of appropriate translations.

Thank you for your comment. The committee discussed your comment and noted that some of the recommendations are tailored to the individual with cystic fibrosis and their family members or carers (as appropriate) can understand. The recommendations will not include translation issues because this is not specific to cystic fibrosis. The committee also included a recommendation which directs readers of this guideline to the NICE guideline CG138 "Patient experience in adult NHS services: improving the experience of care for people using adult NHS services". The CG138 guideline recommends: "Establish the most effective way of communicating with each patient and explore ways to improve communication. Examples include using pictures, symbols, large print, Braille, different languages, language or communications aids, or involving an interpreter, a patient advocate or family members".

NHS England Short 1.3.5

- Ear, nose and throat surgeon should be included in this list to help with the common problem of nasal polypos and recurrent sinusitis.

Thank you for your comment. ENT surgeons were included in the protocol as an extended member of the MDT and their importance is discussed in the full guideline. ENT surgeons have been added to the recommendation as suggested.

NHS England Short 1.4.1 and 1.4.2

- Section 1.4.1 states that a common complication of arthritis (1.4.1) and Section 1.4.2 states the less common complication of CF-related arthritis. This is not clear and one normally uses the term CF-related arthropathy to cover all forms of joint pains.

Thank you for your comment. The committee discussed your comment and agreed not to change the recommendations on this because arthritis and arthralgia are two different complications, therefore they should be mentioned separately in the recommendations.

NHS England Short 1.5.3

- As a paediatrician, it is surprising that the recommendation suggests that adults can be seen every 3 to 6 months as surely only the most mild adults would be seen as infrequently as twice a year.

Thank you for your comment. The reviews in this recommendation are routine reviews as opposed to the more comprehensive annual, or bi-annual reviews conducted by the MDT. To guide the audiences reading the recommendation, the committee gave some examples of routine review frequency for different age groups, with frequency decreasing with age. The ranges of frequencies provided in the recommendation are not mandatory, only examples, and should be tailored to the individual with cystic fibrosis. A greater description of the committee’s discussion on this area is provided in the full guideline section titled “Evidence to recommendations”.

NHS England Short 1.8.2

The recommendation notes that lung function testing can be done by children and young people who can do this. It would be worth mentioning that this is usually from 5-6 years of age.

Thank you for your comment. The committee discussed your comment and decided not to mention a usual minimum age because it would be up to the paediatrician’s judgement to decide who is able to do lung function testing with spirometry. This has now been specified in the “Evidence to recommendations” section in the full guideline.

NHS England Short 1.8.3

It is controversial to suggest “consider measuring lung clearance index (LCI) at each routine review (page 34)” and it would be inappropriate for them to have LCI every time in clinic, given the length of time the test takes in each individual and if one adds in the time taken to clean equipment between patients, it would be impossible logistically for this to be carried out. It is also certainly not clear whether there is any evidence that it is a useful thing for routine review in every clinic.

The committee then actually put uselessness of LCI as one of their recommendations for research (page 34) therefore feel it is inappropriate to put this in as a major recommendation.

Thank you for your comment. The recommendation has now been amended to state “at a routine review” rather than “at each routine review”. The section “Evidence to recommendations” in the full guideline has now been modified to mention that no evidence was found on LCI. In the same section it is noted that LCI is currently in its infancy in the UK, but could provide additional information in people with cystic fibrosis. As a result the committee made recommendations to consider the use of LCI for those clinics that have access to the equipment and ability to interpret the results. The recommendation states to “consider measuring LCI, which means that health care professionals would consider whether to do so based on their clinical judgement. To enable stronger recommendations in the future, a research recommendation to assess if LCI is a useful and cost-effective tool for the routine assessment and monitoring of changes in pulmonary status in people with cystic fibrosis was prioritised by the committee.

NHS England Short 1.8.4

The recommendation on respiratory secretions for microbiology refers to including mycobacteria but this should be termed non-tuberculous mycobacteria.

Thank you for your comment. The committee discussed your comment and agreed that non-tuberculous was the right term, so the recommendation has been amended to state non-tuberculous mycobacteria.

NHS England Short 1.8.6

The recommendation notes that people with CF with lung disease who have symptoms that are not controlled by the healthcare professional, can decide whether remote telemedicine or face to face assessment is needed. They then suggest a number of appropriate devices that allow them to family members on the telephone or nurse practitioners who are to measure oxygen saturation and FEV1, and take respiratory secretion samples, at home. Many people would be able to measure weight and

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of assessments to consider, all of which would need face to face assessment apart from the review of the part history. This needs clarification.

NHS England Short 1.6.7 This is a controversial recommendation which states ‘think about doing a chest CT for children with CF who have not had one before to detect features that other tests would miss (for example, early bronchiectasis)’. If one takes this recommendation literally, it would suggest that every child should have a CT scan. The recommendation should be more specific as to which children and how often this should be done because the majority of children do not require a CT chest scan and the radiation issue has never been resolved properly in terms of future cancer risk, given they may have repeated CT scans. This is not to say that no child should have a CT scan, obviously there are a number of clinical circumstances in which this is an important investigation but this should not be routine because one has not been done before.

NHS England Short 1.6.1 0 There is a discussion about using bronchoalveolar lavage to obtain airway samples in children and young people under certain situations. The recommendation does not mention the use of induced sputum which is an increasingly useful technique in children, including those at quite a young age, and it avoids the need for general anaesthetic and bronchoscopy with a relatively simple outpatient procedure.

NHS England Short 1.6.1 1 The recommendation on airway clearance technique requires comment from the physiotherapy group. The recommendation is vague and recommends discussing the use of airway clearance techniques with people with cystic fibrosis who do not have lung disease. It is likely that all children with CF do have lung disease to a degree which has been well shown in studies in London and Australia looking at CT scans, lavage for inflammation and infant lung function and LCI. It is standard protocol for all children to have routine physiotherapy. The next section (1.6.12) to offer training in airway clearance techniques for children who have lung disease should go with the above recommendation so this could be amended to state that all parents should be offered training in airway clearance techniques.

NHS England Short 1.6.1 5 The recommendation says do not offer high frequency chest wall oscillation as an airway clearance technique. On principle, this is fine but would suggest it should say ‘Do not routinely offer; this as there are exceptional circumstances in which case this form of physiotherapy is necessary, for example, children with autism who will not allow manual percussion.

NHS England Short 1.6.1 6 The recommendation suggests using non-invasive ventilation to help with airway clearance techniques in people who have moderate or severe lung disease. It is a useful technique in those with severe lung disease but generally, those with moderate are most unlikely to need this and even more so unlikely to carry it out at home.

NHS England Short 1.6.1 7 The recommendation suggests offering a mucoactive agent to people with CF who have respiratory symptoms or other evidence of lung disease. The European Cystic Fibrosis Society and the US Guidelines suggest offering mucoactive agents (Pulmozyme) to all children aged 6 years and over. Is there a reason that the NICE Guidelines differ from these recommendations.

NHS England Short 1.6.2 2 The recommendation suggests that fluoxacinil prophylaxis should be given to children and consider continuing in up to 6 years of age, this is quite old now and is not standard UK practice and 2-3 years of age far more likely to be the current recommendation.

of length or height at home, and clinical history could be reviewed using telemedicine. Therefore the committee agreed that the guideline should recommend to decide whether to provide a remote telemedicine or face-to-face assessment depending on the assessments that are needed. The section “Evidence to recommendations” in the full guideline has been modified to specify that these assessments could be performed at home.

Thank you for your comment. The recommendation has been amended to specify low-dose CT scan. The committee noted that the recommendation states to think about a low-dose chest CT scan rather than stating to perform this on any child that has not had a CT scan before.

Therefore, performing the CT scan would be subject to clinical judgement based on individual circumstances. This has now been explained in the section “Evidence to recommendations” in the full guideline.

NHS England Short 1.6.7 Thank you for your comment. The recommendation has been amended to mention sputum induction as an example of non-invasive upper airway respiratory secretion sampling, which would be performed before thinking about broncho-alveolar lavage.

NHS England Short 1.6.1 Thank you for your comment. The recommendations have now been amended. The guideline notes that there is no evidence to discuss the use of airway clearance techniques with people with cystic fibrosis who do not have clinical evidence of lung disease and their parents or carers (as appropriate) and to provide them with training in airway clearance techniques and to explain when to use them. A separate recommendation states to offer training in airway clearance techniques to people with cystic fibrosis who have clinical evidence of lung disease and their parents or carers (as appropriate). The recommendation on people with no clinical evidence of lung disease has been kept separate from the recommendation on people with clinical evidence of lung disease because the former may not have to use airway clearance techniques on a regular basis. However training on airway clearance techniques should cover ways to identify the need for performing these techniques. This would allow people with cystic fibrosis to start independently when appropriate rather than delaying the use of these techniques until a health care professional has identified the need. On the other hand, the committee agreed that when a patient has clinical evidence of lung disease or has received a treatment that produces sputum, such as mucolytic treatment, performing airway clearance techniques on a regular basis has a strong rationale and is often helpful in relieving symptoms of cough and breathlessness.

NHS England Short 1.6.1 Based on their experience and expertise, the committee noted that NIV could be used in people with cystic fibrosis who have moderate or severe lung disease and cannot clear their lungs using standard airway clearance techniques. This is because it is known that NIV unloads the respiratory muscles, therefore, it reduces the symptoms associated with respiratory muscle fatigue in moderate and severe lung disease such as reduced oxygen and breathlessness. The Committee also agreed that NIV can be beneficial as a short-term option in moderate disease, when people have difficulty clearing their airways using other clearance techniques, by unloading the respiratory muscles and reducing fatigue. The recommendation on NIV has been modified accordingly.

NHS England Short 1.6.1 Thank you for your comment. The recommendation has been amended to refer to clinical evidence of lung disease rather than respiratory symptoms or other evidence of lung disease. As explained in the full guideline under “Consideration of clinical benefits and harms”, the committee discussed whether a mucoactive or mucolytic agent should be prescribed to everyone who has cystic fibrosis. However, taking into account the potential adverse effects, as well as the inconvenience and the cost of treatment, it was agreed not to recommend it to everyone; instead, the Committee agreed that it should be offered to people with cystic fibrosis who have clinical evidence of lung disease.

NHS England Short 1.6.2 Thank you for your comment. The recommendation has been amended to state to offer fluoxacinil prophylaxis against respiratory Staphylococcus aureus infection from the point of diagnosis up to age 3, and to consider continuing up to 6 years of age. The rationale for these age cut-offs has been added to the full guideline in the “Evidence to recommendations” section. The committee noted that a beneficial effect (decreased number of children in whom S aureus was isolated) was observed for the comparison oral fluoxacinil versus placebo + antibiotic “as required” at 2 and 3 years of follow-up. There was no evidence on fluoxacinil after 3 years. Therefore, the committee recommended to offer fluoxacinil up to age 3. The committee noted that the same beneficial effect was observed for the comparison between another anti-

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| NHS England | Short | 1.6.3 | This is not standard practice. Whilst people will continue with inhaled antibiotics, certain patients do not receive extended courses of oral. The same follows for if they are clinically unwell. |
| NHS England | Short | 1.6.3 | 0 | The recommendation suggests that patients have deteriorated despite regular inhaled antibiotic treatment or have developed Aztreonam or nebulised Tobramycin or Tobramycin DPI. NHS England policy states that Tobramycin is second line and Aztreonam is third line – this is based on acquisition cost and should be reflected in the NICE Guideline. It would also be worth mentioning the use of inhaled Levofloxacin which is in the late stage of NHS England recommendation process where once finalised, will be offered as a fourth line inhaled antibiotic for adults and by the time the NICE Guidelines are published, the Levofloxacin recommendation will be published. |
| NHS England | Short | 1.6.4 | 4 | The recommendation suggests that if patients have deteriorated despite regular inhaled antibiotic treatment or have developed Aztreonam or nebulised Tobramycin or Tobramycin DPI. NHS England policy states that Tobramycin is second line and Aztreonam is third line – this is based on acquisition cost and should be reflected in the NICE Guideline. It would also be worth mentioning the use of inhaled Levofloxacin which is in the late stage of NHS England recommendation process where once finalised, will be offered as a fourth line inhaled antibiotic for adults and by the time the NICE Guidelines are published, the Levofloxacin recommendation will be published. |
| NHS England | Short | 1.6.5 | 4 | The recommendation suggests that if Azithromycin has not helped, to consider oral corticosteroids and this is controversial given long term oral corticosteroids are associated with side effects and this is generally not a treatment that is undertaken. |
| NHS England | Short | 1.7.5 | The recommendation suggests that tests for exocrine pancreatic insufficiency should be repeated annually in children and young people if the initial result is normal. It will usually be repeated once or twice in a baby with a normal level, but usually this would only be repeated if symptoms suggest rather than routinely every year. |
| NHS England | Short | 1.7.7 | 0 | In discussing acute onset of abdominal pain with no features of DIOS, they suggest abdominal ultrasound or abdominal CT scan. This should mention that one would consider a surgical opinion at that point as well, particularly in children. |

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<tr>
<td>NHS England</td>
<td>Short</td>
<td>17.1</td>
<td>5</td>
<td>The recommendation suggests considering surgery as a last resort for DIOS if not responding to treatment. This should also discuss the role of colonoscopy and gastroenterology as well. Thank you for your comment. The committee agreed that the recommendation to manage suspected distal intestinal obstruction syndrome with supervision from specialists who have expertise in recognising and treating the condition and its complications indirectly referred to specialty areas such as colonoscopy and gastroenterology. The committee discussed your suggestion and decided not to specifically mention the role of colonoscopy and gastroenterology in the recommendations not to make them too detailed. However, the section “Evidence to recommendations” has now been modified to specify that the expertise of specialists who supervise management of suspected DIOS should also cover the specialty areas of colonoscopy and gastroenterology.</td>
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<td>NHS England</td>
<td>Short</td>
<td>17.1</td>
<td>8</td>
<td>The recommendation mentions the use of liver ultrasound if liver function tests were abnormal. There is no discussion of any role of liver ultrasound screening for liver disease in children. Thank you for your comment. The committee discussed your comment and decided not to recommend routine ultrasound screening for liver disease because the evidence did not support this. The recommendations state to perform a clinical assessment and liver function blood tests at the annual review. The committee agreed that decisions on the tests to be included in the clinical assessment should be made at individual centres using clinical judgement. This means that individual centres would not be prevented from including an ultrasound scan at annual review. The committee noted that it is currently common practice to perform blood test investigations to look for evidence of liver disease. The committee recognised that ultrasound can detect evidence of liver disease, for example changes in liver echogenicity as well as advanced changes suggestive of portal hypertension. It can also detect the presence of gallstones which sometimes occur in cystic fibrosis. Ultrasound scanning is commonly used to monitor cystic fibrosis-related liver disease. The committee agreed that this may not be necessary if there was no evidence of liver disease, but a liver ultrasound scan should be performed if the blood liver function tests were abnormal. This has now been clarified in the “Evidence to recommendations” section in the full guideline.</td>
</tr>
<tr>
<td>NHS England</td>
<td>Short</td>
<td>17.2</td>
<td>8</td>
<td>The recommendation discusses the use of DXA bone scans but does not mention any role of routine screening in children. This has now been clarified in the “Evidence to recommendations” section in the full guideline.</td>
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<td>Oxford Adult Cystic Fibrosis Centre</td>
<td>Full</td>
<td>176</td>
<td>31</td>
<td>CF specialist nurses commonly undertake a much wider role than implied in this guideline. CF specialist nurses in our unit are involved in the clinical assessment of the unwell CF patient, are often non-medical prescribers, deliver trials of nebulised medications, administer and monitor home courses of IV antibiotic therapy in addition to the roles suggested in the guideline. Greater recognition of the extended scope of CF nursing roles is advised. Thank you for your comment. Some examples about the clinical role of a specialist nurse have now been included in the recommendation.</td>
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<tr>
<td>Oxford Adult Cystic Fibrosis Centre</td>
<td>Full</td>
<td>176</td>
<td>31</td>
<td>Although a social worker is included in the core members of the CF MDT, there is no recommendation on the role and scope of practice for the CF social worker. Thank you for your comment. A recommendation has been added to the section on the multidisciplinary team to include some examples about the role of the social worker as part of the MDT. These include adjusting to long term treatment but also support and advice relating to education or employment.</td>
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<tr>
<td>Oxford Adult Cystic Fibrosis Centre</td>
<td>Full</td>
<td>18</td>
<td>26</td>
<td>The role of CFTR modulators is not included either in what is or is not covered by the guideline. This is a fairly major omission and will limit the usefulness of the guideline. Thank you for your comment. CFTR modulators were not included in the scope as current clinical practice in this area was considered to be consistent and effective, relative to the other areas under consideration. For completeness, a recommendation referring to the NICE technology appraisal on lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation has been added.</td>
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<tr>
<td>Oxford Adult Cystic Fibrosis Centre</td>
<td>Full</td>
<td>530</td>
<td>17-24</td>
<td>Line 17-24 feels out of place as they sound like concluding statements when further exploration of enteral feeding and appetite stimulants follow from these paragraphs. As a result this section does not flow logically. Thank you for your comment. These paragraphs have been deleted from the full guideline.</td>
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Oxford Adult Cystic Fibrosis Centre | Full | 531 | 18 | Line 18 refers to supplement costs of £4.36 and that is based on Calogen. This supplement is not reflective of first line supplements used in CF.

Thank you for your comment. The supplement has been changed to Scandihaze in the section you refer to.

Oxford Adult Cystic Fibrosis Centre | Full | 672 | Gene
eral | The discussion and recommendations offer no advice on the risk or management of potential cross-infection with Mycobacterium abscessus. This issue is of considerable concern to the CF community and deserves more careful consideration in this document.

Thank you for your comment. The recommendations specific to Pseudomonas aeruginosa and Burkholderia cepacia complex were based on the clinical and economic evidence identified. The committee did not make recommendations specific to Mycobacterium abscessus because no evidence was identified to make recommendations in addition to those that were not pathogen specific. All recommendations in this section except for those two that refer to Pseudomonas aeruginosa and Burkholderia cepacia complex should apply to all people with cystic fibrosis, including those with Mycobacterium abscessus. This has now been explained in the section "Evidence to recommendations" in the full guideline.

Oxford Adult Cystic Fibrosis Centre | Short | 11 | 25 | Routine review for adults with CF is recommended "every 3 or 6 months" in this section but in Section 6.1.6 review is recommended "at least every 3 months." This advice should be consistent.

Thank you for your comment. The committee recommended routine reviews at least every 3 months for adults with cystic fibrosis with clinical evidence of lung disease. A separate recommendation relating to the general population of adults with cystic fibrosis mentions an example of frequency of 3 to 6 months. As explained in the section "Evidence to recommendations", frequency of routine reviews would vary based on individual needs, therefore "3 to 6 months" is given as an example rather than as a standard to be followed for all adults. Given that the recommendation states "for example", it does not prevent more frequent or less frequent reviews and does not contradict any other routine review timetables in the guideline.

Oxford Adult Cystic Fibrosis Centre | Short | 20 | 12-21 | There is a typo in the spelling of "Haemophilus influenzae" throughout – needs an e on the end.

Thank you for your comment. We have corrected the spelling of Haemophilus influenzae throughout.

Oxford Adult Cystic Fibrosis Centre | Short | 22 | 26-27 | Does the recommendation on inhaled corticosteroids need clarification for those patients with coexisting CF and asthma?

Thank you for your comment. The committee agreed it would be inappropriate to amend the recommendation for asthma as this would not be treated using an immunomodulatory dose.

PARI Medical Ltd. | Full | 283 | 32 | This is an example line reference; please delete the word 'mask' – most patients using PEP therapy in the UK do so using a mouthpiece.

In our view following PEP with the word 'device' rather than 'mask' would be a more appropriate. Perhaps using this more neutral expression throughout the document would more accurately reflect the practice of HCPs we encounter.

Thank you for your response. Management of the upper airways was not part of the scope of this guideline. In section "What the guideline is about" of Appendix A: Scope, it is specified that the guideline does not cover "Specialist management of cystic-fibrosis-related ear, nose and throat (ENT) disorders".

PARI Medical Ltd. | Full | General | Gene
eral | We are concerned that this recommendation may underrepresent the management and care of the upper airways with sinonasal nebuliser developments in order to offer the most appropriate delivery systems.

The CF Trust recently published an updated guideline: "Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis".

- It was published on 25th April 2017.
- It can be found here: https://www.cysticfibrosis.org.uk/the-work-we-do/clinical-care/consensus-documents

Section 6 specifically includes management of the upper airways & section 6.3 specifically includes the use of delivery systems for sinonasal inhalation of vibrating aerosols (PARI Sinus nebuliser); we believe that the new NICE guidance should also include the therapeutic option with vibrating aerosols (e.g. with the PARI Sinus device) for upper airway management.

Thank you for your comment. We have deleted the term "mask" from this paragraph, from a few included studies, from the comparison headings and from the section linking evidence to recommendations.

PARI Medical Ltd. | Full | General | Gene
eral | In cystic fibrosis very often the upper airways are involved. The term of the "united airways" mainly developed by Hoiby et al puts emphasis to the fact that there is a very close relation between the upper and the lower airways. Upper and lower airways are in fact united to one system with overlapping diseases and symptoms [14,15].

In CF chronic rhinosinusitis and nasal polyps are very common, bacterial infections of the paranasal cavities are additional threats. The patients’ quality of life and their overall health are relevantly impaired [14,15].

Mucolytic agents as dornase alfa and isotonic (0.9%) as well as hypertonic (6%; 7%) saline solutions which are regularly used for the treatment of the CF lung can also be effective in the upper airways. But the deposition of inhaled drugs into paranasal sinuses is substantially limited if traditional nebulisers are used. With the PARI SINUS™ nebuliser it has been shown in deposition studies that the administration of aerosols in the paranasal sinuses is possible [14,15].

In CF the antibiotics Colistin and Tobramycin are widely used for the treatment of pseudomonas aeruginosa or staphylococcus aureus infections in the lower respiratory tract. Recent publications show that the upper airways are often colonized with bacteria of the same genus in the lower airways. Hence, a comprehensive treatment of upper and lower airways seems to be consistent.

Thank you for your response. Management of the upper airways was not part of the scope of this guideline. In section "What the guideline is about" of Appendix A: Scope, it is specified that the guideline does not cover "Specialist management of cystic-fibrosis-related ear, nose and throat (ENT) disorders".

Thank you for your comment. The committee noted that there was more clinical uncertainty about management of lower airways therefore this was prioritised in the scope. With regards to your comment about the PARI SINUS™ nebuliser, different agents were compared in the mucocutaneous and antimicrobials review, however comparisons within agents to compare delivery systems were not included as comparisons of interest in the protocol. The type of delivery system (when reported) was extracted from the included studies and is reported in appendix J.

Thank you for suggesting these studies. The study by Wilson et al. (2014) is about eradication of paranasal sinus pathogens, which was out of the scope of this guideline. The following studies do not evaluate interventions included within the scope of this guideline: DiCicco 2014, Fenn 2014, Mauz 2009, Chartson 2011, Goddard 2012, Lavin 2013. The following study was excluded from the review on mucocutaneous agents: Mauz 2014. The exclusion reason was "Data is poorly reported and cannot be pooled" (please see appendix H for lists of excluded studies).

The following study is a literature (non-systematic) review and therefore was not eligible for inclusion in reviews in this guideline: Kang 2015.
The following literature shows the rationale for a concentrated approach in the treatment of upper airway problems in CF:

1. **Overall role of Sinonasal complications /CRS.**


2. Validation via SNOT Score: Relevant publications:


Concept of united airways:


Pulsating aerosol / PARI SINUS as treatment option


Info aus dem “Economic Dossier für PARI SINUS / France”? (let me know if you need more on this)

Economic value arguments can especially rely on:

The role of UAWs as a bacterial reservoir;

This study on eradication of early Pseudomonas aeruginosa infection was not a randomized controlled trial and therefore not eligible for inclusion: Hoiby 2005.

The following study is about a case report and therefore not eligible for inclusion in reviews in this guideline: Mainz 2011b.

The following study reports on 2 case reports therefore would not be eligible for inclusion in reviews for this guideline: Mainz 2012.
<table>
<thead>
<tr>
<th>Profile Pharma</th>
<th>Full</th>
<th>453</th>
<th>13-25</th>
<th>The Pari e-flow is mentioned as a fast nebuliser. The I-neb has similar or better treatment times with the added advantage of recording when it is used and so monitors adherence.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profile Pharma</td>
<td>Full</td>
<td>658</td>
<td>37</td>
<td>Only the I-neb can currently measure adherence electronically. Thank you for your comment. The I-neb has been added as another example.</td>
</tr>
<tr>
<td>Profile Pharma</td>
<td>Full</td>
<td>668</td>
<td>44-45</td>
<td>The I-neb can objectively measure adherence. Thank you for your comment. The review question on psychological assessment evaluated methods of assessment of adherence to drug treatment and used electronic monitoring of adherence or pharmacy records as the reference standards. One included study (Daniels 2011) compared the index tests of self-report and clinician-report to the reference standard of electronic monitoring with the I-neb nebulizer system. Another study (Siracusa 2015) compared the index tests of self-report and pharmacy refill history to the reference standard of electronic monitoring with the Medication Event Monitoring System (MEMS). The evidence statements from both studies mention that there was an overestimation of adherence by the index tests compared to the reference standards. The section “Evidence to recommendations” in the full guideline has been modified and it now states that the committee noted that adherence is extremely difficult to measure in both clinical practice and research, unless a particular objective measuring tool is employed (for example electronic monitoring or pharmacy records), which is rare in routine clinical practice. The committee noted that the I-neb is by far the commonest method of electronic monitoring in the UK. The committee stressed that adherence problems are common in people with chronic conditions, and those with a number of concurrent treatments, and are not specific to cystic fibrosis. They agreed that the overarching principles from the NICE guidance on Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence [CG76] is applicable to people with cystic fibrosis. Therefore, the committee decided not to make a recommendation specific to measuring adherence in cystic fibrosis care.</td>
</tr>
<tr>
<td>Profile Pharma</td>
<td>Full</td>
<td>General</td>
<td>The importance of adherence is emphasised throughout the document. At present only one device can measure true adherence as it records each time it is used. This is the I-neb nebuliser. Thank you for your comment. The review question on psychological assessment evaluated methods of assessment of adherence to drug treatment and used electronic monitoring of adherence or pharmacy records as the reference standards. One included study (Daniels 2011) compared the index tests of self-report and clinician-report to the reference standard of electronic monitoring with the I-neb nebulizer system. Another study (Siracusa 2015) compared the index tests of self-report and pharmacy refill history to the reference standard of electronic monitoring with the Medication Event Monitoring System (MEMS). The evidence statements from both studies mention that there was an overestimation of adherence by the index tests compared to the reference standards. The section “Evidence to recommendations” in the full guideline has been modified and it now states that the committee noted that adherence is extremely difficult to measure in both clinical practice and research, unless a particular objective measuring tool is employed (for example electronic monitoring or pharmacy records), which is rare in routine clinical practice. The committee noted that the I-neb is by far the commonest method of electronic monitoring in the UK. The committee stressed that adherence problems are common in people with chronic conditions, and those with a number of concurrent treatments, and are not specific to cystic fibrosis. They agreed that the overarching principles from the NICE guidance on Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence [CG76] is applicable to people with cystic fibrosis. Therefore, the committee decided not to make a recommendation specific to measuring adherence in cystic fibrosis care.</td>
<td></td>
</tr>
</tbody>
</table>

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not to make a recommendation specific to measuring adherence in cystic fibrosis care.

Thank you for your comment.

Royal Brompton and Harefield Hospitals NHS Foundation Trust
Full 658 18-29 Strengths and Difficulties Questionnaire (SDQ) is neglected here as a tool – this a well validated, widely used tool useful for screening across emotional, behavioural and social dimensions in children from ages 4 -17 – should have been included in the review.

Thank you for your comment. The Strengths and Difficulties Questionnaire (SDQ) was not prioritized by the committee in the review protocol. The reason for this is that the SDQ is not universally accepted as a good tool for people with physical health conditions though it is a useful screen for use in general mental health practice.

Royal Brompton and Harefield Hospitals NHS Foundation Trust
Full 658 31-36 Far too "medical model" – particularly, because we have emphasised that clin psychs are embedded in the teams in the aspiration that there is prevention of the mental health disorder – in contradiction to this, only evidence of confirmed psychiatric diagnosis has been explored.

Thank you for your comment. For other psychological and behavioural problems listed in the protocol (such as school phobia), the reference standard was "as reported by the study" so the inclusion criteria went beyond confirmed psychiatric diagnosis.

Royal Brompton and Harefield Hospitals NHS Foundation Trust
Full 658 9-13 Comment 1: Missing – promote good psychological health (not just looking for problems). Comment 2: The clinical psychologist can also play a role in identifying whether other challenges of a psychological nature (e.g. enuresis, school absence) may be wholly or partially attributable to having a chronic health condition or not.

Thank you for your comment. The introduction has been modified to state that the role of the psychologist is to promoted psychological health. Moreover, the introduction now also states that the clinical psychologist can also play a role in identifying whether other challenges of a psychological nature (for example school absence or tics) may be wholly or partially attributable to having a chronic health condition or not. The example of enuresis was replaced by the example of tics in order to have an example relevant to both children and adults.

Royal Brompton and Harefield Hospitals NHS Foundation Trust
Full 658 6-8 And vice versa – emotional difficulties for other reasons can impact on CF treatments.

Thank you for your comment. The introduction has been modified to state that vice versa, emotional difficulties for other reasons can impact on CF treatments.

Royal Brompton and Harefield Hospitals NHS Foundation Trust
Full 658 3 Should instead state "Clinical Psychologist, with good links with the CF specialist MDT, can offer preventative model of working, by offering strategies to colleagues, patients and/or family and carers to explore their emotional wellbeing. If necessary the Clinical Psychologist can also offer further assessment and intervention, or facilitate onward referral for more intractable mental health difficulties which may, or may not, be attributable to the diagnosis of cystic fibrosis.

Thank you for your comment. The recommendations state that clinical psychologists are members of the MDT rather than external professionals with links to it. The introduction has been modified to replace the term core MDT with the term specialist CF MDT. Moreover, the introduction has been modified to state that clinical psychologists can offer a preventative model of working, by offering strategies to colleagues, patients and family and carers to explore their emotional wellbeing. If necessary the clinical psychologist can also offer further assessment and intervention, or facilitate onward referral for severe mental health conditions which may, or may not, be attributable to the diagnosis of cystic fibrosis.

Royal Brompton and Harefield Hospitals NHS Foundation Trust
Full 658 6 Rather than "will be aware of" should be "Can hold in mind".

Thank you for your comment. We have amended the sentence to say "...can hold in mind any likely impact of cystic fibrosis treatments on emotional functioning...".
<table>
<thead>
<tr>
<th>Trust</th>
<th>Full</th>
<th>659</th>
<th>Table 3</th>
<th>EAT – no info re ages beyond “adolescents” – should give an age.</th>
<th>Thank you for your comment. The age (15 and over) for young people has been added to the table.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>660</td>
<td>Table 3</td>
<td>There is a cost to the questionnaires (e.g. PI-ED is approx. £1.00 per questionnaire) would be helpful to make sure this is in the health economic model.</td>
<td>Thank you for your comment. The cost of questionnaires has been added as a consideration in the full guideline. The age range for each questionnaire was added to the table in the full guideline. With regards to GAD-7, the full guideline now states that it is intended for use in adults but has been used in young people aged 13 and over. For HADS, PHQ-2 and PHQ-9, the full guideline now states that they are for use in adults and young people aged 13 and over.</td>
</tr>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>666</td>
<td>36-40</td>
<td>Suggest to delete everything from &quot;They noted that even following transplant……&quot; to end of that paragraph; and instead should highlight that adherence is extremely difficult to measure in both clinical practice and research, unless a particular objective measuring tool is employed (Daniels study-electronic measuring i-neb system), which is rare in routine clinical practice.</td>
<td>Thank you for your comment. The section &quot;Evidence to recommendations&quot; has now been modified to delete the section of the paragraph after &quot;They noted that even following transplant&quot; as suggested in your comment. Moreover, the same paragraph now states that the committee noted that adherence is extremely difficult to measure in both clinical practice and research, unless a particular objective measuring tool is employed (for example -electronic monitoring or pharmacy records), which is rare in routine clinical practice. The evidence used two different methods for electronic monitoring as reference standards to measure adherence: the i-neb was used in one study and the Medication Event Monitoring System (MEMS) was used in another study; however the committee noted that the i-neb is by far the commonest method for electronic monitoring in the UK. The committee stressed that adherence problems are common in people with chronic conditions, and those with a number of concurrent treatments, and are not specific to cystic fibrosis. They agreed that the overarching principles from the NICE guidance on Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence (CG76) is applicable to people with cystic fibrosis. Therefore, the committee decided not to make a recommendation specific to measuring adherence in cystic fibrosis care.</td>
</tr>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>667</td>
<td>30</td>
<td>Delete &quot; who are treatment compliant&quot; and replace with &quot;people with cystic fibrosis and/or their carers who are believed to be adherent to treatment, or where adherence is measured with objective measures (e.g. sweat test with use of hancalor).</td>
<td>Thank you for your comment. &quot;who are treatment compliant&quot; has been deleted to address your comment.</td>
</tr>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>668</td>
<td>18-20</td>
<td>Should be: “are more likely to be accepting of this role”</td>
<td>Thank you for your comment. We have amended the sentence to say “are more likely to be accepting of this role.”</td>
</tr>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>668</td>
<td>25 - 27</td>
<td>The team clinical psychologist can support the rest of the team in this by holding psychological wellbeing in mind, and supporting staff if they would like to think through the responses they get from patients (and or family members), and provide training to staff on ……</td>
<td>Thank you for your comment. The section &quot;Evidence to recommendations&quot; in the full guideline has been modified to state that the team clinical psychologist can support the rest of the team by holding psychological wellbeing in mind, and supporting staff if they would like to think through the responses they get from patients (or family members), or provide training to staff on delivery of basic emotional support.</td>
</tr>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>668</td>
<td>23-24</td>
<td>Should be recommendations. Very important for all MDT members to have a role in enquiring about a patient (or family member/careers) emotional wellbeing; with the clinical psychologist taking a lead in the MDT to support MDT members to do this confidently and safely, and offer additional clinical psychology level support when necessary.</td>
<td>Thank you for your comment. The committee discussed your comment about recommending informal but frequent “screening” by the psychologist and multidisciplinary team members by regularly asking questions about emotional wellbeing as well as physical health. The committee agreed that this should be covered in the section &quot;Evidence to recommendations&quot; in the full guideline rather than in the recommendations, because it is standard clinical practice to informally ask about a person’s emotional wellbeing and physical health, especially with regular patients, and this is not specific to cystic fibrosis. The committee decided not to specify in the recommendations that the psychologist should support MDT members because it is expected of all members of an MDT that they would support each other through advice and consultation in relation to their respective areas of expertise.</td>
</tr>
<tr>
<td>Royal Brompton and Harefield Hospitals NHS Foundation Trust</td>
<td>Full</td>
<td>668</td>
<td>32</td>
<td>Should be: “Information provided to people with CF and/or their families/careers…..”</td>
<td>Thank you for your comment. We have amended the sentence to “Providing information to people, and their family or carer, with cystic fibrosis…”</td>
</tr>
</tbody>
</table>
A psychological screening should be offered as part of the annual review to all patients, families and carers. A referral for further assessment and intervention by this clinical psychologist or another mental health practitioner should be discussed with the patient/family and referral should be made if a serious mental health problem is identified. If this opportunity is declined by the patient/family, and this decision is considered to be to the detriment to the patient and or family members physical or mental health, then this necessitates discussion with the CF MDT with involvement of the safeguarding lead professionals.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.
| Trust | Short | 1.6.7 | | Ambiguous wording would imply we should be doing a CT on diagnosis at screening of newborns. Same page, CXR should mention *pneumothorax* or even if ABPA or PE suspected | in the recommendation are not mandatory, only examples, and should be tailored to the individual with cystic fibrosis. A greater description of the committee’s discussion on this area is provided in the full guideline section titled “evidence to recommendations” |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 13 | | Thank you for your comment. The committee noted that the recommendation states to think about a low-dose chest CT scan rather than stating to perform this on any child that has not had a CT scan before. Therefore, performing the CT scan would be subject to clinical judgement based on individual circumstances. This has now been explained in the section “Evidence to recommendations” in the full guideline. The committee also discussed your comment on additional indications to perform a chest X-ray but decided not to include these, because the recommendation focuses on exacerbations. Therefore these additional indications do not apply. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 14 | 1.6.1 | 0 | Induced sputum should also be listed | Thank you for your comment. The recommendation has been amended to mention sputum induction as an example of non-invasive upper airway respiratory secretion sampling, which would be performed before thinking about broncho-alveolar lavage. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 16-17 | 1.6.2 | 6 | Why not treat MRSA? Are they referring to chronic infection? In the earlier sections, need to specify MSSA or MRSA or both, its confusing 1.6.30 very loose: what is ‘new’? what is ‘recent’? | Thank you for your comment. The recommendations have been modified and they now state that for people of new evidence of MRSA respiratory infection (with or without pulmonary exacerbation), specialist microbiological advice should be sought on treatment to eradicate it. However, antibiotics should not be routinely used to suppress chronic MRSA in people with stable pulmonary disease. If a person with chronic MRSA respiratory infection becomes unwell with a pulmonary exacerbation or shows a decline in pulmonary function, specialist microbiological advice should be sought. The committee discussed your comment about why recommendations first only mention Staphylococcus aureus, and then specify MSSA or MRSA. They agreed that recommendations follow the logical treatment pathway for dealing with all Staphylococci infection and only when this is MRSA or MSSA do specific recommendations on these pathogens need to be followed. The committee gave a definition of new *Pseudomonas aeruginosa* infection: recent respiratory secretion sample cultures. The committee agreed that clinical judgement should define recent. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 20 | 1.4.4 | 4 | Probably not correct to lump MAI and abscessus in the same section any more, management differs. The whole section is poor | Thank you for your comment. The committee decided not to make more detailed recommendations, which would require us to differentiate between different non-tuberculous mycobacteria, because no evidence was found on non-tuberculous mycobacteria. Recommendations on this pathogen have now been amended to state to seek specialist microbiological advice on which antibiotics to use and on the duration of treatment. Moreover, the full guideline mentions that there is existing consensus guidance on the management of non-tuberculous mycobacteria in a publication by Floto et al. (2016) titled “US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis” (http://thorax.bmj.com/content/71/Suppl_1/t1) |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 23 | 1.7.5 | | Should this be done annually in a child with 2 mild mutation? | Thank you for your comment. The committee discussed your comment and agreed the test should be done at diagnosis and then repeated if there are symptoms or signs suggesting malabsorption. Therefore the committee removed the recommendation to repeat the test annually. The committee noted that this recommendation does not prevent centres from including this test as part of an annual assessment but it doesn’t mandate to do so. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 27 | 1.7.2 | 8 | This suggests that there should be no routine BMDs but probably not enough evidence to suggest this practice can be stopped | Thank you for your comment. The Committee agreed it was cost-ineffective and burdensome for people to receive regular scans if their management strategy would not change. The committee’s discussion on this area is provided in the full guideline section titled “evidence to recommendations” |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | 28 | Comment 1: Rather than “serious mental health issue” this should state “significant emotional challenges affecting psychological wellbeing” (e.g. school anxiety; low mood; etc.) Comment 2: Consider (in discussion with the family) Tier 2 referral and/or onward referral to local psychological wellbeing services for further support (e.g. school counsellor, CAMHS). Comment 3: What about referring to NICE guidance for treatment of mental health conditions in children. | Thank you for your comment. Comment 1. The Committee discussed this suggestion but decided to use the term “severe mental health condition” instead, because significant emotional challenges affecting psychological wellbeing could also be dealt with by the specialist clinical psychologist in the CF specialist MDT and would not necessarily prompt referral to a mental health practitioner. Some examples of severe mental health conditions are provided in the full guideline in the section “Evidence to recommendations”: psychosis, high level of risk of self-harm or need for psychiatric care. Comment 2. The section “Evidence to recommendations” in the full guideline has also been modified to state that the clinical psychologist should also consider (in discussion with the family) Tier 2 referral or onward referral to local psychological wellbeing services for further support (for example with the school counsellor or CAMHS). Comment 3. The reference to NICE guidelines has now been changed so that no specific
Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 28 3-4

Comment 1: No mention of family and carers of children with cystic fibrosis – this should be stated in this recommendation.

Comment 2: as point 23 above

Thank you for your comment. The recommendation has been amended to state that the specialists involved should be aware that people with cystic fibrosis and their family members or carers may need emotional support and some may need specialist psychological support.

Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 3

Diagnosis: should stress that diagnosis on clinical grounds alone is much less common, and should be the 3rd not 2nd bullet point. Wording suggests that a gene test is the first test if CF is suspected, which doesn’t really tally with the new international guidelines on the diagnosis of CF that still suggests sweat test is the gold standard diagnostic test

Thank you for your comment. The recommendation has now been modified. Diagnosis on clinical manifestations alone is now the last bullet point and we have specified that this is rare. The recommendation only mentions that the blood spot immunoreactive trypsin test would be followed by a sweat and gene test. The Committee decided not to go into more detail in the recommendation itself; however a reference has now been added in the section “Evidence to Recommendations” to the Guidelines for the Performance of the Sweat Test for the Investigation of Cystic Fibrosis in the UK, 2nd Version, by the Royal College of Paediatrics and Child Health.

Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 4

The list of triggers is incomplete. Should include a family history, male infertility due to azospermia, hereditary disorders, unexpected isolation of a ‘CF’ organism such as Ps aer or M abscessus, nasal polyps should be mentioned specifically

Thank you for your comment. Family history has been added to the recommendation. The recommendation already included obstructive azospermia. The committee decided not to include haemorrhagic disease of the newborn and portal hypertension of unknown cause because they are very rare. The Committee decided not to include isolation of P aeruginosa or M abscessus because these pathogens are common in people without cystic fibrosis. Likewise, the Committee decided not to include nasal polyps because they are very common in people without cystic fibrosis therefore they would not prompt an assessment for cystic fibrosis on their own. Moreover nasal polyps are rare in children.

Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 5 3

Replace ‘English’ with ‘in their first language’ in these multicultural days and use of an interpreter where necessary

Thank you for your comment. We have changed the wording of the recommendation from information in clear English to information that people with suspected or diagnosed cystic fibrosis and their family members or carers (as appropriate) can understand. The recommendations will not include translation issues because this is not specific to cystic fibrosis. The committee also included a recommendation which directs readers of this guideline to the NICE guideline CG138 “Patient experience in adult NHS services: improving the experience of care for people using adult NHS services”. The CG138 guideline recommends: “Establish the most effective way of communicating with each patient and explore ways to improve communication. Examples include using pictures, symbols, large print, Braille, different languages, sign language or communications aids, or involving an interpreter, a patient advocate or family members”.

Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 6 8-16

The theme of these comments comes across as too adult patient focussed Line 12: At times of change or transition (e.g. starting school) … (then onto adult focussed eggs of transition). Line 14: “during pregnancy” – should be “family planning”, either parent or parents considering having more children. Missing: considering new treatments, etc. due to deterioration in health (e.g. CFRD) or transplantation.

Thank you for your comment. The following has been added to the recommendation to address your comment: “starting or changing school; fertility, including family planning, pregnancy and infertility; waiting for or having organ transplantation. Cystic fibrosis related complications (which would include CFRD) are also included in the recommendation.

Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 6 9-10

Should instead say “all people with cystic fibrosis and their family members or carers need emotional support, and some may require specialist psychological support”.

Thank you for your comment. The committee discussed your comment and the stem of the recommendation has been amended to state to be aware that people with cystic fibrosis and their family members or carers may need emotional support and some may need specialist psychological support.

Royal Brompton and Harefield Hospitals NHS Foundation Trust

Short 8 24-26

Psychologists do not just work with patients at outpatient clinics and inpatient stays. They may also work with them at separate psychology outpatient appointments and by telephone calls, community visits; school/social care meetings/etc

Thank you for your comment. The recommendation has been modified to state that the specialist clinical psychologists should assess and advise people with cystic fibrosis and their family members or carers (as appropriate) at outpatient clinic visits and (if needed) at other outpatient...
<p>| Hospitals NHS Foundation Trust | Short | 8 | 7.9 | This statement minimises the role of the CF CNS’s (ie does not acknowledge their nursing expertise, etc.) This statement also potentially absolves other professionals of their responsibilities in also advocating and coordination communication (although it is acknowledged that the CF CNS is well positioned to take a lead on this) | Thank you for your comment. The recommendation has been amended to include more examples about the clinical role of a specialist nurse. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | 8 | 1.3.13 should also advise on discharge from hospital | Thank you for your comment. The recommendation has been modified and it now states that the specialist pharmacist should advise people on medicines optimisation during inpatient admissions, on discharge from hospital, at outpatient clinic visits and at annual review. The recommendation now also states that they should advise healthcare professionals on all aspects of medicines use and prescribing. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | 8-9 (over page) 27 (Page 8) – 7 (Page 9) | Page 9, Line 7: The guideline should state that routine access may need to be from local services as well not just centre care. It may be better for some patients and families, especially for psychiatry. | Thank you for your comment. The committee discussed your suggestion and decided not to make this addition because it is implied. Moreover, the NICE guideline NG43 “Transition from children’s to adults’ services for young people using health or social care services” |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | 9 | Should include ENT surgery | Thank you for your comment. ENT surgery has been added to the list. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | 9 | 27-28 Guideline should define “successful (transition)” – or re-word “successful is subjective. Maybe ‘transition from paediatric to adult service is completed’. | Thank you for your comment. This recommendation has been deleted from the guideline and readers are instead directed to NICE guideline NG43 “Transition from children’s to adults’ services for young people using health or social care services” |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | 9 | 29-30 Missing at end of recommendation: “... to contribute to future service planning and development” (Otherwise asking for feedback is meaningless) | Thank you for your comment. The committee discussed your suggestion and concluded not to make this addition because it is implied. Moreover, the NICE guideline NG43 “Transition from children’s to adults’ services for young people using health or social care services” goes into more detail about issues relating to feedback and service planning. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | General | 1.3.10 No mention of where and when CNS’ do their work. No mention as for other professional groups that they work in outpatient/inpatients/community/telecommunications | Thank you for your comment. The recommendations on the cystic fibrosis specialist nurses have been amended to state that they are in a unique position to coordinate care and communication between other members of the team, and act as advocates for people with cystic fibrosis and their family members or carers. Key clinical roles of cystic fibrosis specialist nurses should include: support during and after diagnosis and when starting treatment; triage; advanced clinical assessment; coordinating home intravenous antibiotic services including intravenous antibiotics. The committee decided not to specify any settings where cystic fibrosis specialist nurses perform their role because they agreed that their role involves working across all settings. |
| Royal Brompton and Harefield Hospitals NHS Foundation Trust | Short | General | 1.5.2 No mention of the role of CNS’ nursing assessment at Annual assessment | Thank you for your comment. We have included a nurse and social worker in the assessment bullet point that refers to the annual review. |
| Royal College of General Practitioners | General | At present there is only 5 references to GPs and no acknowledgement of their role | Thank you for your comment. The guideline is mainly concerned with the specialist care and treatment of people with cystic fibrosis. This is usually delivered by specialist MDT teams in specialists CF centres. The majority of the guideline is concerned with the work of those centres and the practitioners who work within them. However the Committee agreed with the RCGP that the guideline should say more about the role of GPs in relation to patients with CF. A new recommendation has therefore been added into the service delivery section of the guideline that sets out some of the key tasks and responsibilities of the GP in relation to supporting people with CF and their families. The recommendation covers prescribing routine CF medicines, annual immunisations, certification of appointments, during inpatient admissions, and at their annual review. The full guideline also mentions some examples of further outpatient appointments: community visits, schools or social care meetings. This section also mention telephone calls, however this was not included in the recommendation not to make it too detailed or over prescriptive, because it would be up to the psychologist and the person they are seeing to agree the setting of their appointment. | The Standards for the Clinical Care of Children and Adults with cystic fibrosis in the UK Second edition. December 2011 from the Cystic Fibrosis Trust defines some of roles to include The GP is responsible for prescribing much of the routine therapy recommended by the Specialist CF Centre. The Specialist CF Centre must ensure that the GP is adequately informed about the medication recommended particularly when it may be unfamiliar or used out of product license. It is reasonable to expect the GP to provide adequate amounts of medication – a minimum of one |</p>
<table>
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<tr>
<th>Royal College of Nursing</th>
<th>Short</th>
<th>7</th>
<th>28</th>
<th>MDT specifics – W.T.E guidance would be beneficial as a minimum for example half a day specialist nurse cover if part of a wider role.</th>
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<td>Thank you for your comment. WTEs are provided in appendix K for a range of clinic sizes. However, the Committee did not want to include WTEs in their recommendations to prevent interpretation of a minimum. Instead, the Committee agreed WTEs should depend on the complexity of people with cystic fibrosis at each clinic. The Committee's discussion on this area is provided in the full guideline section titled “Evidence to recommendations”</td>
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<tr>
<td>Royal College of Nursing</td>
<td>Genera l</td>
<td>General</td>
<td>Gene ral</td>
<td>The Royal College of Nursing welcomes proposals to develop this guideline. The RCN invited members who care for people with cystic fibrosis (CF) and other respiratory conditions to review the draft document on its behalf. The comments below reflect the views of our members.</td>
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<td>Thank you for your comment.</td>
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<td>Royal College of Nursing</td>
<td>Genera l</td>
<td>General</td>
<td>Gene ral</td>
<td>The draft guidelines appear quite comprehensive and set out key outlines for services.</td>
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<td>Thank you for your comment.</td>
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<td>Royal College of Nursing</td>
<td>Short</td>
<td>10</td>
<td>1.4.1</td>
<td>“almost all males with CF are infertile” – this is too colloquial, the statement should be more specific</td>
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<td>Thank you for your comment. This recommendation has been amended to state male infertility caused by obstructive azoospermia (almost all males with cystic fibrosis are infertile). The recommendations in this guideline use plain English in order to be more accessible to people without medical knowledge. There was no evidence on the prevalence of infertility so it was not possible to be more specific. The full guideline explains more in detail the reasoning of the committee behind this recommendation.</td>
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<tr>
<td>Royal College of Nursing</td>
<td>Short</td>
<td>10</td>
<td>1.4.1</td>
<td>Cystic Fibrosis Related Diabetes (CFRD) – affects 1:2 adults (evidence?) maybe this should say “affects up to 1:2 adults”.</td>
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<td>Thank you for your comment. The recommendation already stated “affects up to 1 in 2 adults”. The full guideline mentions that the UK CF Registry 2015 Annual Data Report showed that the prevalence of people on CFRD treatment among people aged 16 or older was 32%. The Committee agreed that the prevalence of people on CFRD treatment was likely to underestimate the prevalence of people with CFRD because many centres do not know how to accurately test for it. Therefore, based on their clinical experience and expertise, the Committee recommended to be aware that cystic fibrosis-related diabetes is common in people with cystic fibrosis, and it specified that it affects up to 1 in 2 adults.</td>
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<tr>
<td>Royal College of Nursing</td>
<td>Short</td>
<td>11</td>
<td>1.5.2</td>
<td>There is no mention of annual chest x-ray. This is important.</td>
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<td>Thank you for your comment. The recommendation states that a comprehensive annual review includes a pulmonary assessment and refers to the recommendations in the section on pulmonary monitoring. The section on pulmonary monitoring recommends to include a chest X-ray at each annual review in relation to pulmonary assessment.</td>
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<tr>
<td>Royal College of Nursing</td>
<td>Short</td>
<td>11</td>
<td>1.5.3</td>
<td>Perhaps local DGH’s need this guidance re regular review, but it is not set in stone. It needs to be patient specific</td>
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<td>Thank you for your comment. Based on their clinical experience and expertise, the committee agreed to recommend more frequent routine reviews after diagnosis and in early life. Following those initial years, the person’s condition is likely to become more predictable. To guide the audiences reading the recommendation, the committee gave some examples of review frequency for different age groups, with frequency decreasing with age. The ranges of frequencies provided in the recommendation are not mandatory and should be tailored to the individual with cystic fibrosis. A greater description of the committee’s discussion on this area is provided in the full guideline section titled “Evidence to recommendations.”</td>
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<tr>
<td>Royal College of Nursing</td>
<td>Short</td>
<td>11</td>
<td>1.5.3</td>
<td>Should read “at least every 3 or 6 months as adults”</td>
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<td>Thank you for your comment. The NHS service specifications for cystic fibrosis refer to the CF Trust Standards of Care 2011, which specify that patients should be reviewed with a frequency appropriate to their individual needs. For this reason, the committee provided examples of review frequencies in their recommendation to guide the audience reading the recommendation and allow the frequency to be tailored to the individual. Reviewing each adult every 3 months may not be cost-effective when an adult is stable, but the recommendation does not prevent a review every 3 months in adults if this is considered to be appropriate. A greater description of the committee’s discussion on this area is provided in the full guideline section titled “Evidence to recommendations.”</td>
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<tr>
<td>Royal College of Nursing</td>
<td>Short</td>
<td>12</td>
<td>1.8.3</td>
<td>Do all centres do routine lung clearance? Not sure about this, especially as not all centres have access to LCI or experience in using. Also, perhaps it should say … if normal lung function, but child has symptoms e.g. low weight gain, recurring cough, normal cough swabs etc then consider LCI.</td>
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<td>Thank you for your comment. The committee noted that LCI can be a useful tool to assess disease progression as it could provide additional respiratory information to spirometry. However, the committee added that LCI is currently in its infancy in the UK. As a result, the committee made recommendations to consider the use of LCI for those clinics that have access to the equipment and ability to interpret the results. To enable stronger recommendations in the future, a research recommendation to assess if LCI is a useful and cost-effective tool for the routine.</td>
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assessments and monitoring of changes in pulmonary status in people with cystic fibrosis was made by the committee. The committee discussed your suggestion to consider LCI only if there are symptoms, however agreed that LCI can also be considered in asymptomatic people with the objective to obtain more information than from spirometry and detect any issues early on.

Royal College of Nursing
Short 13 1.6.5

Definitely appropriate.

Thank you for your comment.

Royal College of Nursing
Short 13 1.6.7

Should 1.6.7 be after 1.6.8?

Thank you for your comment. The committee discussed your comment and agreed not to change the order of these recommendations because the two recommendations are about different populations: the first recommendation is about children with cystic fibrosis who have not had a CT scan before, the second recommendation is about people with cystic fibrosis who are receiving or have received treatment for an exacerbation of lung disease.

Royal College of Nursing
Short 16 1.6.2

Are there any alternative medication to be given if the patient is allergic to penicillin?

Thank you for your comment. We have amended the recommendation to state that if children are allergic to penicillin, an alternative oral anti-staphylococcal aureus agent should be considered.

Royal College of Nursing
Short 18 1.6.3

Unclear as to when to use dry powder inhaler (DPI) medication – could this be re-written in a simpler format?

Thank you for your comment. The committee agreed that the results from an ultrasound scan could lead to a change in the management strategy when, for example, cirrhosis and portal hypertension (with Doppler) are detected. Given that an ultrasound can add additional information to an abnormal liver function blood test, a recommendation in that subgroup was considered as a cost-effective use of ultrasound scans.

Royal College of Nursing
Short 23 1.7.4

“Short term trial of appetite stimulant” – could this be clarified, how long is “short term”?

Thank you for your comment. We have added up to 3 months as an example in the recommendation.

Royal College of Nursing
Short 25 1.7.1

Should an annual liver ultrasound be recommended? This is not mentioned in this section.

Thank you for your comment. One of the recommendations states to perform a liver ultrasound scan if liver function blood tests (performed at the annual review) are abnormal. The section “Evidence to recommendations” in the full guideline explains that the committee noted that if abnormal liver function blood tests are the first indication of liver disease, there are potential cost savings to the NHS if those tests can replace ultrasound scans at the annual review. This saving is particularly the case in adults who are unlikely to develop liver disease without prior suspicion. Following this, the committee agreed that a recommendation in favour of liver function blood tests as the first assessment was warranted. However, the committee agreed that the results from an ultrasound scan could lead to a change in the management strategy when, for example, cirrhosis and portal hypertension (with Doppler) are detected. Given that an ultrasound can add additional information to an abnormal liver function blood test, a recommendation in that subgroup was considered as a cost-effective use of ultrasound scans.

Royal College of Nursing
Short 26 1.7.2

There is no mention of how often CFRD should be tested for in this group of patients.

Thank you for your comment. We could not include the frequency of testing in the recommendation as the focus was on the type of monitoring as opposed to the frequency. Moreover, the committee were reluctant to provide a frequency based on consensus, as the frequency should be tailored to the individual with cystic fibrosis according to their need and risk factors. Therefore, the frequency should be determined by clinical decision.

Royal College of Nursing
Short 26 1.7.2

Should "excessive thirst" also be mentioned here?

Thank you for your comment. The committee did not include excessive thirst in their recommendation as this is a feature of Diabetes Mellitus, rather than CFRD and it not often the key indicator someone with CF would present with.

Royal College of Nursing
Short 27 1.7.2

There is no mention of frequency of bone scans or of age of starting bone scans

Thank you for your comment. The committee agreed that the recommendations on BMD should apply to children and adults. The starting age of bone scans is redundant as this depends on the presence of those risk factors highlighted in the recommendation.

In the full guideline section titled “evidence to recommendations” it is suggested that scans could be repeated on an annual basis if the BMD SDS score is less than -2.0. However, the committee did not state the frequency of bone scans in their recommendations as this would be individualised to the patient using clinical expertise.

Royal College of Nursing
Short 29 1.8.6

Include age appropriate toys in rooms. Cleaning of toys and rooms between patients. We do not use same toys in same clinics, but the rooms are used again, though cleaned and aired between patients.

Thank you for your comment. The committee agreed that toys and rooms should be cleaned. The committee made a recommendation to prevent cross-infection among people with cystic fibrosis in outpatient and inpatient care using microbiological surveillance and a local infection control strategy. The full guideline clarifies that a local infection control strategy would cover interventions such as cleaning of rooms and equipment, closing the doors of rooms in the hospital or the outpatient clinic and effective ventilation in gyms to remove exposure of airborne cross-infection. The committee noted that cleaning of toys would also fall within the remit of a local infection control strategy, therefore this did not need to be specifically mentioned in the recommendations. The committee also noted there are existing NICE guidelines on preventing and controlling infection. Therefore, the committee incorporated a reference to these guidelines and focussed their recommendations on cross-infection concerns specific to people with cystic fibrosis.

Royal College of Nursing
Short 29 1.8.7

Even during clinic visits, there can be a problem of contact when visiting other hospital’s communal areas such as pharmacy.

Thank you for your comment. The pharmacy has been added to the recommendations on cross-infection. Hospital communal areas are also considered to be covered by referring to diagnostic and treatment facilities.

Royal College of Nursing
Short 3 1.1

It would be beneficial if the National Screening Programme is mentioned as the 1st point.

Thank you for your comment. The recommendation has now been modified and infant screening is mentioned in the first bullet point.

Royal College of Nursing
Short 5 1.2.3

It would be helpful for the information to be provided in a range of languages or patients/carers should have access to translation services.

Thank you for your comment. We have changed the wording of the recommendation from information in clear English to information that people with suspected or diagnosed cystic fibrosis and their family members or carers (as appropriate) can understand. The recommendations will include age appropriate toys in rooms. Cleaning of toys and rooms between patients. We do not use same toys in same clinics, but the rooms are used again, though cleaned and aired between patients.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

29 of 39
Royal College of Nursing

Short 5

1.2.3 The point ....... Implications for "independent living" ....... Suggests that people with CF are disabled in some way.

Thank you for your comment. Independent living has been changed to living independently. This refers to all stages of life, for example moving out of the family home to go to university, which would present new challenges such as finding privacy to perform daily treatments.

Royal College of Nursing

Short 5

1.2.6 ...... "Including those aimed at children" ...... gives the impression that these are groups that meet. We do NOT encourage any adults to meet with their children who have CF. Perhaps this should be revised for clarity, i.e. written or online resources.

Thank you for your comment. We have changed the first bullet to refer to available resources and support, such as local support and advocacy services. The word "groups" has been deleted from the recommendation to avoid giving the impression that these are groups that meet. The section "Evidence to recommendations" also mentions that the committee strongly recommends that support groups do not take place face to face in order to prevent cross-infection which can lead to further complications. Information about online support groups and advocacy services would be beneficial. Facilitating access to parent or carer only face to face social support groups can be considered if there is a demand. But with these, the risk to the groups of children meeting socially must be emphasised.

Royal College of Nursing

Short 6

1.3 Service delivery — there is no mention in this section about patient’s route for admission (e.g. Patients should be able to refer themselves directly to the respiratory ward for admission if required)

Thank you for your comment. We have added waiting for or having organ transplantation to this recommendation.

Royal College of Nursing

Short 6

1.2.9 This list should also include ......"on transplant list" ...... as another option

Thank you for your comment. The recommendation has been amended to include waiting for or having organ transplantation.

Royal College of Nursing

Short 7

1.3.5 We feel that it might not be appropriate/reasonable for all CF teams to provide a member on call for 24 hours per day 7 days per week. Might be better to have a number for patients to phone (e.g. CF ward) and the call can then be escalated if appropriate.

Thank you for your comment. We have added waiting for or having organ transplantation.

Royal College of Nursing

Short 7

1.3.5 The role of CF team is to also promote the empowerment of people, therefore at night, weekends etc. families should also be encouraged to contact their local hospital for urgent enquiries, as there are instances where CF teams will be unavailable.

Thank you for your comment. The recommendation has been changed to state that the specialist cystic fibrosis centre should have a point of contact available at all times (day or night) for urgent enquiries from people with cystic fibrosis and their family members or carers (as appropriate). Following this, the route for admission would be individualised to the patient according to their needs and severity. The committee agreed it would be inappropriate for all patients to be able to refer themselves as this may not take into account the opportunity cost of resources.

Royal College of Nursing

Short 7

1.7 It would be prudent to specify what level of contact (day and night) is the minimum as this is currently left to interpretation

Thank you for your comment. The committee agreed that the recommendation did not need to be more specific about the level of contact people can expect as a minimum because each centre will have their own process for providing this. There should be existing clear processes in place for accessing out of hours at each clinic.

Royal College of Nursing

Short 8

1.3.1 0 There is no mention of IV antibiotic training. Also very vague description of CF CNS role generally.

Thank you for your comment. The recommendation has been amended to include more examples about the clinical role of a specialist nurse including home IV services and IV access. Also note that IV antibiotic training is included as a recommendation in the section on service configuration which states to make arrangements (including providing equipment and expert support) for people to have intravenous antibiotic therapy at home, when this is appropriate.

Royal College of Nursing

Short 9

1.3.1 6 Should read "Begin to discuss the transition process ..."

Thank you for your comment. The recommendation has been amended as you suggested.

Royal College of Nursing

General Gene

ral We only read and commented on the short version of the guideline, so acknowledge that there may be a lot more detail in the full version. However, these short version of the guidelines do seem vague and we presume they are to be used in conjunction with the CF Trust’s consensus documents?

Thank you for your comment. Recommendations are based on the best available evidence and the committee’s knowledge and expertise. NICE does not endorse consensus documents without a rigorous reviewing process and consultation process. However, any changes to current clinical practice are highlighted in the full guideline with for example, reference to NHS Service Specifications.

Royal College of Nursing

General Gene

ral There is no mention at all of lung transplantation or end of life care which we consider are major components of CF care.

Thank you for your comment. The guideline scope did not include lung transplantation or end of life care as key areas to be covered. However, one theme identified in the review on information and support was end of life care, this is reported in the full guideline. The recommendations on information and support state that when appropriate, people with cystic fibrosis and their family members or carers should be provided with opportunities for discussion with relevant expert professionals on organ transplantation and end of life care. The recommendations on information and support also state to be aware that people with cystic fibrosis and their family members or carers may need emotional support and some may need specialist psychological support, in particular when waiting for or having organ transplantation, and when approaching the end of life.

Royal College of Nursing

General Gene

ral We agree that the content is appropriate and have no changes to suggest.

Thank you for your comment.
Royal College of Paediatrics and Child Health  
**Short 11**  
For well babies diagnosed by screening who are doing well, monthly appointments up to a year may be unnecessary. At 6 months after diagnosis, this could be reduced to 6-8 weekly.  
Thank you for your comment. To guide the audiences reading the recommendation, the committee gave some examples of review frequency for different age groups, with frequency decreasing with age. The ranges of frequencies provided in the recommendation are not mandatory, only examples, and should be tailored to the individual with cystic fibrosis. A greater description of the committee’s discussion on this area is provided in the full guideline section titled “evidence to recommendations”.

Royal College of Paediatrics and Child Health  
**Short 12**  
Most secondary care clinics do not have the facilities to measure lung clearance.  
Thank you for your comment. In the full guideline it is noted that LCI is currently in its infancy in the UK, but could provide additional respiratory information to spirometry. As a result the committee made recommendations to consider the use of LCI for those clinics that have access to the equipment and ability to interpret the results. This is a weak recommendation by the use of “consider” and is not mandatory. To enable stronger recommendations in the future, a research recommendation to assess if LCI is a useful and cost-effective tool for the routine assessment and monitoring of changes in pulmonary status in people with cystic fibrosis was prioritised by the committee.

Royal College of Paediatrics and Child Health  
**Short 12**  
Testing for mycobacteria is difficult and probably unnecessary in those who do not produce sputum.  
Thank you for your comment. The committee discussed your suggestion but decided not to delete non-tuberculous mycobacteria from the recommendation. The committee agreed that microbiological investigations should include non-tuberculous mycobacteria even if testing for this pathogen is more difficult than for other pathogens. The committee noted that if people are unable to produce sputum, cough swabs should be analysed, even if the accuracy of the analysis is lower with cough swabs. The committee noted that currently not all laboratories analyse cough swab for non-tuberculous mycobacteria so the recommendation to include this pathogen among microbiological investigations at annual reviews will be a change to current practice in some centres. However they agreed that it was important to undertake all possible efforts to ensure early diagnosis of non-tuberculous mycobacteria.

Royal College of Paediatrics and Child Health  
**Short 14**  
Broncho-alveolar lavage would presumably only be done using bronchoscopy under GA. If this is being done, then a full bronchoscopic examination should also be done. This is not clear.  
Thank you for your comment. The committee discussed your comment and agreed that it was correct but decided not mention bronchoscopy because this recommendation is about the indications for broncho-alveolar lavage (BAL). The committee noted that recommendations on how to perform a BAL are beyond the scope of this guideline.

Royal College of Paediatrics and Child Health  
**Short 15**  
It is not clear here what is meant by ‘mucoactive agents’. Presumably it just refers to saline, DNase and mannitol. It could be misinterpreted as referring to older discredited mucolytics such as N-acetyl-cysteine. This should be clarified.  
Thank you for your comment. The committee discussed your comment and decided to leave the heading as it is because the review looked at more mucovactive agents than the ones included in the recommendations, therefore including all agents in the heading may cause confusion. The mucovactive agents that were considered when drafting recommendations are the ones specified in the protocol for the systematic review on mucovactive agents (please see Appendix D for review protocols). The protocol includes dornase alfa, acetylcysteine, nebulised sodium chloride (saline) hypertonic and isotonic, and mannitol. With regards to acetylcysteine, the full guideline explains why this was not recommended. The committee reviewed the evidence comparing acetylcysteine to placebo. Very low to moderate quality evidence showed no clinically significant differences in F2’1 between acetylcysteine and placebo at 4, 12 and 24 week follow-ups. Likewise, low quality evidence showed no differences in need for additional intravenous antibiotics for pulmonary exacerbation at 24 week follow-up. No clinically significant differences were found in inflammatory markers or quality of life either. The committee also noted that acetylcysteine was not commonly used in clinical practice because of the unpleasant smell and taste. Moreover, acetylcysteine needs to be taken up to 4 times a day, so overall it is less tolerable and more burdensome than other mucovactive agents. Based on this, the committee agreed not to make a recommendation in favour of acetylcysteine.

Royal College of Paediatrics and Child Health  
**Short 15**  
There is no indication at what age DNase should start. Current practice is to start around 5 years of age. It is more effective when the child can manage the nebuliser competently. This should be mentioned.  
Thank you for your comment. The review didn’t include age, but the committee agreed that if a patient had clinical evidence of lung disease, rhDNase would be started regardless of age.

Royal College of Paediatrics and Child Health  
**Short 15**  
There should perhaps be a reference to the practice of using hypertonic saline only during exacerbations, or when there is a need to induce sputum for microbiological diagnosis.  
Thank you for your comment. The committee decided not to add a reference to exacerbations or to the need to induce sputum. No evidence was reviewed on hypertonic sodium chloride when there is a need to induce sputum. One study (Dentice 2016) compared 7% sodium chloride to 0.12% sodium chloride in a population admitted for management of a pulmonary exacerbation. One other study (Wilmott 1996) compared rhDNase to placebo in a population admitted to hospital for at least 1 night for treatment of a chest exacerbation. However none of the included studies compared rhDNase and hypertonic sodium chloride in a population with a pulmonary exacerbation. Therefore, the committee did not make specific recommendations on a first choice mucovactive agent in people with pulmonary exacerbations. The committee reviewed the available evidence comparing rhDNase to hypertonic sodium chloride, which was not specific to exacerbations and showed significant differences in FEV1 in favour of dornase alfa at 3 month follow-up but not at 3
Royal College of Paediatrics and Child Health  Short 16  There is no mention here of using long-term inhaled tobramycin to prevent Staph. aureus, with or without fluoroquinolones, which is common practice. Thank you for your comment. The committee discussed your comment and decided not to recommend inhaled tobramycin as antibiotic prophylaxis to prevent pulmonary bacterial infection with S. aureus because inhaled tobramycin was not included in the review protocol on the effectiveness of long-term antimicrobial prophylaxis to prevent pulmonary bacterial colonisation with S. aureus in people with CF. Therefore, the evidence on this was not reviewed.

Royal College of Paediatrics and Child Health  Short 18  We are disturbed by the inclusion in a NICE guideline of a discounted access scheme from a manufacturer. These schemes come and go and costs change. This should not be enshrined by NICE, as it could lead to accusations of commercial bias in the production of the guideline. DPI products should be recommended or not recommended according to the evidence of their effectiveness. DPIs could be recommended where patients’ adherence to nebuliser treatments is a problem. Thank you for your comment. Significant changes to acquisition costs are highlighted during NICE surveillance and could warrant an update to the guideline in these areas. Recommendations on tobramycin DPI and colistimethate sodium DPI are adopted from NICE TA276 that used the Appraisal Committee’s knowledge and expertise to interpret the clinical and economic evidence to recommend a cost-effective use of NHS resources. DPI products are recommended in this review when nebulised products are contraindicated, not tolerated or not produced an adequate response.

Royal College of Paediatrics and Child Health  Short 21  The guidance about NTM management appears to be less aggressive than other published guidance. Other guidance suggests full treatment if cultures are positive even if the patient is well. Thank you for your comment. Recommendations are based on the best available evidence and the committee’s knowledge and expertise. The strength of NICE recommendations reflects the quality of the evidence that supports them. Unfortunately no relevant evidence was identified to justify stronger recommendations in this area.

Royal College of Paediatrics and Child Health  Short 25  Abdominal surgery for any reason should only be carried out in a specialist centre, with the involvement of the CF team. Thank you for your comment. The committee agreed that the recommendation does not need to specify that surgery should be carried out in a specialist centre, as all CF-related care should be managed by the CF centre.

Royal College of Paediatrics and Child Health  Short 25  Some definition of abnormal LFTs is needed. Liver enzyme levels often fluctuate in the absence of significant liver involvement. If the threshold is too low, UDCA may get prescribed unnecessarily. I suggest ‘if liver enzyme levels (ALP, ALT, GGT) are above twice the upper limit of normal on at least two occasions, at least one month apart’. Thank you for your comment. The committee discussed your suggestion and decided not to include a definition of abnormal liver function blood tests to allow for clinical judgement to decide what tests are abnormal.

Royal College of Paediatrics and Child Health  Short 25  Liver disease can exist even in the presence of relatively normal LFTs. Routine USS can pick up liver problems missed by LFT screening. We suggest routine liver USS at annual review every 2 years, during the high-risk age for new-onset LD i.e. 10-16 years. Repeat annually if LFTs abnormal or any abnormality on scan. If scan normal at age 16, no need to repeat. Thank you for your comment. The committee discussed your comment and decided not to recommend routine ultrasound screening for liver disease because the evidence did not support this. The recommendations state to perform a clinical assessment and liver function blood tests at the annual review. The committee agreed that decisions on the tests to be included in the clinical assessment should be made at individual centres using clinical judgement. This means that individual centres would not be prevented from including an ultrasound scan at every annual review, or every two years. The committee noted that it is currently common practice to perform blood test investigations to look for evidence of liver disease. The committee recognised that ultrasound can detect evidence of liver disease, for example changes in liver echogenicity as well as advanced changes suggestive of portal hypertension. It can also detect the presence of gallstones which sometimes occur in cystic fibrosis. Ultrasound scanning is commonly used to monitor cystic fibrosis-related liver disease. The committee agreed that this may not be necessary if there was no evidence of liver disease, but a liver ultrasound scan should be performed if the blood liver function tests were abnormal. This has now been clarified in the "Evidence to recommendations" section in the full guideline.

Royal College of Paediatrics and Child Health  Short 26  Last bullet point unclear, needs re-writing. Thank you for your comment. If you are referring to the bullet on “excessive tiredness” this is increased tiredness compared to the normal level of tiredness for that individual, so would depend on their history. The committee did not want to quantify "excessive tiredness" as this is relative to the individual.

Royal College of Paediatrics and Child Health  Short 28  Psychologist should not only be available but should actively see families at every visit. Thank you for your comment. The Committee agreed that it was better to have a less prescriptive recommendation which would allow to determine frequency of visits based on individual needs. The section "Evidence to recommendations" relating to psychological assessment mentions that the frequency of visits to the psychologist should be based on individual needs as it would be week follow-up. The evidence was low or very low quality. Due to the limited evidence, the committee relied on their expertise and experience to guide their decision as to whether rhDNase or hypertonic sodium chloride should be the first-line treatment. On balance, they agreed that rhDNase was more effective and tolerable, and insufficient evidence was presented to change currently accepted practice. Therefore, the committee recommended rhDNase as first choice treatment and hypertonic sodium chloride as second choice treatment. Mannitol was recommended as an option in adults who cannot use rhDNase because of ineligibility, intolerance or inadequate response to rhDNase and whose lung function is rapidly declining (forced expiratory volume in 1 second [FEV1] decline greater than 2% annually) and for whom other osmotic agents are not considered appropriate. These recommendations were in agreement with the NICE TA266. The committee also recommended to consider mannitol in children and young people only if there was inadequate response or intolerance to rhDNase and hypertonic sodium chloride. The committee noted that the evidence showed no benefit nor harm of mannitol in children and young people. The committee noted that mannitol is rarely used in clinical practice in this age subgroup. They were aware of issues of poor tolerability and difficulties with the inhaled device in children and young people.
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The Royal College of Radiologists (RCR) and the British Society of Thoracic Imaging (BSTI)  

**Short**  

13  

1.6.7  

Should be added as mention: In patients with cystic fibrosis specific low dose CT protocol should be considered as these patients may require many CT scans during their life with associated radiation dose. Moreover, with modern CT techniques it is possible to get high quality long CT at a much lower dose than previously. Many patients with CF are thin and therefore low dose CT is particularly appropriate.  

Thank you for your comment. We have amended the recommendation to state that the chest CT scan should be low dose. Moreover, in the section “Evidence to recommendations” we have used the rationale provided in your comment to explain why the CT scan should be low dose.

The Royal College of Radiologists (RCR) and the British Society of Thoracic Imaging (BSTI)  

**Short**  

22  

1.6.5  

Consideration on imaging (CXR and/or CT) could also be added to this section on unidentified infective exacerbation.  

Thank you for your comment. The committee discussed your suggestion and decided not to include radiological investigations in this recommendation because this recommendation is about treatment rather than about investigations. Please refer to the section on pulmonary monitoring for recommendations about investigations and use of imaging techniques.

The Royal College of Radiologists (RCR) and the British Society of Thoracic Imaging (BSTI)  

**Short**  

24  

1.7.1  

Consider changing the wording of 1.7.10 about acute onset periumbilical abdominal pain. Perhaps “initially by ultrasound and followed by MRI or CT if the cause is not confirmed via ultrasound and clinical concern persists”…abdominal CT in young and very thin CF patients is a big source of ionising radiation dose and may not be rewarding. This is one area where MRI is already established enough to be clinically useful.  

Thank you for your comment. The committee discussed your suggestion and noted that no evidence was reviewed on diagnosis of DIOS, therefore only consensus recommendations were made. The committee did not feel confident to make recommendations on using one imaging technique before the other based on consensus only. Therefore they decided that the choice of imaging technique should be left to clinical judgement. The committee did not refer to MRI specifically in the recommendations, but stated to consider further imaging, for example…so that the recommendation also indirectly refers to MRI and not only to the abdominal ultrasound scan or to the abdominal CT scan. The committee decided to leave the specific examples referring to abdominal ultrasound scan and abdominal CT scan in the recommendation because these are more commonly performed. The committee also noted that the CT scan is less costly and less time consuming than an MRI scan.

The Royal College of Radiologists (RCR) and the British Society of Thoracic Imaging (BSTI)  

**Short**  

25  

1.7.1  

Consider mention “ultrasound liver elastography” in the liver disease section.  

Thank you for your comment. The section titled “Evidence to recommendations” in the full guideline provides the committee’s discussion on ultrasound liver elastography. The committee agreed there was little evidence to support the use of ultrasound liver elastography (FibroScan®) for early stage detection of liver disease and agreed that because treatment with ursodeoxycholic acid would have already been initiated, the value of adding this test to a diagnostic regimen was diminished.

The Royal College of Radiologists (RCR) and the British Society of Thoracic Imaging (BSTI)  

**Short**  

3  

1.1.1  

Maybe add that “Occasionally, chest CT may have been performed in a symptomatic patient, with no previous diagnosis of Cystic Fibrosis(CF). Confirming the presence of bronchiectasis-features prompting further clinical tests (sweat test etc.) to confirm the diagnosis of CF.”  

Thank you for your comment. This has not been added to this recommendation because it is included in the following recommendation, which lists the symptoms that would prompt an assessment for cystic fibrosis.

The Royal College of Radiologists (RCR) and the British Society of Thoracic Imaging (BSTI)  

**Short**  

8-9  

1.3.1  

Need to add “diagnostic and interventional radiology”.  

And add that “There should be specialist access to thoracic radiology within the MDT team (e.g. requires familiarity with CT appearances of atypical mycobacterial disease, ABPA etc. as mentioned in the document)”  

Thank you for your comment. The committee agreed not to add a “diagnostic radiologist” because the diagnostic radiologist wouldn’t need to be specialist in cystic fibrosis, whereas the interventional radiologist would.

UK Psychosocial Professionals in CF (UKPCCF)  

**Appendix N**  

Title page  

Refers to mental analysis instead of meta analysis  

Thank you for your comment. This has been amended.

UK Psychosocial Professionals in CF (UKPCCF)  

**Full**  

130  

2  

Please consider including need for social work support and social work assessment. CF Specialist social workers support the child and family’s long term adjustment to treatment by providing their educational needs, providing advice and advocacy support for their welfare entitlements, respite care needs and emerging quality of life issues across the life span.  

Thank you for your comment. The recommendations have been amended to include examples of the role of the CF social worker. These include adjusting to long term treatment but also support and advice relating to education or employment. Moreover, in the section “Evidence to Recommendations” related to the information and support review, a sentence has been added to specify that additional support may be needed during times of change, such as starting or changing school, moving from education to work, changing to independent living. The committee noted that social work support is also important at these times and especially liaison with local Social Care services as appropriate.
UK Psychosocial Professionals in CF (UKPPCF) Full 170-174 38 We are concerned that the recommendation for patients to have annual review did not include their social care needs given that the condition is progressive and peoples' social care needs are likely to change. Thank you for your comment. We have included a nurse and social worker in the assessment bullet point that refers to the annual review.

UK Psychosocial Professionals in CF (UKPPCF) Full 171 9 We are concerned that this recommendation may imply that the social care needs of people with CF are not as important as their health needs. The document acknowledged that cystic fibrosis is associated with poor quality of life and clinical outcomes. The role of all the other MDT members is stated in the document but that of social work is not. Instead some of the responsibilities of social workers are assigned to the specialist nurses. Please consider including assessment by a specialist social worker. The CF social workers currently employed by NHS Trusts are integrated within the CF multidisciplinary team and are part of annual reviews. Thank you for your comment. The recommendations have been amended to acknowledge that not every specialist CF MDT team will have access to dedicated social worker. Where social workers are available they are members of the core MDT team. We have also added a recommendation which includes some examples about their role on the MDT. We have also included a nurse and social worker in the assessment bullet that refers to the annual review.

UK Psychosocial Professionals in CF (UKPPCF) Full 174 40 Please consider including the role as a specialist social worker as they work within the CF multidisciplinary team Thank you for your comment. A recommendation has been added to the section on the multidisciplinary team to include some examples about the role of the social worker as part of the MDT. These include adjusting to long term treatment but also support and advice relating to education or employment.

UK Psychosocial Professionals in CF (UKPPCF) Full 177 19 Currently reads “when needed at outpatient and inpatient clinics”. Inpatient care is not in clinic so would better read “when needed at outpatient clinics and during inpatient admissions” Thank you for your comment. "inpatient admissions" has now replaced "inpatient clinics". Moreover, "and (if needed) at other outpatient appointments" has been added after "at outpatient clinics and during inpatient admissions" to make this more clear.

UK Psychosocial Professionals in CF (UKPPCF) Full 177 19 Please include a separate line stating that the specialist social worker should assess and intervene with people with cystic fibrosis at their annual review, and when needed at outpatient clinics and during inpatient admissions. Thank you for your comment. A recommendation has been added to the section on the multidisciplinary team to include some examples about the role of the social worker. This recommendation does not specify the setting where this would take place because social workers are not employed by the NHS and therefore are outside the scope of this guideline, and the recommendation could not be too prescriptive. Moreover, the recommendation on the annual review has been modified to include assessment by the social worker.

UK Psychosocial Professionals in CF (UKPPCF) Full 19 6 We would like it to include - Recognising social, psychological and behavioural problems. NHS Trusts across UK and Ireland have recognised the need for a Specialist CF Social worker to systematically assess and intervene on the emerging social problems due to CF being a lifelong condition. Thank you for your comment. The recommendations have been amended to include examples about the role of the CF social worker. This include adjusting to long term treatment but also support and advice relating to education or employment.

UK Psychosocial Professionals in CF (UKPPCF) Full 19 31 Please consider including - Transition from children’s to adults’ services for young people using health or social care services NICE guideline, 2016 Thank you for your comment. We have directed readers to NG43 Transition from children’s to adults’ services for young people using health or social care services.

UK Psychosocial Professionals in CF (UKPPCF) Full 655 21 Typo – this should read the Thank you for your comment. Unfortunately we cannot identify the typo you are referring to.

UK Psychosocial Professionals in CF (UKPPCF) Full 667 11-12 Currently reads ‘If a severe problem is identified as part of the annual review the person should be referred to a mental health practitioner’. We feel this advice is ambiguous. Clinical Psychologists are able to work with severe problems in people with CF e.g. severe anxiety, severe depression, referral outside the team may not therefore be needed in these cases. Referral outside the CF team should be made when there is a severe mental health condition e.g. psychosis, high level of risk or need for psychiatric care. This would normally involve a “stepping up” of care into specialist mental health services, not to any mental health practitioner. Significant risk would be managed within local mental health services rather than in the CF team. Thank you for your comment. The section “Evidence to recommendations” in the full guideline has now been modified to include specific examples of a severe mental health condition that would prompt referral to a mental health team. The same section currently states that if a severe mental health condition is identified as part of the annual screening such as psychosis, high level of risk of self-harm or need for psychiatric care, the person should be referred to a mental health team. This would normally involve a “stepping up” of care into specialist mental health services.

UK Full 669 27-28 As in comment 14. Thank you for your comment. We understand the request is to change a mental health recommendation.
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<td>We were unclear what “psychosocial indicators” referred to or included.</td>
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<td>“Serious mental health issue” is unclear. Severe mental health problem/condition may be more appropriate term here.</td>
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<td>Sentence does not seem clear. Perhaps should read “to use as a screening test”</td>
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<td>Social worker assessment should be included here.</td>
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<td>6</td>
<td>16</td>
<td>Useful to add “when experiencing major changes in health or serious health events”</td>
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<td>UK Psychosocial Professionals in CF (UKPPCF)</td>
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<td>26</td>
<td>Useful to add “The specialist clinical psychologists should also offer advice/consultation to the CF team on psychological care”</td>
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<td>UK Psychosocial Professionals in CF (UKPPCF)</td>
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<td>26</td>
<td>Social work roles are omitted here although are listed in essential MDT.</td>
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<tr>
<td>University Hospital Southampton</td>
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<td>177</td>
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<td>The specialist pharmacist should be available to advise on medicines and their optimisation during in-patient stay as well as at AR and outpatients (particularly when in-patient ward covered by a non-specialist pharmacist).</td>
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<tr>
<td>University Hospital Southampton</td>
<td>Full</td>
<td>260</td>
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<td>There is internal inconsistency with the recommended review period. Here it recommends at least every three months, whereas elsewhere eg page 171 line 17 it says every 3 or 6 months.</td>
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Thank you for your comment. The committee have not discussed having access to CF specific psychiatrists or psychiatric nurse staff. This recommendation is aimed at when someone is identified as having a severe mental health condition such as psychosis, high level of risk of self-harm or need for psychiatric care, which is not specifically related to their CF or may require pharmacological input or input from community or inpatient psychiatric services. To state “the” mental health practitioner would indicate this should be someone within the CF MDT which may not be the case. The section “Evidence to recommendations” has been amended to specify that the person should be referred to a mental health practitioner who would be part of the local mental health team.

Thank you for your comment. We understand the request is to change a mental health practitioner to “the” mental health practitioner. The committee have not discussed having access to CF specific psychiatrists or psychiatric nurse staff. This recommendation is aimed at when someone is identified as having a severe mental health condition such as psychosis, high level of risk of self-harm or need for psychiatric care, which is not specifically related to their CF or may require pharmacological input or input from community or inpatient psychiatric services. To state “the” mental health practitioner would indicate this should be someone within the CF MDT which may not be the case. The section “Evidence to recommendations” has been amended to specify that the person should be referred to a mental health practitioner who would be part of the local mental health team.

Thank you for your comment. This term has now been modified to indicators of emerging psychosocial problems. The “Evidence to recommendations” section also gives some examples of said indicators: poor school attendance, family break up, anxious thoughts, low mood, missing treatments, financial or home management difficulties, safeguarding concerns, employment support needs or criminality.

Thank you for your comment. This term has now been modified to severe mental health condition.

Thank you for your comment. The research question has been amended to what is the most effective measure of psychological functioning to use as test for thresholds of concern in people with cystic fibrosis.

Thank you for your comment. The committee have included a nurse and social worker in the assessment bullet point that refers to the annual review.

Thank you for your comment. The committee discussed this suggestion and decided that this addition was not needed because the recommendation was more specific and focused on specific times when additional support may be needed due to major changes in health. They specifically mentioned pregnancy, cystic fibrosis related complications, transplantation, approaching end of life.

Thank you for your comment. The committee discussed your suggestion and decided not to specify this because it is expected of all members of a multidisciplinary team that they would support each other through advice and consultation in relation to their respective areas of expertise.

Thank you for your comment. A recommendation has been added to the section on the multidisciplinary team to include some examples about the role of the social worker on the MDT.

Thank you for your comment. The recommendation has been modified and it now states that the specialist pharmacist should advise people on medicines optimisation during inpatient admissions, on discharge from hospital, at outpatient clinic visits and at annual review. The recommendation now also states that they should advise healthcare professionals on all aspects of medicines use and prescribing.

Thank you for your comment. The committee recommended routine reviews at least every 3 months for adults with cystic fibrosis with clinical evidence of lung disease. A separate recommendation relating to the general population of adults with cystic fibrosis mentions an example of frequency of 3 to 6 months. As explained in the section “Evidence to...
University Hospital Southampton Full 260 26 and 41 Although ‘clinical history’ may be considered to include medication review. CF is so complex, with so many long term medications, and with adherence being so important, suggest should include explicit adherence mention to review medication and adherence at each routine clinic appointment and annual review

University Hospital Southampton Full 262 2 Why is this recommendation only for children and young people, not all adults?

University Hospital Southampton Full 459 25 If making recommendations, surely discussion about abscesses being at least a potential contra-indication to transplant needs to be mentioned as influencing treatment decisions? I.e. if abscesses (with sub-speciality differences noted), and PWCF could be a candidate for transplant, then needs eradication. These guidelines seem insufficiently detailed to be adequate to guide these crucial decisions.

University Hospital Southampton Full 460 24 Raised aspergillus serology is not a sufficiently specific statement to justify treatment for ABPA. A raised total IgE is required greater than 500 or 1000ui depending on the guidelines you choose. Aspergillus specific IgG may be raised but is not diagnostic of ABPA. This raises the issue of fungal bronchitis, which is not recognised by all clinicians, but which may warrant a trial of treatment. These recommendations do not seem detailed enough to be useful in this complex area.

University Hospital Southampton Full 530 21 and 45 Despite low quality evidence to support the use of oral supplements, enteral feeding and appetite stimulants (likely due to small numbers) we do find that in clinical practice they are extremely successful for some patients in clinical practice. We wanted to reassure the committee that we don’t want to add to unnecessary treatment burden in this group of patients and are under constant pressure to justify the use of these in the community due to high costs. We therefore closely monitor use of these products and discontinue if no positive outcome.

University Hospital Southampton Full 594 19 We would request that specific mention of the latest type of CGM monitoring devices, "intermittently viewed" CGM (such as eg Freestyle Libre) were specifically mentioned. We would also like to express concern over any guideline that recommends the diagnosis of CFRD based on CGMS, for which no definition of DM exists.

University Hospital Southampton Full 607 34-43 We keep a bone database which includes all patients who have had a bone scan revealing low bone mineral density (osteoopenia/osteoporosis as per WHO Guidelines). A review of the database revealed 50 patients who have a low bone mineral density but do not meet the "high risk" criteria set out in the proposed NICE Guidelines (frequent or long term corticosteroid use, frequent intravenous antibiotic use, severe lung disease, undernutrition, previous low impact fractures, previous transplants, post menopause). This means that if we were to adhere to the NICE guidelines we would have missed the presence of low bone mineral density in 18.5% of our total adult patient group (n=270). We run an innovative joint CF/Rheumatology service with the help of Professor Nigel Arden from University of Oxford and MRC. We would be happy to share our experience with the committee.

University Hospital Southampton Full 708 34 There is no mention of the need for cross infection surveillance using strain typing (for pseudomonas, cepacia and MRSA) or whole genome sequencing for M.abscessus) on a routine basis eg once a year. Without this, how can you tell if CI is a problem or not? This is in the National Service Specification

University Hospital Southampton Full 709 6 The word "managed" is too vague to be useful as it could be interpreted in many different ways. Mixing for PWCF is clearly a bad idea (with good evidence) so change this word to ‘avoided'

University Hospital Southampton Full 719 37 The scoping statement of these guidelines states;
Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.
**Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.**

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<th>Response</th>
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| Vertex Pharmaceuticals (Europe) Ltd | Short 33 | 8-10 | The current draft states ‘By making robust recommendations based on the available evidence and best practise in cystic fibrosis care, this guideline will help improve care for this highly complex condition’ We would make the following comments:  
I. This draft does not make reference to all the available clinical evidence nor commissioning policies relating to the clinical use of Kalydeco (ivacaftor) since 2015 for the treatment of CF patients  
II. This draft fails to reference or include the current clinical practise where Kalydeco (ivacaftor) is routinely used for appropriate patients in CF services across England; and by failing to do so may create unnecessary confusion for clinicians and patients. | Thank you for your comment. CFTR modulators were not included in the scope as current clinical practice in this area was considered to be consistent and effective, relative to the other areas under consideration. For completeness, a recommendation referring to the NICE technology appraisal on lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation has been added. |

*None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*