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Guidelines

Cystic fibrosis: diagnosis and management

• NICE guideline 78 •

REPRINT

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Cystic fibrosis: diagnosis and management

National Institute for Health and Care Excellence

- This *Guidelines* summary covers the key points for secondary care, please see the full guideline at **www.nice.org.uk/ng78** for a complete set of recommendations on:
  - transition to adult services
  - complications of cystic fibrosis
  - pulmonary infections
  - nutritional interventions and exocrine pancreatic insufficiency
  - liver disease
  - cystic-fibrosis-related diabetes
  - bone mineral density
  - psychological assessment

Diagnosis of cystic fibrosis

- Be aware that cystic fibrosis can be diagnosed based on:
  - positive test results in people with no symptoms, for example infant screening (blood spot immunoreactive trypsin test) followed by sweat and gene tests for confirmation **or**
  - clinical manifestations, supported by sweat or gene test results for confirmation **or**
  - clinical manifestations alone, in the rare case of people with symptoms who have normal sweat or gene test results

- Assess for cystic fibrosis and, when clinically appropriate, perform a sweat test (for children and young people) or a cystic fibrosis gene test (for adults) in people with any of the following:
  - family history
  - congenital intestinal atresia
  - meconium ileus
  - symptoms and signs that suggest distal intestinal obstruction syndrome faltering growth (in infants and young children)
  - undernutrition
  - recurrent and chronic pulmonary disease, such as:
    - recurrent lower respiratory tract infections
    - clinical or radiological evidence of lung disease (in particular bronchiectasis) persistent chest X-ray changes
    - chronic wet or productive cough
  - chronic sinus disease
  - obstructive azoospermia (in young people and adults)
  - acute or chronic pancreatitis
  - malabsorption
  - rectal prolapse (in children)
  - pseudo-Bartter syndrome

- Refer people with suspected cystic fibrosis to a specialist cystic fibrosis centre if:
  - they have a positive or equivocal sweat test result
  - their assessment suggests they have cystic fibrosis but their test results are normal
  - gene testing reveals 1 or more cystic fibrosis mutations

Information and support

- Provide people who are newly diagnosed with cystic fibrosis and their family members or carers (as appropriate) with opportunities to discuss their concerns

- Information and support should be provided by healthcare professionals with expertise in cystic fibrosis

- Provide people with suspected or diagnosed cystic fibrosis and their family members or carers (as appropriate) with relevant information that they can understand, and opportunities for discussion on topics such as:
  - their diagnosis
  - monitoring of their condition
  - management choices for their condition
  - possible or existing complications or comorbidities
  - implications for living independently

- Provide people with cystic fibrosis and their family members or carers (as appropriate) with information about their care pathway

- Give information to people with cystic fibrosis and to family members or carers in ways that are individually appropriate. Avoid jargon and use formats that they prefer, for example:
  - face-to-face discussions
  - copies of correspondence
  - written information (such as leaflets)
  - any digital media and reliable internet sources that are available

- When appropriate, provide people with cystic fibrosis and their family members or carers with opportunities for discussion with relevant expert professionals on:
  - available resources and support, such as local support and advocacy services
  - managing the risks of cross-infection
  - implications of the condition for school and education
  - career planning
  - transition to adult care
  - foreign travel
  - fertility and contraception
  - pregnancy and parenting
  - organ transplantation
  - end of life care

- Provide people with cystic fibrosis with information about how to contact other people with cystic fibrosis without risking cross-infection, for example by directing them to online support groups

- For more information on communication, providing information and shared decision-making in adult NHS services, see the NICE guideline on patient experience in adult NHS services

- Be aware that people with cystic fibrosis and their family members or carers will need emotional support and some may need specialist psychological support, in particular:
  - at diagnosis
  - at times of transition (for example, when starting or changing school, moving from education to work, or changing to living independently for the first time)
  - in relation to fertility, including family planning, pregnancy and infertility
  - to cope with complications of cystic fibrosis
  - when waiting for or having organ transplantation
  - when approaching the end of life

Service delivery

Service configuration

- Care for people with cystic fibrosis should be provided by a specialist cystic fibrosis multidisciplinary team based at a specialist cystic fibrosis centre

- Specialist cystic fibrosis centres should:
  - plan patient care (including outpatient and inpatient care), taking into account the risk of cross-infection
  - maintain local and national registers of patients that include information about their clinical condition, treatment and outcomes
  - audit practice and outcomes

- When a shared-care model is used for children and young people, it should include:
  - formal arrangements between the local paediatric team at the shared-care centre and the multidisciplinary team at the specialist cystic fibrosis centre
  - direct involvement of specialist cystic fibrosis multidisciplinary team members
  - an annual assessment and at least one other review per year by the specialist cystic fibrosis multidisciplinary team, in addition to reviews by the local paediatric team

- If available and when clinically appropriate, outreach care for adults with cystic fibrosis may be provided by the specialist cystic fibrosis multidisciplinary team at a local hospital

- 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)

- Consider telemedicine or home visits for routine monitoring when they are more appropriate than outpatient visits and if the person with cystic fibrosis prefers it

- Make arrangements (including providing equipment and expert support) for people to have intravenous antibiotic therapy at home, when this is appropriate

Multidisciplinary team

- The specialist cystic fibrosis multidisciplinary team should include at least one of each (depending on the size of the clinic) of the following professionals, who should have specialist expertise in the condition:
  - specialist paediatricians or adult physicians
  - specialist nurses
  - specialist physiotherapists
  - specialist dietitians
  - specialist pharmacists
  - specialist clinical psychologists

- The specialist cystic fibrosis multidisciplinary team should be led by a specialist paediatrician or adult physician

- The specialist cystic fibrosis multidisciplinary team should either include or have access to social workers

- Social workers should provide advice and support to people with cystic fibrosis and their family members or carers (as appropriate), for example on:
  - help with adjusting to long-term treatment (such as taking regular medicines)
  - education
  - employment
  - government benefits
  - respite care

- Specialist nurses (working with specialist paediatricians or physicians) should coordinate care and facilitate communication between other members of the cystic fibrosis team, and act as advocates for people with cystic fibrosis and their family members or carers (as appropriate). Key clinical roles could include:
  - support during and after diagnosis and when starting treatment
  - triage
  - advanced clinical assessment
  - coordinating home intravenous antibiotic services, including intravenous access

- Specialist physiotherapists should assess and advise people with cystic fibrosis at clinic, at inpatient admissions, during pulmonary exacerbations and at their annual review. Assessment and advice could cover airway clearance, nebuliser use, musculoskeletal disorders, exercise, physical activity and urinary incontinence

- Specialist dietitians should assess and advise people with cystic fibrosis about all aspects of nutrition at outpatient clinic visits, during inpatient admissions and at their annual review

- Specialist pharmacists should advise people with cystic fibrosis on medicines optimisation at outpatient clinic visits, during inpatient admissions, on discharge from hospital and at annual review. They should advise healthcare professionals on all aspects of medicines use and prescribing, and support GPs, community pharmacists and homecare providers to ensure that people with cystic fibrosis get the medicines they need without interruption

- 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 appointments, during inpatient admissions, and at their annual review

- The specialist cystic fibrosis multidisciplinary team should either include or have access to specialist expertise relevant to cystic fibrosis in the following areas:
  - microbiology
  - pulmonary physiology
  - diabetes
  - gastroenterology

- hepatology
- rheumatology
- psychiatry
- interventional radiology
- surgery (gastrointestinal, thoracic, and ear, nose and throat)
- obstetrics
- palliative care

- The specialist cystic fibrosis multidisciplinary team should work with GPs, and provide timely information so that GPs can support people with cystic fibrosis by:
  - prescribing cystic fibrosis medicines:
    - in batches of at least 1 month at a time for routine medicines
    - for longer periods if advised by the specialist team
    - following guidance on arrangements for prescriptions of unlicensed medicines
  - providing routine annual immunisation, including any alterations for people with cystic fibrosis and flu vaccinations for family members and carers
  - managing health problems not related to cystic fibrosis
  - certification of illnesses
  - working in partnership with cystic fibrosis homecare teams, particularly for end of life care
  - providing care for the person's family members or carers

Annual and routine reviews

- Be aware that:
  - the aim of cystic fibrosis care is to prevent or limit symptoms and complications of the condition
  - routine monitoring and annual assessments are crucial in providing effective care

- Offer people with cystic fibrosis a comprehensive annual review that includes the following:
  - a pulmonary assessment
  - an assessment of nutrition and intestinal absorption
  - an assessment for liver disease
  - testing for cystic-fibrosis-related diabetes, from 10 years of age
  - an assessment for other potential or existing cystic fibrosis complication
  - a psychological assessment
  - assessments by a specialist nurse, physiotherapist, pharmacist and social worker
  - a review of their exercise programme

- Provide regular routine reviews for people with cystic fibrosis, and do these more frequently immediately after diagnosis and in early life. For example:
  - weekly in their first month of life
  - every 4 weeks when they are between 1 and 12 months old
  - every 6 to 8 weeks when they are between 1 and 5 years old
  - every 8 to 12 weeks when they are over 5 years old
  - every 3 to 6 months as adults

Pulmonary monitoring, assessment and management

Pulmonary monitoring

- For people with cystic fibrosis who have clinical evidence of lung disease, base the frequency of routine reviews on their clinical condition but review children and young people at least every 8 weeks and adults at least every 3 months. If appropriate, think about using the review schedules described above

- Include the following at each routine review, in relation to pulmonary assessment, for people with cystic fibrosis:
  - a clinical assessment, including a review of clinical history and medicines adherence, and a physical examination with measurement of weight and length or height
  - measurement of oxygen saturation
  - taking respiratory secretion samples for microbiological investigations, using sputum samples if possible, or a cough swab or nasal pharyngeal aspirate (NPA)

  - lung function testing with spirometry (including forced expiratory volume in 1 second [FEV_1], forced vital capacity [FVC], and forced expiratory flow [FEF] 25–75%) in adults, and in children and young people who can do this

- If spirometry is normal at a routine review, consider measuring lung clearance index

- Include the following at each annual review in relation to pulmonary assessment for people with cystic fibrosis:
  - a clinical assessment, including a review of the clinical history and medicines adherence, and a physical examination, with measurement of weight and length or height
  - a physiotherapy assessment
  - measurement of oxygen saturation
  - a chest X-ray
  - blood tests, including white cell count, aspergillus serology and serum IgE
  - taking respiratory secretion samples for microbiological investigations (including non-tuberculous mycobacteria)
  - lung function testing (for example with spirometry, including FEV_1, FVC, and FEF 25–75%) in adults, and in children and young people who can do this

- Consider measuring lung clearance index at each annual review if spirometry is normal

- For people with cystic fibrosis with lung disease who have symptoms that are concerning them or their family members or carers (as appropriate), consider which of the following may be useful:
  - review of clinical history
  - physical examination, including measurement of weight and length or height measurement of oxygen saturation
  - taking respiratory secretion samples for microbiological investigations, using sputum samples if possible, or a cough swab or NPA if not
  - for adults, blood tests to measure white cell count and inflammatory markers such as C-reactive protein
  - lung function testing, for example with spirometry (including FEV_1, FVC, and FEF 25–75%) in adults, and in children and young people who can do this
  - lung clearance index for people with normal spirometry results

- Depending on the assessments that are needed, decide whether to provide a remote telemedicine or face-to-face assessment

- Think about doing a low-dose chest CT scan for children with cystic fibrosis who have not had a chest CT scan before, to detect features that other tests (such as a plain chest X-ray) would miss (for example early bronchiectasis)

- Think about doing a chest X-ray for people with cystic fibrosis during or after treatment for an exacerbation of lung disease (taking account of severity), if:
  - the exacerbation does not respond to treatment **or**
  - a chest X-ray before treatment showed new radiological abnormalities

- Monitor the treatment response during and after an exacerbation of lung disease by assessing whether the symptoms and signs have resolved, and as appropriate:
  - take respiratory secretion samples for microbiological investigations, using sputum samples if possible, or a cough swab or NPA if not
  - test lung function, for example with spirometry (including FEV_1, FVC and FEF 25–75%) in adults, and in children and young people who can do this
  - measure oxygen saturation

- Think about using broncho-alveolar lavage to obtain airway samples for microbiological investigation in people with cystic fibrosis if:
  - they have lung disease that has not responded adequately to treatment **and**
  - the cause of the disease cannot be found with non-invasive upper airway respiratory secretion sampling (including sputum induction if appropriate)

Airway clearance techniques

- 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). Provide them with training in airway clearance techniques and explain when to use them
- 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)
- When choosing an airway clearance technique for people with cystic fibrosis:
  - assess their ability to clear mucus from their lungs, and offer an individualised plan to optimise this
  - take account of their preferences and (if appropriate) those of their parents and carers
  - take account of any factors that may influence adherence
- Regularly assess the effectiveness of airway clearance techniques, and modify the technique or use a different one if needed
- Do not offer high-frequency chest wall oscillation as an airway clearance technique for people with cystic fibrosis except in exceptional clinical circumstances. The specialist cystic fibrosis team will decide whether these circumstances apply, and their decision would then be subject to the NHS England policy on Individual Funding Requests. Be aware that the evidence shows high-frequency chest wall oscillation is not as effective as other airway clearance techniques
- Consider using non-invasive ventilation in people with cystic fibrosis who have moderate or severe lung disease and cannot clear their lungs using standard airway clearance techniques

Mucoactive agents

- Offer a mucoactive agent to people with cystic fibrosis who have clinical evidence of lung disease
- Offer rhDNase (dornase alfa; recombinant human deoxyribonuclease)* as the first choice of mucoactive agent
- If clinical evaluation or lung function testing indicates an inadequate response to rhDNase, consider both rhDNase* and hypertonic sodium chloride or hypertonic sodium chloride alone
- Consider mannitol dry powder for inhalation† for children and young people who cannot use rhDNase and hypertonic sodium chloride because of ineligibility, intolerance or inadequate response
- Mannitol dry powder for inhalation is recommended as an option for treating cystic fibrosis in adults:
  - who cannot use rhDNase because of ineligibility, intolerance or inadequate response to rhDNase **and**
  - whose lung function is rapidly declining (FEV_1 decline greater than 2% annually) **and**
  - for whom other osmotic agents are not considered appropriate

  (This recommendation is taken from NICE technology appraisal guidance 266)
- People currently receiving mannitol whose cystic fibrosis does not meet the criteria above should be able to continue treatment until they and their clinician consider it appropriate to stop
  (This recommendation is taken from NICE technology appraisal guidance 266)
- For recommendations on using lumacaftor–ivacaftor, see the NICE technology appraisal guidance on lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation

Immunomodulatory agents

- For people with cystic fibrosis and deteriorating lung function or repeated pulmonary exacerbations, offer long-term treatment with azithromycin‡ at an immunomodulatory dose
- For people who have continued deterioration in lung function, or continuing pulmonary exacerbations while receiving long-term treatment with azithromycin, stop azithromycin and consider oral corticosteroids
- Do not offer inhaled corticosteroids as an immunomodulatory treatment for cystic fibrosis

Other monitoring, assessment and management

Distal intestinal obstruction syndrome

- Be aware that a variety of conditions can cause acute abdominal pain and resemble distal intestinal obstruction syndrome in people with cystic fibrosis, for example:
  - constipation
  - appendicitis
  - intussusception
  - cholecystitis
- 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
- For people who have an acute onset of peri-umbilical abdominal pain but no other clinical or radiological features of distal intestinal obstruction syndrome, consider further imaging, for example with an:
  - abdominal ultrasound scan **or**
  - abdominal CT scan
- Manage suspected distal intestinal obstruction syndrome in a specialist cystic fibrosis centre, with supervision from specialists who have expertise in recognising and treating the condition and its complications
- Offer oral or intravenous fluids to ensure adequate hydration (and rehydration if needed) for people with distal intestinal obstruction syndrome
- Consider diatrizoate meglumine and diatrizoate sodium solution (orally or via an enteral tube) as first-line treatment for distal intestinal obstruction syndrome
- If diatrizoate meglumine and diatrizoate sodium solution is not effective, consider an iso-osmotic polyethylene glycol and electrolyte (PEG) solution (macrogols) (orally or via an enteral tube) as a second-line treatment
- Consider surgery as a last resort, if prolonged treatment with a PEG solution is not effective
- To reduce the risk of distal intestinal obstruction syndrome recurring:
  - encourage people to drink plenty of fluids
  - optimise pancreatic enzyme replacement therapy
  - consider advising regular treatment with a stool-softening agent such as lactulose or a PEG solution

Exercise

- Advise people with cystic fibrosis and their family members or carers (as appropriate) that regular exercise improves both lung function and overall fitness
- Offer people with cystic fibrosis an individualised exercise programme, taking into account their capability and preferences
- Regularly review exercise programmes to monitor the person's progress and ensure that the programme continues to be appropriate for their needs

- Provide people with cystic fibrosis who are having inpatient care with:
  - an assessment of their exercise capacity
  - the facilities and support to continue their exercise programme (as appropriate), taking into account the need to prevent cross-infection and local infection control guidelines

Preventing cross-infection

- For recommendations on preventing and controlling infection, see the NICE guidelines on infection control in primary and community care and healthcare-associated infections, and the NICE quality standard on infection prevention and control

- To prevent cross-infection among people with cystic fibrosis in outpatient and inpatient care, use microbiological surveillance and a local infection control strategy that includes cohorting

- Inform people with cystic fibrosis, their family members or carers (as appropriate) and staff involved in their care about the risk of cross-infection and how to avoid it

- Each specialist cystic fibrosis clinic should be organised to prevent cross-infection. Separate people individually during the clinic, including by organising:
  - the use of communal areas
  - attendance at diagnostic, treatment and pharmacy facilities

- 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

- Consider keeping people with cystic fibrosis who have intermittent isolation of *Pseudomonas aeruginosa* separate from people who do not have this infection, for example by using separate outpatient clinics. Help people with cystic fibrosis plan their inpatient attendance to avoid contact with each other, for example when they use:
  - hospital restaurants, schools and recreation areas
  - diagnostic, treatment and pharmacy facilities

- During inpatient care, give people with cystic fibrosis individual rooms with en-suite facilities

* At the time of publication (October 2017), rhDNase did not have a UK marketing authorisation for use in children under 5 years of age with cystic fibrosis for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

† At the time of publication (October 2017), mannitol dry powder for inhalation did not have a UK marketing authorisation for use in children with cystic fibrosis for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

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Full guideline available from

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