Cystic Fibrosis our focus

Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis (2020)

Fourth edition - November 2020

Fighting for a Life Unlimited

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1. Foreword

1.1 Document development

This document is the updated “Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis” (2017). It incorporates relevant information from the ACPCF/Cystic Fibrosis Trust endorsed “Standards of Care” (2020) and “Clinical Guidance for the Physiotherapy Management of Screened Infants with Cystic Fibrosis and Screen Positive Inconclusive Diagnosis” 2020 (Appendix I) to complete a comprehensive support document for physiotherapists working in cystic fibrosis (CF). It covers infants, children and adults with CF.

All contributors are professionals working in the specialist field of cystic fibrosis. The ACPCF acknowledges the invaluable input of other health professionals and have consulted in areas where additional expertise is pivotal, eg respiratory physiology. This document has been developed independently of any funding bodies.

1.2 How to use this document

The Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis aims to be a useful tool and comprehensive reference document for all physiotherapists and clinicians involved in the delivery of care to people diagnosed with cystic fibrosis. It can also be used as a reference document for people with CF and their families/carers. The endorsement process of the document by the Cystic Fibrosis Trust has included review by relevant experts as well as peer review.

This document is intended to support physiotherapists to develop local guidelines tailored to their specific needs and circumstances in caring for people with CF. Good clinical practice points highlight areas of experienced clinical practice that are relevant to clinicians, but that do not currently have substantive evidence to support them. There are a number of appendices, which have been compiled by the authors and are currently in use in clinical practice. The updated Infant Guidelines are also included, which outline the recommendations for the management and ongoing care of newly diagnosed, possibly asymptomatic infants with CF and those who present with a screen positive but inconclusive diagnosis.

1.3 Review of the document

As we enter a new era of cystic fibrosis care and the implementation of modulator therapies, many aspects of care are likely to change with increasing regularity and it is anticipated that this will be need to be a “live” document with relevant changes made to each section as they are needed. Cystic fibrosis transmembrane conductance regulator (CFTR) modulators are a class of drugs that act by improving production, intracellular processing, and/or function of the defective CFTR protein. These drugs represent an important advance in the management of CF because they target the production or function of the mutant CFTR protein rather than its downstream consequences. Their indications and efficacy depend upon the CFTR mutations present in each individual and for these reasons we will likely see personalised changes in the management of CF care, which will undoubtedly include physiotherapeutic management.

1.4 Grading scheme for recommendations in the document

In this document the evidence used to support the recommendations has been graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE gives the clinician a useful tool in making clear, pragmatic interpretations of strong versus weak recommendations. As few areas of physiotherapy management in CF have sufficient and robust evidence, it is of paramount importance to inform the clinician about:

- the quality of the evidence *(QoE) (high, moderate, low or very low)*;
- which outcomes are critical; and
- the overall strength of the recommendation (strong or weak) to better inform their clinical reasoning and decision process.

Although recommendations overall may be graded as 'strong' (ie the degree of confidence that the desirable effects outweigh the undesirable) the quality of the evidence may be moderate or low, due to the methodological issues within the studies available.

Where there is no evidence to either support or refute practice, no recommendation is made. Additionally, there is an occasional requirement for further research into specific fields of physiotherapeutic management of CF and these points have been highlighted by the authors of the relevant sections.

2. Physiotherapy National Standards of Care for people with Cystic Fibrosis (2020)

How to use the standards

The standards have been developed in association with the following documents (note these may be updated or superseded since publication of this document), which should be consulted as required.

- NHS England National Service Specification – Cystic Fibrosis adult https://www.england.nhs.uk/wp-content/uploads/2018/08/Levofloxacin-nebuliser-solution-for-chronic-Pseudomonas-lung-infection-in-cystic-fibrosis-adults.pdf
- NHS England National Service Specification – Cystic Fibrosis children https://www.england.nhs.uk/wp-content/uploads/2018/07/a01Sb-spec-cystic-fibrosis-child.pdf
- Clinical Commissioning Policy: Inhaled Therapy for Adults and Children with Cystic Fibrosis https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a01-policy-inhld-thrpy-cf.pdf
- Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis Third Edition (Cystic Fibrosis Trust, 2017)
- Clinical Guidance for the Physiotherapy Management of Screened Infants with Cystic Fibrosis (ACPCF Physiotherapy Guidance Paper 2020)
- Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient. Section 3, Cystic Fibrosis (Joint BTS/ACPRC guideline 2009)
- Quality Assurance Standards for Physiotherapy Service Delivery (CSP 2013)
- Code of Members Professional Values and Behaviour (CSP 2011) https://www.csp.org.uk/publications/code-members-professional-values-and-behaviour
- *Pseudomonas aeruginosa* Infection in People with Cystic Fibrosis. Suggestions for Prevention and Infection Control. Second Edition. (Cystic Fibrosis Trust, November 2004)
- Methicillin-resistant *Staphylococcus aureus* (MRSA). (Cystic Fibrosis Trust, April 2008)
- The *Burkholderia cepacia* complex. Suggestions for Prevention and Infection Control Second Edition. (Cystic Fibrosis Trust, September 2004)
- Laboratory Standards for Processing Microbiology Samples from People with Cystic Fibrosis (Cystic Fibrosis Trust, September 2010)
- NTM guidelines: Suggestions for Infection Prevention and control of *Mycobacterium abscessus*. (Cystic Fibrosis, Trust 2017) (Amended March 2018)
- National Consensus Standards for the Nursing Management of Cystic Fibrosis (Cystic fibrosis Trust, 2001)
- Nutritional Management of Cystic Fibrosis (Cystic Fibrosis Trust, 2016)
- Pharmacy Standards of Care (Cystic Fibrosis Trust, 2011)

European Cystic Fibrosis Society guidelines:

- European Cystic Fibrosis bone mineralisation standards (Journal of Cystic Fibrosis, 2011)
- European Cystic Fibrosis Society Standards of Care: Framework for the Cystic Fibrosis Centre (2014)
- European Cystic Fibrosis Society Standards of Care: Best Practice guidelines (2014)
- European Cystic Fibrosis Society Standards of Care: Quality Management in cystic fibrosis (2014)
- Guidelines for the diagnosis and management of distal intestinal obstruction syndrome in cystic fibrosis patients (Journal of Cystic Fibrosis, 2011)
- Best practice guidance for the diagnosis and management of cystic fibrosis-associated liver disease (Journal of Cystic Fibrosis, 2011)
- End of Life Care for Patients with Cystic Fibrosis (Journal of Cystic Fibrosis, 2011)
- Guiding principles on how to manage relevant psychological aspects within a CF team: Interdisciplinary approaches (Journal of Cystic Fibrosis, 2011)
- New clinical diagnostic procedures for cystic fibrosis in Europe (Journal of Cystic Fibrosis, 2011)
- Chronic *Pseudomonas aeruginosa* infection definition: EuroCareCF Working Group report (Journal of Cystic Fibrosis, 2011)
- Pulmonary exacerbation: Towards a definition for use in clinical trials. Report from the EuroCareCF Working Group on outcome parameters in clinical trials Journal of Cystic Fibrosis Volume 10 (2011)
- Travelling with cystic fibrosis: Recommendations for patients and care Team members (Journal of Cystic Fibrosis, 2010)
- Guidelines for the management of pregnancy in women with cystic fibrosis (Journal of Cystic Fibrosis 2008)

NICE guidance:

- Cystic fibrosis: long-term azithromycin (NICE 2014)
- Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis (NICE 2013)
- Mannitol dry powder for inhalation for treating cystic fibrosis (NICE 2012)
- Cystic fibrosis: diagnosis and management (NICE 2017)
- Cystic fibrosis: Quality standard [QS168] (NICE 2018)

The majority of people with CF in the UK receive all or some of their care from a specialist CF centre. In some circumstances, particularly in the care of children, network care arrangements between a specialist CF centre and the network clinic have been developed.

A safe and effective specialist CF service will require a team with appropriate levels of experience, knowledge and skill.

The standards are set out under the following headings:

1. Staffing
2. Service provision
3. Facilities
4. Equipment
5. Clinical standards
6. Infection Control
7. Professional development and training

Standard 1: Staffing

People with cystic fibrosis will be cared for by physiotherapists with an appropriate level of expertise in the physiotherapy management of cystic fibrosis.

CF specialist centres

A CF specialist centre must be led by a Principal CF Physiotherapist (Band 8).

Definition of a principal CF physiotherapist

- Works within in a regional centre with a minimum of 50 people with CF.
- Has a minimum of 5 years' experience working as an Advanced CF Physiotherapist (Band 7).
- Maintains CF-specific continuing professional development including annual attendance at National and International Conference.
- Required to undertake CF-specific clinical audit, quality improvement and research.
- Required to provide CF specialist clinical education at graduate and post-graduate level.

The Principal CF Physiotherapist post must be underpinned by Advanced CF Physiotherapist post(s) (band 7 or above).

Definition of advanced CF physiotherapist

- Works within in a centre/clinic with a minimum of 50 people with CF (adults or paediatrics) or working in a network clinic with responsibility of delivering CF specialist care under the supervision of a regional centre.
- Has a minimum of 3 years' experience assessing and treating a CF specialist caseload.
- Maintains CF-specific continuing professional development including annual attendance at National and International Conference.
- Required to teach and supervise the specialist physiotherapists.

The number of Advanced CF Physiotherapist posts will depend on the size of the centre and the role and responsibilities of the posts.

The complexity of the caseload requires robust cross cover arrangements between the Principal CF Physiotherapist and the Advanced CF Physiotherapist posts.

In addition to these posts, multidisciplinary teams in large and/or complex specialist CF centres benefit from the strategic leadership and expertise provided by a Consultant Nurse or a Consultant Allied Health Professional Post.

Recruitment to these pivotal physiotherapy posts will be undertaken in collaboration with the Clinical Director of the CF centre.

Staffing will include an appropriate skill mix to meet the recommended staffing levels.

	75 patients	150 patients	250 patients	>250 patients
Adult Centres (WTE)	2	4	6	Increase of 2 WTE / 75 patients
Paediatric Centres (WTE)	2	3	4	Increase of 1 WTE / 100 patients

The recommended qualified physiotherapy staffing levels: (working group, 2015)
The table shows the recommended Whole Time Equivalent (WTE) of qualified Physiotherapists for a 5-day physiotherapy service. Please note that these staffing levels refer to both specialist centres and network clinics. Staffing levels for adult centres will be maintained at the ratio of 2 WTE physiotherapists per 75 people with CF to reflect the requirements of larger numbers of adult patients as we see life expectancy improve. In addition, as patients become older, they will potentially present with other co-morbidities necessitating increased supportive care (eg cancer, heart disease).

The mechanism for weekend, on-call and 7-day provision will not impinge on the weekday staffing levels. Guidance within the Chartered Society of Physiotherapy (CSP) seven-day extended hours service pack will be observed (CSP 2014a).

Continuity of care is known to improve health outcomes and patient satisfaction for people with long-term conditions. Continuity of care can be supported by the use of static specialist CF Physiotherapists to both underpin the lead posts already described and to consistently achieve the recommended staffing levels. It is also recognised that rotational physiotherapy posts (Band 6 and Band 5) create the opportunity to train and build a CF specialist workforce and offer succession planning for the future. However, rotational staff should be used cautiously, with careful consideration to ensure that skill mix, continuity of care and the stability of staffing levels all underpin workforce planning.

A safe and effective specialist CF service requires a team with the levels of experience, knowledge and skill as recommended below. This should be used as a framework for local application.

Definition of a Specialist Physiotherapist
Physiotherapists developing clinical expertise in the physiotherapy management of CF, in either a static or wider rotational post, or community staff who treat individuals with CF as part of a mixed caseload.

- Working in either a specialist centre or a CF network clinic.
- At least 2 years post qualification.
- Will have access to specialist advice from the principal CF Physiotherapist or Advanced CF Physiotherapy Practitioner.
- Maintains own competencies and skills through continuing professional development relevant to CF practice.

Definition of a physiotherapist
Qualified physiotherapists in a wider rotational post.

- Requires daily supervision and specialist advice from the Principal CF Physiotherapist, Advanced CF Physiotherapist or Specialist Physiotherapist. Will not be required to work in isolation of CF specialist physiotherapists

Definition of technical instructors (non-graduate physiotherapists) and Physiotherapy Assistants
This staffing group must work within their scope of practice (CSP scope of practice for physiotherapy assistants (2014)).

- Must be an ongoing competency-based training, development and assessment programme in place.
- Must have access at all times to support and advice from the principal CF Physiotherapist, Advanced CF Physiotherapist or Specialist Physiotherapist.

Network clinics

Care at each clinic visit and inpatient stay must be either delivered by, or directly supervised by, an Advanced Physiotherapist (Band 7).

The Advanced Physiotherapist must have strong links and regular two-way communication with the Principal CF Physiotherapist at the specialist CF centre.

Continuity of care is known to improve health outcomes and patient satisfaction for people with long-term conditions. Continuity of care is best achieved by the use of static Specialist CF Physiotherapists (band 6) to both underpin the lead posts already described and to achieve the recommended staffing levels. Non-specialist rotational physiotherapy posts (Band 6 and Band 5) will be used cautiously as they cannot contribute to continuity of care and have a large training requirement. These will represent no more than 10% of the CF physiotherapy work force.

Where clinical posts are shared with other services, there must be strategies in place to ensure that the demands from other services do not result in a disproportionate amount of time spent providing care to the non-CF case load.

All physiotherapists who are permanently part of teams providing care for people with CF must:

- have access to training and continuing professional development opportunities in CF; and
- follow the Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis (ACPCF 2020).

Standard 2: Service provision

Individuals with CF will receive supportive physiotherapy interventions from appropriately skilled individuals at all stages of their life in a range of different care settings. This will be supervised and directed by the Principal CF Physiotherapist in partnership with an Advanced CF Physiotherapist.

Care setting outpatients

Multidisciplinary clinic

All individuals with CF will receive the following care.

- They will be seen by a Specialist Physiotherapist at each clinic visit. Clinic physiotherapy provision will be supervised, and long-term plans directed by an Advanced or Principal CF Physiotherapist.
- They will see the Principal CF Physiotherapist at least twice a year (one of these may be the annual review visit) and more frequently if required
- They will have open access to specialist physiotherapy support between clinic visits when needed such as during a course of antibiotics, after a change of technique or if any concerns arise. Appropriate facilities and technology will be in place to provide this intervention either face to face or remotely. This should be based on clinical need alongside consideration of easy and convenient access to care.

Annual review

NICE quality standard QS168 (2018) requires members of CF MDT to meet annually to review assessment results and treatment for all people with CF. Disease progress must be reviewed and care adjusted as needed to prevent or limit symptoms, complications and disease progression. In order to fulfil this requirement the following conditions will be met.

- The physiotherapy annual review will be carried out by the Principal CF Physiotherapist or an Advanced CF Physiotherapist. The Principal CF Physiotherapist will provide regular clinical supervision to the Advanced CF Physiotherapists undertaking annual review assessments and plans.

- There will be sufficient time allocated at annual review to address airway clearance, exercise plans (including exercise testing), inhalation therapies (and associated devices), musculoskeletal/posture and continence issues and gastro-oesophageal and sinus disease.
- There will be treatment/referral pathways in place for management of musculoskeletal, continence or sinus issues should they arise.
- An individualised, goal-orientated physiotherapy plan will be developed in partnership with the person with CF (and carers if appropriate) and communicated to the physiotherapy and multidisciplinary team.
- There will be processes in place for submission of accurate physiotherapy-related national registry and quality dashboard data, subject to patient consent and national requirements.

Inpatients

There will be adequate staffing and appropriate skill mix to ensure that the following conditions are met.

- Inpatient care packages are delivered by a team led by an Advanced CF Physiotherapist, with oversight and expert intervention easily available from a Principal CF Physiotherapist.
- All individuals with CF admitted to hospital for inpatient care will have access to physiotherapy assessment and treatment. There will be an initial assessment and regular review of patient progress by an Advanced CF Physiotherapist.
- People with CF who are admitted to hospital will be entitled to optimisation of physiotherapy and will be offered a minimum of twice-daily treatment, more regularly if required (unless an alternative regimen is agreed by the person/carer and the Advanced CF Physiotherapist).
- Individuals with CF and/or their carers will not be expected to provide their own inpatient physiotherapy because of shortfalls in physiotherapy staffing levels.
- Individuals with CF admitted for inpatient care will have opportunities to carry out targeted exercise programmes on a daily basis.
- Physiotherapy to support airway clearance will be available at weekends in line with weekday treatment plans. It will be delivered by physiotherapists trained and competent in CF physiotherapy provision.
- An emergency on-call physiotherapy service will be available to inpatients with CF during out of hours if required.

Community

Home care physiotherapy (where appropriate) will be provided by an Advanced CF Physiotherapist at times of particular need, for example:

- at diagnosis;
- to provide school visits on starting primary or secondary school if required;
- when additional support is required to implement changes to a treatment plan eg airway clearance modifications, new inhaled therapy regimens, exercise programmes;
- to support with delivery of exercise programmes where additional support may be required eg prehab, accessing community gyms, change in health status;
- to support during the peri-natal period;
- to support adherence with complex treatment regimens;
- to assist the provision of palliative care at home;
- to resolve complex oxygen/non-invasive ventilation issues; and/or
- where optimisation of physiotherapy is required during home IV treatment.

Specific life stages

New diagnosis

- All newly-diagnosed people with CF (either through newborn screening or later diagnosis) will see a Principal CF Physiotherapist.
- Care may be provided jointly by the Principal CF Physiotherapist and the Advanced CF Physiotherapist, but there will be a clear management plan with oversight and input from the Principal CF Physiotherapist and regular communication.
- For infants “Recommendation of Practice” stated in the Clinical Guidance for the Physiotherapy management of Screened Infants with Cystic Fibrosis (ACPCF Physiotherapy Guidance Paper 2020) will be followed.
- For late diagnosis, following assessment, a physiotherapy management plan will be advised appropriate to clinical manifestation.

- Frequency of input will be tailored to the individual, but frequent assessment and advice will be required in the months following diagnosis. Access to physiotherapy will be weekly in the months following diagnosis.

Transition

- All people with CF transitioning from paediatric to adult CF care will have appropriate input from the relevant adult, paediatric and network physiotherapy services throughout the transition process, utilising a coordinated and documented transition program such as Ready Steady Go Hello.
- Processes will be in place to allow ongoing communication between the relevant physiotherapy services during transition in order to optimise the support provided to the individual and their families.
- The Principal or Advanced CF Physiotherapist will carry out the initial physiotherapy consultation on transition to adult services. An individualised physiotherapy plan will be developed in partnership with, and communicated to, the person/carer and the receiving physiotherapist and multidisciplinary team.

Surgery

All people with CF undergoing surgical procedures (eg port insertion, PEG insertion) should have access to specialist physiotherapy to optimise respiratory status pre-operatively and provide appropriate support in the post-operative period. Depending on the severity of disease, the surgery and the associated risks, physiotherapy plans and modifications will likely require regular review and oversight from the Advanced and Principal Physiotherapists.

Pregnancy

There should be regular specialist physiotherapy support throughout and after pregnancy for modification and optimisation of airway clearance, exercise programmes, inhaled therapies and screening for musculoskeletal and continence issues, with appropriate referral pathways in place. All pregnant mothers with CF will have an assessment by the Advanced and/or Principal Physiotherapist during hospital admissions or when changes to inhaled treatments or airway clearance techniques are required.

Transplantation

- There will be appropriate specialist physiotherapy support in the work up for transplantation with oversight from the Principal Physiotherapist for the optimisation of airway clearance, inhalation therapies, exercise, oxygenation and ventilation needs. Where appropriate, complementary therapies may be considered for symptom relief.
- There will be communication between the physiotherapy team at the individual's CF centre and the transplant centre with a clear physiotherapy management plan.
- There will be appropriate specialist physiotherapy input following transplantation for support, with exercise programmes and inhalation therapies. Additional input should be provided as required, eg for optimisation of airway clearance or sinus management.

End of life care

There will be appropriate specialist physiotherapy input throughout the stages of end of life care, with oversight and expertise provided from both the Principal and Advanced CF Physiotherapists to support individuals with symptom relief through optimisation of airway clearance, oxygenation and ventilation as required. Complimentary therapies may be considered for pain relief, breathlessness and anxiety management.

Physiotherapy intervention

All physiotherapists carrying out physiotherapy interventions for people with CF will have received appropriate competency-based training and will be directed under the supervision of the Advanced or Principal CF Physiotherapy. Where patients' needs are acute or complex (for example NIV set ups) treatments should be directed by the Advanced or Principal Physiotherapist and opportunities for supervision sought to ensure experience and learning is shared.

Airway clearance techniques

- All individuals undergoing changes to airway clearance techniques will receive the necessary education and support, with age appropriate verbal and written instruction.
- Processes will be in place for regular assessment and monitoring of treatment response, including any adverse effects.
- A structured adherence programme will be available to support individuals with changes to treatment regimes.

Exercise

- All individuals undergoing changes to exercise programmes will receive the necessary education and support, with age-appropriate verbal and written instruction.
- Processes will be in place for regular assessment and monitoring of treatment response, including any adverse effects.
- A structured adherence programme will be available to support individuals with changes to treatment regimes.

Inhalation therapies

- All people with CF will have a regular, structured review of inhaled therapies (including mucoactive agents), with any alterations to drug regimens or delivery devices being discussed with the Principal or Advanced CF Physiotherapy Practitioner.
- All people with CF will have access to inhaled therapies in accordance with the NHS England policy or the policy of their devolved nation.
- New inhaled therapies will be initiated by the specialist CF centre or by the network clinic in discussion with the specialist CF centre.
- Appropriate delivery devices will be provided, with replacement of consumables at the recommended intervals.
- For any new inhaled therapy, a formal drug response assessment will be undertaken. A supervised test dose will be carried out in the hospital environment with objective assessment for post-dose broncho-constriction, according to local protocol and standard operating procedures (Appendices VIa-e).
- Physiotherapy staff undertaking drug response assessments will have undergone appropriate competency-based training.
- All individuals undergoing changes to inhaled therapies will receive the necessary education and support, with age-appropriate verbal and written instruction.
- Processes will be in place for regular assessment of lung function and subjective reporting to ensure on-going tolerance and identification of any adverse effects.
- Delivery methods will take into consideration optimisation of drug delivery and adherence to treatments.
- A structured adherence programme will be available to support individuals with changes to inhaled treatment regimes.

Non-invasive ventilation (NIV)

- Physiotherapy staff initiating or altering NIV, either for ventilatory failure or supporting airway clearance techniques/exercise, will have undergone appropriate competency-based training and supervision.
- All individuals with CF will receive the necessary education and support, with age-appropriate verbal and written instruction and supervised treatments where needed.
- Processes will be in place for regular assessment and monitoring treatment response, including any adverse effects.

Musculoskeletal management

- Processes will be in place to ensure annual assessment and monitoring of posture with ongoing support as required.
- All individuals with CF should be screened for musculoskeletal signs and symptoms, with referral pathways in place to access musculoskeletal specialists where appropriate.
- All individuals with CF should be screened for urinary and faecal incontinence, with referral pathways in place to access continence specialists where appropriate.
- All individuals with CF will receive the necessary education and support, with age-appropriate verbal and written instruction.

Sinus management

- All individuals with CF should be screened for sinus symptoms, with referral pathways in place to access ENT specialists where appropriate.
- All individuals with CF will receive the necessary education and support, with age-appropriate verbal and written instruction.

Standard 3: Facilities

People with CF will have access to age-appropriate facilities for their physiotherapy care as inpatients and outpatients.

- Facilities will recognise the need for privacy and dignity when carrying out airway clearance and exercise, this should include single rooms for airway clearance and ensuite facilities where possible.
- Adequate facilities for exercise will be available to people with CF as inpatients, eg gym with adequate range of exercise equipment and sufficient space/facilities for aerobic exercise and exercise testing to be carried out.
- Facilities for physiotherapy treatment must enable adherence with national and local infection control policies.

Standard 4: Equipment

All people with CF will be provided with appropriate respiratory and exercise equipment and will be trained in its use and maintenance.

- There must be written protocols regarding the use of the equipment used by and issued to people with CF.
- People with CF will be provided with the respiratory equipment they require for use at home, eg to nebulise medication, for airway clearance, for oxygen delivery and humidification.
- People with CF/carers will be trained in the use of equipment supplied for home use.
- Written instructions regarding the use and maintenance of equipment provided for home use (including cleaning/disinfection/sterilisation as applicable) will be offered to all people/carers and will be in line with manufacturers guidance.
- All equipment used by people in hospital or at home will be serviced and maintained (including cleaning/disinfection/sterilisation as applicable) according to the manufacturer's instructions and/or national and local policies.
- There must be a clear and adequate budget available for the provision of respiratory equipment, including advanced, fast and efficient nebuliser devices eg vibrating mesh technology (VMT) nebulisers. There will be clear responsibility as to who holds this budget.

Standard 5: Clinical standards

Physiotherapy clinical care will be based on the best evidence available; ACPCF, CF Trust and NICE guidelines, protocols and consensus documents will be followed.

- Copies of all documents listed at the start of this document will be available in all hospital areas where people with CF receive care.
- All physiotherapy staff caring for people with CF will be expected to read these documents during their induction period and areas for training and development identified.
- There must be evidence that the physiotherapy service provided for individuals with CF is regularly evaluated through clinical audit and quality assurance programmes.

Standard 6: Infection control

All physiotherapists working with people with CF will consider issues of hygiene and the prevention of cross-infection.

- All staff will have knowledge of and work to: Local Infection Control Policies, CF Trust guidelines relating to prevention and infection control with *Burkholderia cepacia* complex, *Pseudomonas aeruginosa*, *Mycobacterium abscessus* and MRSA in people with CF. Local Infection Control Policies should make specific reference to physiotherapy management in different settings.
- All people with CF will have their own home respiratory equipment eg airway clearance devices, nebuliser devices and consumables, oxygen equipment and NIV.
- Some respiratory equipment eg Intermittent Positive Pressure Breathing (IPPB), High Frequency Chest Wall Oscillation (HFCWO), High flow Nasal Oxygen (HFNO), Ultrasonic nebulisers, Cough Assist and NIV devices may be used by more than one person in the hospital setting. Local standard operating procedures relating to minimisation of cross-infection between people with CF will be in place for these devices.
- Physiotherapists will have access to records of individual microbiological status and be able to identify people at high risk of cross-infection.

- There will be rigid adherence to infection control policies when carrying out airway clearance, exercise, nebulisation and spirometry.
- All staff, including weekend staff, will take all reasonable precautions to reduce the risk of cross-infection in accordance with local policy. This will include rigorous hand-washing, decontamination of pulse oximeters, stethoscopes and exercise equipment between people with CF, wearing of aprons and gloves for airway clearance and careful handling of respiratory secretions (sputum pots to be covered and disposed of at least daily and soiled tissues disposed of immediately).
- All staff should be aware of the physiotherapy guidance around infection control and methods of decontamination of equipment found in the Standards of Care and Good Clinical Practice for the physiotherapy management of children and adults with CF Fourth Edition (2020).

Standard 7: Professional development and training

Physiotherapists caring for people with CF have a professional responsibility to keep up to date with current CF research and to continually update their skills and knowledge to provide the best possible clinical care.

All physiotherapists with permanent posts providing care to people with cystic fibrosis must adhere to the below requirements.

- Ensure they maintain their continuing professional development in general respiratory care and ensure they have adequate clinical skills to follow the Standards of Care and Good Clinical Practice for the physiotherapy management of children and adults with CF Fourth Edition (2020).
- Will be a member of, and regularly contribute to, the ACPCF specialist interest group and will attend local ACPCF meetings
- In addition to supporting local or regional CF study events, they will attend at least one national CF meeting annually. This will be the annual national ACPCF study event or a national CF study day/conference.
- Where appropriate submit research, case reports or quality improvement work to national and international conferences.
- The Principal CF Physiotherapist will attend annually a national and/or international conference. They will demonstrate knowledge of current CF research and be involved in CF research locally as appropriate.
- Have an annual appraisal and be able to provide evidence of meeting professional development plans.
- Seek feedback from people with CF using the physiotherapy services, to ensure that they continue to meet their needs, and feedback can be used to help direct future service improvements.

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The UK CF annual registry data report (2018). Available at: https://www.cysticfibrosis.org.uk/the-work-we-do/uk-cf-registry/reporting-and-resources

The following documents pertaining to prevention and control of infection are available at: https://www.cysticfibrosis.org.uk/the-work-we-do/clinical-care/consensus-documents

- *Pseudomonas aeruginosa* Infection in People with Cystic Fibrosis. Suggestions for Prevention and Infection Control. Second Edition. November 2004
- Methicillin-resistant *Staphylococcus aureus* (MRSA). April 2008
- The *Burkholderia cepacia* complex. Suggestions for Prevention and Infection Control Second Edition. September 2004
- Laboratory Standards for Processing Microbiology Samples from People with Cystic Fibrosis (September 2010)
- US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of *non-tuberculous mycobacteria* in individuals with cystic fibrosis." Floto RA, et al. Thorax 2016

Transition to Adult Services. Ready Steady Go: Available at: https://www.uhs.nhs.uk/OurServices/Childhealth/TransitiontoadultcareReadySteadyGo/Transitiontoadultcare.aspx

3. Outcome measures

Outcome measures are used for a variety of reasons including to assess the impact of the disease on daily function, assist in clinical decision making, assess the efficacy/effectiveness of treatment interventions within clinical practice and research, to assess the cost/benefit of a service and potentially to commission funding for a service. An outcome measure should be assessed for important clinimetric properties such as validity, reliability and responsiveness to treatment. The use of outcome measures relevant to physiotherapy are restricted by their complexity and feasibility. Feasibility is multifaceted and refers to financial, practical and ethical considerations, as well as patient and assessor acceptability and ease of use in the clinical setting (eg high resolution CT scan, radioisotope aerosol labelling carry risk to the patient; Lung Clearance Index is not yet used clinically but primarily in the research setting).

For the purpose of this document we have concentrated on outcome measures that could potentially be used to evaluate physiotherapy interventions.

3.1 Airway clearance

There is great difficulty in selecting outcome measures in cystic fibrosis. Many patients, especially in the paediatric population, have normal or near-normal imaging, clinical scores and exercise tolerance and do not produce sputum. This makes the selection of sensitive, responsive and clinically valid outcome measures in the evaluation of airway clearance techniques challenging. In a complex disease such as CF, other changes in treatment (not limited to airway clearance techniques) may affect outcomes.

Historically, outcome measures of convenience, which are easy to measure, were used in clinical trials. Alternative outcome measures are now emerging which may be useful both for the short-term assessment of ACT effect and for longer-term monitoring.

Outcome measures for airway clearance effect

Routine airway clearance techniques (ACTs) are recommended as part of CF management. There are many different ACTs and physiotherapists need to work together with their patients to create a regime suitable for each person. Assessment of the effect of ACTs needs to consider the relevance of the outcome measure. A measure assessing amount of sputum cleared will probably not be useful in a non-productive patient. Likewise, a patient with severe CF lung disease may not be able to complete a lengthy or effortful breathing test such as a multiple breath wash out or spirometry.

There are several papers illustrating the methodological and ethical issues in assessing ACTs[1-3] and currently there is a debate about what is a sensitive, responsive and clinically valid outcome measure to use when evaluating the effect of airway clearance. Most outcome measures used to assess ACT have no agreed minimally clinically important difference, which can make interpretation of change difficult.

Historically commonly used outcome measures have included spirometry, oxygen saturations and sputum volume or weight. While these are both readily accessible and easy to use within a clinical or research setting, several papers have questioned their validity and responsiveness when used to assess ACT effect.[1-6]

In relation to sputum, it has been suggested that amount of sputum cleared is not specific to airway clearance or alveolar recruitment, not sensitive to small changes and has limited repeatability as it is subject at times to the preference of the person whether or not to expectorate.[5,6] Sputum also could be swallowed, cleared after an ACT session, or contaminated by saliva, all which can result in over- or underestimations of ACT effect. Taking these difficulties into account, sputum volume or weight can be helpful when evaluating ACT effect in an appropriate individual. If used, strict controls on the methodology should be adopted such as use of graduated sputum containers for volume or calibrated scales for weight, to ensure accuracy.

Forced expiratory volume (FEV_1) is the most commonly used spirometric measure to assess ACT effect, but it can be difficult to demonstrate a change in this as it is effort dependent[7] and it may not be sensitive enough to detect small but possibly clinically significant changes as those over a session of ACT or in patients with mild disease.[3-5,8,9] Often now FEV_1 is found to be within normal limits, especially within the paediatric population and even rate of FEV_1 decline which has been suggested as a useful outcome, is thought to be minimal for a stable CF population. Furthermore, the nature of completing a forced expiratory manoeuvre, such as FEV_1, may create an airway reaction, which in its own way may influence the results of airway clearance, and there is no recognised best time point for performing spirometry after airway clearance.[10] Allowing for these potential problems, spirometry, when performed with a standardised technique, can be used on an individual basis to monitor a response to treatment and may provide clinicians with useful information.

Some studies investigating ACT effect have been published recently using other outcome measures such as the lung clearance index (LCI) which is derived from the multiple breath wash out test,[11-13] electrical impedance tomography (EIT),[14-16] radioaerosol techniques[17,18] or impulse oscillometry (IOS).[19-21] However, these studies are of variable quality due to small sample sizes, single treatment sessions or lack of detail into methodology. While the evidence for these newer measures is emerging, most are accepted for use as assessment tools in other contexts, but they have not been validated for use when assessing ACT effect. They often involve expensive equipment and/or lengthy test procedures which currently limits their use clinically. Work is being done comparing some of these newer measures against the historical measures of FEV_1 and sputum weight to assess ACT effect, and so far, good reliability and validity have been reported between study visits, but responsiveness over a session of ACT is yet to be established.[22] For example, changes in LCI in response to interventions such as airway clearance techniques can show heterogeneous results. Once obstruction within the airway is relieved, it allows a previous poorly-ventilated, distal lung unit to contribute to the LCI, increasing overall inhomogeneity and thus increasing LCI indicating a worsening of ventilation despite clearing the obstruction.[23]

Several studies have used the number of exacerbations over a set time period as an outcome measure, which a large robust multicentre trial[24] reported to be a valuable measure when comparing physiotherapeutic interventions. However, in a complex disease such as CF, other changes in treatment which are difficult to control for (not limited to ACTs) may affect outcomes during such a time period and need to be carefully considered when reporting changes.

Patient reported outcomes (eg CFQ-R quality of life questionnaire or VAS scales) can be easy to use and possibly the most useful in those with milder disease. Patient preference is key to a successful ACT regime and may be the most meaningful outcome to patients.

Many systematic reviews recognise a variety of outcome measures, while suggesting that further work is required to identify the most appropriate outcome measures for use in airway clearance interventions.[5,25-33] Future work needs to focus on clinimetric properties, reliability and acceptability for use across the disease trajectory (mild through to severe disease) and identifying a minimally clinically important difference for each outcome measure.

Recommendations

- Physiotherapists should use the best clinically applicable outcome measures to assess the efficacy of airway clearance techniques on an individual basis *(QoE – high)*.
- Outcome measures used may include:
  - spirometry;
  - sputum volume, weight, colour, ease of expectoration;
  - patient reported outcomes such as VAS scales or preference;
  - healthcare utilisation eg time to next exacerbation; and
  - physiological assessments such as LCI, IOS, radioaerosol techniques or EIT *(QoE – moderate)*.

Good practice points

- Factors influencing the choice of outcome measure for airway clearance need to be assessed prior to selection of an outcome measure to use. These include:
  - clinimetric properties of the test;
  - clinical relevance to the individual; and
  - context of use for eg ease of use in day to day practice or clinical trial.
- Outcome measures should be completed by professionals who are skilled and trained in performing that test, and in interpreting the results.
- Physiological assessments such as LCI, IOS, radioaerosol techniques or EIT may be used to evaluate the effect of airway clearance, however, it is acknowledged that to date their use for this purpose is still to be fully evaluated.

Outcome measures for long-term monitoring

Identification of change within a patient is essential at all stages for effective CF management, from the infant detecting early signs of lung disease to the end-stage patient requiring complex interventions. While in CF it is difficult to attribute change to the long-term effect of physiotherapeutic interventions alone, it is important for physiotherapists to be aware of the health status of their patients to help tailor airway clearance and exercise programmes to each individual and to assess each individual's response.

Traditionally CF physicians have used lung function decline (particularly FEV_1) to monitor health status. It is now recognised that early progression of lung disease is possible, in the absence of any notable symptoms and without changes in lung function, possibly even before lung function is adequately performed by the patient. Alternative outcome measures are now being utilised, which include computed tomography (CT)-based imaging, magnetic resonance–based imaging (MRI), the lung clearance index (LCI), which is derived from the multiple breath washout (MBW) test, impulse oscillation system (IOS), forced oscillometry technique (FOT) and quality of life.

Early progression of lung disease, in the absence of any associated symptoms, can be identified using CT-based imaging, with approximately one-third of patients diagnosed by newborn screening showing evidence of bronchiectasis at the age of 3 years.[34] There are limitations to the use of routine CT imaging due to the long-term cumulative exposure to radiation.

MRI–based imaging could be the radiation-free alternative, but many questions regarding its sensitivity and specificity remain. The information gained is limited on which of the MRI changes are clinically relevant and which, if tracked over time, can be correlated with a decline in respiratory function, as is currently the most widely utilised outcome measure.

MRI seems to be able to identify regional mucus plugging, which is of clinical importance.[35] However, scoring combines bronchiectatic changes and bronchial wall thickening, both of which may respond differently to therapeutic interventions, thus making the scoring system less meaningful.

LCI derived from the MBW test is a useful measurement of ventilation inhomogeneity and may go some way to identification of early airway dysfunction and tracking of disease progression,[36,37] particularly in the younger patients in whom spirometry is unreliable.[35] The MBW technique involves recording the clearance of an inert tracer gas from the lungs during tidal breathing. LCI is defined as the number of lung turnovers (ie multiples of FRC) required to reduce end tidal marker gas concentration to 1/40th of the starting value. A study by Horsley et al[38] found healthy control LCI values ranging between 5.0-7.5 and LCI values in CF subjects ranging from 6.3-20.4.

Stanojevic[37] found that a higher LCI score was associated with an increased frequency of pulmonary exacerbations and was closely linked to those individuals using inhaled antibiotics for chronic infection. When compared with healthy controls, LCI was elevated in people with CF during periods of upper respiratory infection, depicted by a cough.[37]

Kraemer et al[39] found that progression of CF lung disease is detected earliest by LCI, followed by FEF_{25-75}, FVC and finally FEV_1, and high rates of subjects had abnormal lung function that was not detected by FEV_1.

Compared with spirometry, LCI better reflects structural lung abnormalities shown on HRCT, therefore there is potential LCI could reduce the number of HRCTs being performed.[40,41] It can also be useful for detecting degree of lung damage in those children unable to give full effort in forced expiratory manoeuvre.[42] Stanojevic[37] found that a higher LCI score was associated with an increased frequency of pulmonary exacerbations and was closely linked to those individuals using inhaled antibiotics for chronic lung infection, especially *Aspergillus fumigatus* and *Pseudomonas aeruginosa*.

Although an extremely useful tool and whilst increasingly used as an outcome in clinical trials, as a reproducible measure, MBW is time consuming and test duration increases with disease severity. It also requires skilled operators and there are issues with tolerability and co-operation in the younger population, making feasibility in a clinical setting difficult.[41] Mulligan et al[42] found that children <6 years old struggled to perform washout in a technically correct manner, although a clear learning effect was observed with improved technique and shorter testing times on repeat visits.

Success rates are influenced by patient age and sedation is often used in infants and pre-school children to increase co-operation and feasibility. Stahl et al[35] found substantially higher success rates for LCI in those <3 years old with use of sedation than seen in previous studies of non-sedated infants. Kieninger et al[43], however, suggests that infants aged 3-14 weeks can produce similar results when tested in natural, non-rapid eye movement sleep as those in previous studies who were sedated, and suggests it may better reflect natural regulation of lung physiology. While feasible in younger infants, it becomes more challenging in older infants who may then require sedation and this in turn may reduce comparability.

While some studies look at decreasing washout time in an attempt to increase feasibility in a clinical setting (by decreasing washout to 1/20 rather than 1/40 of initial concentration) it may not be suitable in patients with mild disease as there is potential to miss information on ventilation distribution during later stages of washout.[44]

Standardisation of LCI is ongoing. Variables in protocols, such as washout time, interface, differences in the gas, requirement of sedation, and body position that are required for MBW measurements across different age groups can influence results.[35]

Saunders et al[41] suggests LCI is most useful as a monitoring tool in infants and pre-school children, and also in older patients with well-preserved spirometry. In contrast, for those patients with marked airflow obstruction, LCI adds little clinical information and is more cumbersome than spirometry.

Ratjen[34] suggests that the use of LCI and MRI in parallel would enable appreciation of their sensitivity and specificity and their responsiveness to therapeutic interventions, with long-term monitoring in those with normal spirometry to test strategies that may delay or prevent irreversible lung damage.[35]

Impulse oscillometry system (IOS) requires tidal breathing and no expiratory manoeuvres, it is easier and fairly comfortable to perform, and therefore may be more suited to the younger or severely affected patient for whom other outcome tests are unreliable or too challenging to perform. IOS is suited to exploring both resistance of the respiratory system (the “in phase” part of impedance) and reactance (the “out of phase” part of impedance) and for this reason evaluates both central and peripheral airways.[19] A study by Buchs[19] assessing the impact of 2 weeks of treatment on 34 patients using standard spirometry and IOS concluded that IOS was not as sensitive as FEV_1 at monitoring response to a course of therapy, but there was indication of improvement in the peripheral airway reactance.

Within-breath forced oscillometry technique (FOT) measuring mechanical impedance and reactance may provide additional information on top of more commonly-used tests such as spirometry, body plethysmography, or LCI.[45] In a study of 33 children, CF lung disease affected reactance (peripheral airways) more than resistance (central airways), indicating that airways obstruction occurred at a peripheral level.[35] This suggestion of the occurrence of dynamic airways compression may eventually lead to expiratory flow limitation (EFL), frequently associated with chronic dyspnoea.[46,47] Dyspnoea is frequently the first symptom that people with CF present to their primary physician. Steven[48] suggests that expiratory flow limitation, as characterised by pulmonary hyperinflation, has a closer relationship to chronic dyspnoea than FEV_1.

It is likely that EFL has significant clinical implications in CF, as two of the most important treatments, exercise and chest physiotherapy, rely on the ability to increase expiratory flow rates.[46] This may impair airway clearance and cause excessive dyspnoea and fatigue

during treatment.[46] The clinical importance of hyperinflation during exacerbations is further underlined by demonstrating that it is indices of increased air-trapping, rather than FEV_1, that were the strongest predictors of dyspnoea severity.[47]

EFL when identified at rest, may be indicative of accelerated lung function deterioration in subjects with CF.[49] Vilozni[49] explored the longitudinal effect of EFL on lung function and clinical condition in CF and demonstrated that onset of EFL correlates with a moderately reduced FEV_1 without associated pulmonary exacerbation. Following the onset of EFL there is significant clinical deterioration, eg increased frequency of hospitalisation and spirometry changes thus increasing morbidity.

The ease of measuring EFL by relating the flow decay of both tidal flow and $FEF_{25–75\%}$ should be considered as an aid in explaining sudden continuous falls in FEV_1 without the presence of exacerbation.[49]

Rate of exacerbations or time to next admission or infection have been used as outcome measures for long-term monitoring. When using these measures, it is important to acknowledge the multiple influences on the CF patient during a time period which may not be wholly attributable to one intervention. It is also essential to clearly define the parameters and definition of an exacerbation to ensure accurate reporting of events throughout the whole CF healthcare team.

Quality of life (QoL) and subjective health reporting are considered to be important predicators of survival, with many studies finding reduced QoL scores associated with poorer lung function and 6-minute walking distance (6MWD).[36] However, even though QoL data and 6MWD represent global estimations of disease progression, they are not sensitive enough to replace spirometry or LCI.[36] Furthermore, Ratjen[34], reports that although functional assessments can reflect disease severity, the consequences of repeated infection and inflammation in CF is structural lung damage which may not be identified by a functional assessment.

Recommendations

- Physiotherapists should use the best clinically-applicable outcome measures for the long-term monitoring of patients, in partnership with the wider CF team and being aware of the requirements of each individual patient *(QoE – high)*.
- The outcome measures used may include:
  - spirometry;
  - healthcare utilisation eg rate of exacerbations;
  - lung clearance index;
  - CT or MRI imaging;
  - IOS; and/or
  - patient reported outcomes such as quality of life (*QoE – high*).

Good practice points

Physiotherapists should be aware of the health status of their patients to help tailor airway clearance and exercise programmes to each individual and to assess each individual's response.

- Factors influencing the choice of a long-term monitoring outcome measure include:
  - clinimetric properties;
  - ease of use in practice including equipment availability and training of staff; and
  - clinical relevance to the individual.
- For LCI use, it is essential that the equipment is suitable for the patient, and that tests results completed with differing equipment or protocols must not be extrapolated.
- LCI, alongside microbiological results and interventions is most useful as a monitoring tool in infants, pre-school children, those unable to perform reliable spirometry and also in older patients with well-preserved spirometry.[50]
- IOS may be useful to track changes after IV antibiotic therapy, but this improvement may be insufficiently evaluated using IOS alone so should be combined with another outcome measure.

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3.2 Induced sputum

Sputum collection is essential to detect changes in pathogens and guide the management of respiratory disease. It may be one of the most valuable methods for monitoring disease activity as lung function and imaging may be insensitive especially in the case of younger children.[1,2] Spontaneously expectorated samples have been shown to be representative of lower airway secretions.[3] However, there are many people with CF, particularly children, who are unable to spontaneously produce a valid sample.

Bronchial-alveolar lavage (BAL) is often considered the "gold standard" for obtaining sputum to identify microbial and inflammatory changes in the airways. However, this technique is expensive, requires sedation, is risky, invasive and is potentially limited to certain areas of the lungs.[1,2,4,5,6]

Some studies show that sputum induction provides as valid a sample as BAL, but is cheaper, easier to do, non-invasive and reproducible.[4,7,8] Other studies have shown induced sputum sampling to be superior to samples obtained by BAL[2,6,7,9-11]. Some studies have indicated that sputum induction has produced a more representative sample of the bronchial tree than spontaneously expectorated sputum.[11-14]

Sputum induction has been demonstrated to be safe to use with young children with a large number of papers demonstrating that it is well-tolerated and that there were no adverse events.[1,4,5,8,15,16] Some studies have included children as young as one month old with a high percentage of success.[1,2,8,17] Sputum induction has not been found to promote significant inflammatory changes in the airways.[2,5] Sputum induction, with or without suction combined, has been demonstrated to have a statistically significantly higher microbial content than cough swabs when compared directly.[2,8]

To date there has not been a universally agreed procedure for sputum induction.[11] Precautions/ contraindications to this technique are considered to be similar to those in the TB sputum induction guidelines.[19] Consideration should be given to the fact that sputum induction can cause bronchospasm and excessive coughing and should not be carried out in people with CF where this can be harmful.[20]

The various components of induced sputum will be discussed individually.

Technique considerations

Oral hygiene
It is considered good practice to rinse out the mouth with water and/or brush teeth to get rid of any potential contaminants.[3,12,19,20]

Short acting bronchodilator prior to induced sputum
A number of studies used a short-acting bronchodilator prior to commencing induced sputum.[1-4,9,11,13,15,22,16] However, some studies omitted to pre-dose with a bronchodilator considering that they can have a paradoxical effect and increase airway instability.[5] There was no significant fall in FEV_1 in these groups.[5,22]

Nebuliser
It has been suggested that the nebuliser device used, the size of the respirable particles of aerosol generated and rate of aerosol generation may affect the success of the procedure, however, when nebulisers were directly compared this was not substantiated.[23,24] The majority of studies reviewed used ultrasonic nebulisers for the technique. Other studies used mesh or jet nebulisers without adversely affecting the samples obtained.

Saline concentration
There are no valid direct comparisons of the concentration of hypertonic saline used for sputum induction. Due to the irritant nature of hypertonic saline, higher concentrations may be more effective but may have a higher risk of bronchospasm.[5,25] This was reversible with use of a short-acting bronchodilator. Some studies have suggested that higher concentrations may be more effective, however, it is unclear whether it was the duration of nebulised saline that resulted in successful samples.[23] Studies looking at the effect of mucociliary clearance in relation to concentration of hypertonic saline in CF found that higher concentrations (7% and 12%) significantly improved mucociliary clearance.[25] If a patient is at risk of bronchospasm, it is recommended to start at a lower concentration and gradually increase it until a sample has been obtained.[19]

Monitoring
The majority of studies have performed spirometry to monitor for changes in FEV_1 during induced sputum.[8,13,15,15,26] Observing the patient for adverse effects as well as continual SpO_2 monitoring and auscultation are adequate, with use of short acting bronchodilator to reverse any clinical signs of bronchospasm.[1,2,4,21] Some studies used SPO_2 monitoring. Induced sputum should be stopped if $SpO_2 < 90\%$[3,27] or if the patient is showing signs of bronchospasm.

Airway clearance techniques
There are no published studies looking at the direct effect of airway clearance techniques with induced sputum. One study suggested that samples are only obtained from the central airways[12] as the sputum is generally only cleared by a cough; however, other studies have found evidence of sputum from the peripheral airways and alveolar space,[6,8,9,11,28] which may suggest that samples from the periphery may be easier to yield if airway clearance techniques are employed in combination.

Suction/cough swabs
In order to gain an effective sample, the option of performing oropharyngeal suction or a cough swab following sputum induction can be used. There was no significant difference in culture yield observed between post induction sputum samples collected by nasopharyngeal suction, voluntary expectoration or oropharyngeal suction in one study.[17]

Oropharyngeal cough swabs, in combination with induced sputum, was previously found effective in obtaining valuable samples,[21] however, a recent study found no additional bacterial yield post sputum induction with cough swabs.[2]

Cough swabs are unable to accurately assess for fungal or mycobacterial infections and therefore should not be used for this purpose.[16,17]

Pain/discomfort
These procedures can be distressing for patients. A study looking at pain associated with sputum sampling methods found that patients can experience mild to moderate pain with cough swabs and induced sputum.[14]

Infection control
There have not been any studies that specifically look at infection risk with CF during sputum induction. There is no mention of infection control precautions detailed in the studies reviewed and there is continued debate as to whether use of nebulisers and chest physiotherapy are aerosol-generating procedures.[29] It was found that nebulisers did produce aerosol, but with variable particle size. A study looking at *Pseudomonas aeruginosa* in cough aerosol reported that it remained viable in the air in 78% of patients after 45 minutes.[30]

Currently we are unaware of the transmissibility of bacteria such as *Mycobacterium abscessus,*[31] how long their aerosol remains viable and how far they travel. It is suggested that the treatment room be left empty for as long as possible following a procedure, in concordance with local infection control policies and dependent on air exchanges per hour. Ideally the procedure would take place in a negative pressure room.[16]

For additional information on infection control please see section 14 of this document.

Sputum induction is carried out when clinically indicated or to obtain an alcohol and acid fast baccili (AAFB) sample to assess for mycobacteria. There is some evidence to suggest the routine inclusion of sputum induction and AAFB sampling at annual review can detect non-tuberculous mycobacteria sooner than clinical signs[16] and may help to allow appropriate cohort segregation and improve infection control.[32]

Recommendations

- Induced sputum should be considered when clinically indicated as a means of sampling the microbiome (a community of microorganisms, such as bacteria, fungi, and viruses) that inhabit a particular environment) of the CF lung, particularly in patients who do not expectorate sputum *(QoE – moderate)*.
- Monitoring should be continuous *(QoE – moderate)*.
- Stop induced sputum if there is subjective or objective wheeze, if SpO_2 falls below 90% or a fall in FEV_1> 20% (if using Spirometry) *(QoE – low)*.
- Induced sputum will be performed in a clinical area with resuscitation equipment available *(QoE – moderate)*.
- Perform induced sputum in a room with the door closed where the air from the room is exhausted to the external environment, unless a well maintained HEPA filtration unit is in place *(QoE – moderate)*.
- Avoid anyone entering the room for 1-2 hours after induced sputum procedure, depending on the frequency of air exchanges *(QoE – moderate)*.
- Consult local infection control and prevention guidelines *(QoE – low)*.

Good practice points

- Consider use of induced sputum in place of cough swabs for pathogen surveillance in non-productive patients.
- Consider that this technique may be distressing for the patient, so try to alleviate this as able for example by use of distraction techniques.
- Brush teeth with a new toothbrush and water and rinse mouth with water prior to carrying out induced sputum to help avoid contamination of the sample.
- Consider using short-acting bronchodilator prior to sputum induction.
- Use an ultrasonic nebuliser if available, taking into consideration infection control policies.
- Use a low output device, eg jet nebuliser, if high output devices are not tolerated or not available. There is no current evidence evaluating vibrating mesh nebulisers in induced sputum.
- Use a higher concentration if able for induced sputum to optimise mucociliary clearance, ie 7%.
- Consider starting with a lower concentration of hypertonic saline, ie 3%, if the patient is at known risk of bronchospasm.
- Process samples produced later in the procedure if possible.
- Oropharyngeal suction with soft catheter and sputum trap can be performed if the patient is unable to expectorate.
- Oropharyngeal cough swab can also be considered if expectorated sputum or suction is not possible, however, the value of such a sample is questionable and can give false negative results.

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3.3 Exercise outcomes and exercise counselling

This chapter provides a contemporary overview of best practice recommendations for exercise testing people with CF. Several key articles have been published providing expert consensus on exercise testing practices for people with CF. We recommend these accompany the guidelines presented here.[1,2,3] Recommendations for the assessment of habitual physical activity and sedentary behaviours are also provided.

Exercise testing

Why perform an exercise test?
Exercise testing offers an integrated, objective assessment of the efficiency and performance of the lungs in combination with the cardiovascular, respiratory, and musculoskeletal systems of the patient. This information cannot be obtained from more static methods such as monitoring lung function, radiological investigations or measures of nutritional status that are routinely used in clinical practice. Much focus has been on the evaluation of aerobic fitness, since several studies have demonstrated that better aerobic fitness (peak oxygen uptake [VO_{2peak}]) is associated with greater 7-12 year survival in people with CF.[1,4,5]

Over the shorter-term, exercise evaluations can facilitate assessment of interval changes in clinical status, such that tests identifying poor exercise capacity for the degree of lung function deficit warrant prompt attention and act as an early warning of clinical deterioration. Exercise evaluations can assist with transplant stratification,[6] and for this reason, at least annual exercise testing is recommended for all patients by the Cystic Fibrosis Trust[7] and European CF Society.[8]

It is important to remember the wealth of information an exercise test provides, offering not only an indication of an individual's function but also the mechanism(s) responsible for any impairment to this (see figure in Appendix II). This information can also help us understand the response to treatment eg new modulator therapies.

People with CF may feel that participating in exercise testing demonstrates their ability to exercise at a higher intensity than anticipated thus freeing them from personal uncertainty and/or parental fears regarding future activities.

Exercise test results can facilitate exercise programmes tailored to the needs of each individual, eg improving fitness or maintenance in those with significant ventilatory limitation but good fitness levels[3] (see example Case Study Patient in Appendix IIb).

Who should perform an exercise test?
Annual exercise testing as a minimum is recommended for all people with CF, although the age at which routine and regular exercise testing begins depends on the type of exercise testing undertaken, as well as the physical and mental development of the child. Cardiopulmonary exercise testing (CPET) is recommended from 10 years of age.[8] This is as a guide for those using a cycle ergometer, as the participant must maintain a standard pedal speed and meet the minimum height requirement (128 cm for most cycle ergometers), which may preclude some children. Paediatric cycle ergometers are available and technically acceptable tests can be achieved in younger children.

Younger children (≥ 6 years) should be tested using validated field-based tests, eg 10 m modified shuttle walk test (MSWT) or iSTEP.[9] Even younger children can start to be tested to facilitate familiarisation with the exercise testing protocols and procedures and to encourage exercise participation.

When should an exercise test be performed?
Interval exercise testing is recommended for all children and adults with CF.[8] Exercise testing before and after significant change or intervention is recommended, eg before/after a new treatment (eg CFTR modulator)[10] or exercise programme. In addition, exercise testing plays a vital role in pre-transplant assessment, with both field tests and laboratory based CPET being validated for this purpose.[6]

A case study example, represented with permission from Urquhart & Saynor (2018)[3] identifying the need for intervention and the subsequent evaluation of the test is presented in Appendix II.

What to do when preparing for an exercise test?
CPET:

- Avoid strenuous exercise for 24 hours before CPET.
- Refrain from eating for at least 2 hours before CPET.

- For individuals currently taking bronchodilators, usual pre-exercise bronchodilator and dose should be administered at least 10 minutes before the test.

Field tests:

- Avoid strenuous exercise for 2 hours before test.
- Refrain from eating for at least 1 hour before test.
- For individuals currently taking bronchodilators, usual pre-exercise bronchodilator and dose should be administered at least 10 minutes before the test.

10m-MSWT:

- Pre-recorded audio instructions played prior to test.
- To help the participant establish the first very slow speed of walking, the operator can walk alongside for the first shuttle.

In patients with CF-related diabetes mellitus (CFRD):[11,12,13]

Exercise testing, although not often prolonged, is usually strenuous and therefore a risk factor for hypoglycaemia in patients with CFRD. When testing patients who are prescribed insulin (or some oral hypoglycaemic agents) the following should be considered.

- Ensure that no more than three hours have elapsed since the preceding meal and that the meal contained adequate carbohydrate.
- Ensure that the patient is adequately hydrated.
- Ensure that appropriate snacks and fast-acting glucose are on hand during and after the exercise test if required to correct hypoglycaemia.
- Where possible, avoid injecting insulin in areas likely to be heavily involved in the exercise eg the thighs and gluteals.
- Blood glucose levels should be monitored and recorded before and after the exercise test, taking any necessary steps to avoid hypoglycaemia. Delayed hypoglycaemia can occur up to 24-36 hours post-exercise, so monitoring should continue as such. Recording and sharing exercise blood glucose data can aid the patient with ongoing self-management.
- Blood glucose must be 4 mmol or higher prior to exercise testing and a 10 g snack, such as a biscuit or banana, is recommended if blood sugar is below 7 mmol.
- Salt supplementation may be considered.

What exercise test should be performed?

Standardised exercise testing is recommended in several countries, but there is no current agreement on a single best exercise test to accommodate all individuals with CF, who differ in age and disease severity.[8]

Tests to evaluate anaerobic fitness (eg Wingate) and muscular fatigue/strength are available. Much of the focus to date has been on the evaluation of aerobic fitness in people with CF, given the association between this outcome measure and survival,[1,14] hospitalisation risk[15] and quality of life.[16]

Available tests of aerobic fitness range from comprehensive cardiopulmonary exercise testing (CPET) to 'field' tests.

CPET

CPET is conducted using either a cycle ergometer or treadmill (with most European centres preferring to use cycling). Cycle ergometry with breath-by-breath analysis of gas exchange and ventilation offers a comprehensive exercise assessment of ventilatory, circulatory, and metabolic parameters during various exercise intensities. Workload is progressively increased incrementally during CPET using a 'step' or ramp protocol, such that exercise responses up to and including maximal exercise can be measured within 8–12 minutes.

Key measures of interest include VO_{2peak}, VO_2 at the ventilatory anaerobic threshold (AT), and peak minute ventilation ($V_{Epeak)}$ in addition to peak power output (W_{peak}), change in SpO_2 (ΔSpO_2), time to exhaustion, and perceptions of effort and breathlessness. Measurement of VO_{2peak} by CPET is regarded as the gold-standard method to evaluate an individual's aerobic fitness. Additional outcome measures allow us to evaluate the mechanism(s) of any exercise limitation such as measures of pulmonary gas exchange and ventilation, as well as heart rate (HR), SpO_2 and subjective indicators of effort and breathlessness.

The Godfrey cycle ergometer test is the recommended protocol for people with CF >10 years,[8,17] with monitoring of SpO_2, pulmonary gas exchange, ventilation and HR. The stepwise increments (10–25 watts per minute) are based on the individual's height, anticipating an 8–12 minute test duration. This allows us to collect data during several different exercise intensities that may be relevant to activities of daily living and exercise prescription.

The European Respiratory Society Statement on Standardisation of CPET in chronic lung diseases[2] suggests using continuous ramp protocols, since the increments increase continuously, similar to physiological responses. Ramp testing protocols are both safe and valid for use in children with CF[18] and adults and/or those with more severe CF lung disease.[19]

For those seeking to undertake treadmill testing, various well-established protocols exist for CPET, including Bruce, Balke, modified Balke, and Naughton protocols, during which treadmill speed and/or slope is increased over time. The modified Bruce protocol is recommended for treadmill testing in CF.[8] It should be noted that none of these protocols, including their modifications, allows a linear increase of work rate as a ramp or minute-by-minute increment. For predictive equations to estimate VO_2 from treadmill data please refer to the Statement on Exercise Testing.[8]

Irrespective of exercise modality, in line with the European Respiratory Society Statement on Standardisation of CPET in chronic lung diseases[2], a brief resting period before initiation of exercise should be included to allow the patient to familiarise with the testing apparatus and the tester to obtain measures of SpO_2, arterial blood sampling (in selected cases only), echocardiogram (ECG), blood pressure, V_E and gas exchange variables at rest. Resting measures, especially the respiratory exchange ratio (RER), can be particularly useful for identifying patients who may be demonstrating an anticipatory hyperventilatory response prior to exercise, which can be common when a mouthpiece/face mask is fitted, and can be compared with data obtained during maximal effort. If maximal exercise endpoints are unclear, supramaximal exercise testing to verify VO_{2peak} can be considered.[18,20]

Field tests

Some clinics will not have access to the equipment necessary for CPET.[21] In these cases, other options for aerobic fitness testing include field tests, such as incremental shuttle tests, submaximal treadmill, walking tests and step tests. These are logistically easier to perform as they are usually portable and require less formalised equipment. Although it should be noted that whilst field testing can be incremental and maximal for many patients (eg severe lung disease, deconditioned), not all individuals will elicit a peak response.[23] Moreover, field tests give only limited information about exercise capacity, reasons for exercise limitations and potential exercise-associated adverse reactions.[22] During field testing, there is also no clear way to establish whether a maximal effort has been given due to the limited outcome measures collected. However, they are low cost, easy to administer, often quick and can be useful in assessing exercise tolerance, functional exercise capacity and guiding exercise prescription. The reader is directed to the Consensus Statement on Exercise Testing for standard operating procedures for these tests.[8]

Field tests can also provide an opportunity for more meaningful exercise education as they often involve more functional activities. The 6 minute-walk test (6MWT) is simple, requires minimal equipment and is one of the most commonly used self-paced exercise tests. Reliability and validity work has been conducted in both adults and children/young people with CF.[23-25] In addition, the 1 year minimally important clinical difference (33 m) for this test has recently been calculated for the first time to facilitate its use as an additional outcome measure in people with CF, particularly as part of the annual review process.[25] 6MWT will be grossly submaximal for all but the sickest people with CF and its use should be reserved for pre-transplant assessment.

Sit-to-stand (STS) testing can also provide a useful alternative to assess exercise capacity that may particularly suit those with limited space. Although the cardiorespiratory demand has been shown to be lower than that of CPET, the 1-minute STS test (1-min STS), can elicit a substantial cardiorespiratory response and provide valid outcome measures that are functionally relevant, eg STS repetitions, and demonstrate strong correlations with CPET outcomes.[26] Such testing offers a more clinically practical alternative, with minimal equipment or space needed, and simple outcomes that provide insight into an individual's functional capacity.

3-Minute Step Test (3MST):
The 3MST is a feasible and acceptable measure of submaximal exercise performance in children and adults and a useful tool in the assessment of oxygen desaturation. The test is short in duration, simple to carry out and has low cost and minimal space and equipment requirements. However, the submaximal nature and ceiling effect of the 3MST limits its usefulness clinically across the age spectrum.[27-29] It is recognised to be submaximal for almost all participants but the most sick who may desaturate, and for this reason a near maximal field test such as the shuttle tests would be preferred.

The Chester Step Test (CST):
The CST is a 10-minute submaximal standardised multistage test and, like the 3MST, has minimal space and equipment requirements. The CST was originally designed for workplace screening and is now widely used for exercise prescription in the UK cardiac population.[30,31] In healthy individuals one study reported a ceiling effect and a positive relationship between predicted VO_{2max} using the CST and measured VO_{2max}. However, a subsequent study questioned this prediction validity. The CST has been found to be highly reproducible in patients with chronic obstructive lung disease and reliable in patients with bronchiectasis, but too challenging for both groups.[32,33]

To date no studies have been published in adults with CF where an incremental exercise step test has been investigated to assess exercise tolerance or determine maximum oxygen uptake (VO_{2max}).[34] As part of a small feasibility study, Button and Wilson developed The Alfred or 'A-Step' test. Although there are no published reviews of this, the proposed test will allow for early detection of decline in physical function in the day-to-day clinical setting. This test is an incremental, maximal, externally paced step test with a protocol suitable for adults with CF, which is applicable to all ages, levels of fitness and disease state and is in line with current exercise testing recommendations.

Incremental field tests
A number of incremental field tests have demonstrated validity and reliability for testing people with CF. Appropriately designed incremental field tests should continue beyond a physiologically feasible level of exercise and thus enable subjects to exercise to volitional fatigue.

The modified test 10 m-MSWT is available in 15-level and 25-level versions and allows subjects to run as necessary. The test is concluded when participants state subjectively that they are unable to continue or fail to make the course marker on two consecutive beeps.

These MSWT's have proven reliability, repeatability and sensitivity in people with CF[35,36, 37]. A predication equation (Equation 2) for this test has also been proposed[38] ,

Distance walked (m) = 219.5 + (281.2 x sex) – (9 * age (years)) + (15.9 x FEV_1 % predicted)

N.B. This equation is only appropriate for use with moderate-severe CF lung disease ($FEV_1 \leq$ 67% predicted) and is based on a relatively small sample of 127 adults with CF (aged 17-52 years).

The iStep test, an incremental step test developed to test children and young people with CF, has some proven validity and feasibility,[9] demonstrating a near-maximal physiological response in 66% of participants (n = 24). However, there was suggestion of a ceiling effect with 50% of participants completing all 5 levels.

Alternative forms of exercise testing
Alternative components of fitness can be measured and may prove useful in exercise counselling and in the management of muscular and postural issues. These include assessment of muscular strength and endurance,[39] flexibility and core strength/stability. Other forms of exercise testing assessing short-term muscle performance (eg the Wingate Test and isokinetic testing), have been used for scientific purposes, but rarely in a clinical setting.

There is a growing body of evidence to support peripheral skeletal muscle abnormalities in people with CF,[40] which may contribute to increased fatigability and reduced physical activity participation. This may further exacerbate exercise intolerance and reduce health-related quality of life thus increasing risks of hospitalisation and poorer survival in people with CF. Peripheral muscle testing in CF should be considered for clinical and research purposes, notably for early detection and monitoring of limb muscle abnormalities, to design and evaluate targeted therapies.

Development and validation of suitable testing protocols should help to increase its uptake. A test should evaluate all components of muscle function (ie strength, endurance, power, fatigability) that may be impaired in pw CF, and should be valid, reliable and feasible, with normative reference data available to assist with data interpretation.[40]

Handgrip strength offers a simple global indicator of muscle strength and has been used in people with CF.[41,42]

A more comprehensive assessment of peripheral muscle strength can be done using chairs with a fixed strain gauge offer an attractive (often under-utilised) alternative for measuring limb muscle strength in both healthy individuals[43] and those with chronic respiratory disorders.[44] Such chairs are also easily transportable and have been used to assess muscle function in other chronic respiratory conditions.[45,46]

Assessment of respiratory muscle function should also be considered. Respiratory muscle performance in CF is a key determinant of aerobic fitness.[47] Impairment of (inspiratory and expiratory) respiratory muscles is a common clinical finding in people with primary lung disease. It is unclear whether people with CF exhibit respiratory (inspiratory and/or expiratory) muscle dysfunction or preserved respiratory muscle function.[48,49] However, respiratory muscle function is influenced by a variety of factors including hyperinflation, nutritional status,[48] systemic corticosteroid use, *Pseudomonas aeruginosa* colonisation, inactivity, and chronic inflammation.[47] Multiple CF-related comorbidities, including thoracic kyphosis and postural abnormalities, may also create a restrictive lung dysfunction that elevates the demand imposed on the respiratory pump.[50,51] Thus, individuals with CF commonly exhibit an imbalance between the ventilatory load and the capacity of the respiratory muscles, which is exemplified by the adoption of inefficient breathing patterns[52] that may contribute to exercise intolerance.

Looking to the future of exercise testing in CF

Given that people with CF are living longer and are fitter than ever, it is important to consider the needs and sporting interests of the individual. Sport-specific modalities of testing where possible and the provision of an appropriate level of challenge should be utilised in our more active CF population. Since single exercise tests may not reflect day-to-day activities, a combined approach, assessing the relationship with whole-body exercise, may be needed.[39] Using these complementary approaches will enable us to further understand the function of people with CF. Multimodal assessments of aerobic fitness and skeletal muscle function, using reproducible tests,[18,43] represent an important next step in our exercise testing practices for people with CF.

What outcome measures should be reported from an exercise test?

Dependent on the exercise test chosen and the equipment available, there are several outcome measures that should be used for exercise testing. Some are specific to the test such as work rate and VO_{2peak} for CPET, distance covered and steps completed for field tests, but several key measures should be obtained across testing modalities and protocols. Objective measurement of HR and SpO_2 will be measured before, during and after an exercise test and during recovery, as a minimum. Monitoring should be continuous and recorded if equipment allows, to facilitate a more thorough assessment. If an individual does desaturate during exercise, the corresponding intensity of exercise (eg HR, work rate, effort rating) can then be used to guide 'safe zones' within their exercise prescription.

The use of subjective measures of perceived exertion, breathlessness or fatigue should also be used to assess symptoms during exercise testing. Numerous pictorial scales are now available to assist in the collection of this type of information (eg OMNI,[53] and Dalhousie).[5,54] Readers should refer to the statement on exercise testing for further details.[2]

The following statement is also recommended by the European Respiratory Society to ensure more standardised instruction and collection of subjective data: *"During every stage of exercise, we are going to ask you about the intensity of your breathlessness and leg discomfort at that point in time. As you should avoid speaking during the test, you will use a finger of your hand to point which number between 0 and 10 best reflects the intensity of each of these sensations".*

CPET tests generate a large dataset usually displayed in a series of graphs, known as the 9-panel plot (see Appendix IIb and IIc Figures 1 and 2), which are used to measure or estimate key exercise parameters including VO_2, V_{Epeak}, and the anaerobic threshold (AT). After checking data quality, one should first review VO_{2peak} and maximum workload to assess whether they are normal relative to appropriate (age, sex, and ethnicity) normative reference data. In addition, it is important to consider whether maximum effort has been reached with respect to HR_{peak}, respiratory exchange ratio at peak exercise and whether VO_{2peak} has plateaued at the end of exercise. If maximal exercise endpoints are unclear, supramaximal exercise testing to verify VO_{2peak} can be considered.[18-20] An abnormally low exercise capacity is defined as $VO_{2peak} < 80\%$ predicted. It is important to note that it is not only

VO_{2peak} that has prognostic value in CF, W_{peak} as well as other submaximal measure have utility in this context.[8,55]

The next challenge is to identify whether reduced VO_{2peak} may be due to cardiovascular and/or peripheral muscle disease, or as is more likely in more severe CF, the result of deconditioning and/or ventilatory limitation. A schematic overview of how to determine exercise function and/or cause of any dysfunction in individuals with CF[56] is presented in Appendix IIa.

The normal mechanism for exercise termination in a healthy individual is cardiac limitation, with HR_{peak} being attained (no cardiac reserve) and V_E falling short of estimated maximal voluntary ventilation (MVV)– exercise V_E < 85% MVV.[8] The physiology in children differs from adults, and expected HR_{peak} falls with age, whilst children with CF often achieve a HR_{max} > 200 beats/min during CPET.

AT onset provides a submaximal indicator of an individual's aerobic fitness. Deconditioning results in an early onset AT, indicative of reduced efficiency to transfer and utilise O_2 at the muscular level. An AT occurring < 50% predicted VO_{2peak} (in the absence of cardiac disease or muscle abnormalities) is likely to be associated with deconditioning and can be improved with training.

Efforts should be made to report the findings and outcomes of exercise tests in a standardised manner. To assist with this, a guidance document was recently published which provides a standardised template for reporting CPET results.[2] To summarise, a clinical exercise report should typically include four components:

- Basic information on the patient
- Technical report
- Response to exercise (aerobic/anaerobic performance, cardiovascular response, ventilatory response, gas exchange response, metabolic response)
- Report summary

Refer to Radtke[2] for more details on each of these sections and to obtain the template, which is also included in the appendices of this document (see Appendix IIf). A recently published review by Urquhart and Vendruscolo[57] offers advice on how to interpret and use CPET outcome measures to guide exercise counselling in children with CF.[56]

Assessment of habitual physical activity and sedentary behaviour

Assessment of the habitual physical activity behaviours of people with CF is an important consideration, taking into account the amount and intensity of activity, as well as sedentary behaviours. A recent survey exploring perceptions of physical activity monitoring among children and young people with CF and their health care professions (HCPs) reported that HCPs recognised the potential benefits of the devices in clinical practice.[57] However, physical activity assessment is not commonplace or consistent in clinical practice. This section aims to summarise some of the assessment methods available to guide the incorporation of physical (in)activity assessment in the clinical setting. The reader should also make use of several key articles published on this topic,[58,59] as well as the European expert position statement on the assessment of physical activity in people with CF.[60]

Motion sensors, activity questionnaires and diaries are all useful to gauge an individuals' general physical activity behaviours and, as with exercise testing, the purpose of data collection will guide the choice of tool used. The range of tools also differ in terms of cost and ease of use. The current recommendation from the European position statement is that activity monitors (eg SenseWear or ActiGraph) offer informed choices to facilitate a comprehensive assessment of physical activity and should as a minimum report on dimensions of physical activity including energy expenditure, step count and time spent in different intensities and sedentary time[60]. It should be noted that recent data suggests that people with CF enjoy wearing monitoring devices and had good compliance with wrist-worn devices and that devices providing feedback were the preferred choice.[57]

Sophisticated activity monitoring can eliminate the subjective evaluation of activity; however, it is more technical and costly to offer in most clinical settings.

Simple pedometers may offer an inexpensive method of obtaining a measurement of PA, and there is some evidence for supporting their use in people with CF.[58] The current recommendation is the DigiWalker pedometer offer a comparatively inexpensive alternative to obtain some measurement of physical activity,[60] although they are more limited in the information, they provide concerning the different components of physical (in)activity.

Questionnaires provide an appreciation of the person's perception of their physical activity, but not data reflecting symptoms whilst active. It may however be useful as a screening tool to guide further discussion about exercise patterns, goal setting and subsequent exercise prescription. It should be noted that questionnaires depend on patient recall and are subjective so should be used with caution. Although there is insufficient data to recommend the use of one diary over another, it is currently recommended that the Habitual Activity Estimation Scale (HAES) is a reliable and valid instrument that can be used to assess activities of varying intensity in people with CF.[60]

In the future, new technologies such as the LifeShirt® may be useful to allow cardiopulmonary assessments to be made in the field. However, the role of these devices in clinical practice is yet to be established.

The increase in use of commercially available activity monitors offers an opportunity to measure the physical activity patterns of individuals longitudinally,[57] which can also act as a useful focus for physical activity counselling.

Summary

Exercise testing is a standard of care and at least annual interval testing should be undertaken, to provide an accurate dynamic assessment of physical function that may not be detected by other assessments such as pulmonary function. Traditional testing of lung health using spirometry tells us how much and how fast air exits the lungs, whereas exercise testing measures the efficiency and performance of these lungs in combination with cardiovascular, pulmonary and musculoskeletal systems during exercise. Exercise testing provides precise information that is of prognostic importance, as well as allowing us to further understand individual pathophysiology of exercise limitation and individually tailor exercise programmes for people with CF. Assessment of habitual physical activity and sedentary time should also be considered where possible to provide a more comprehensive insight into both the individual's activity and fitness.

Recommendations

- Exercise testing is recommended as part of the routine assessment of pw CF at least annually *(QoE – high)*.
- Exercise testing is recommended to assess for changes in overall management (eg examining efficacy of intervention, pre/post admission or modifying exercise prescription) *(QoE – high)*.
- Exercise testing is essential to monitor response to exercise training, to assess fitness and to allow safe and effective exercise prescription *(QoE – high)*.
- Exercise testing is recommended in people with CF aged 10 years and older, but can be started at a younger age to aid familiarisation in later years *(QoE – moderate)*.
- The gold standard (CPET) should be used where possible and in the absence of gas analysis an incremental ramp protocol should still be implemented *(QoE – moderate)*.
  - Acceptable alternatives may be:
  - cycle ergometry without gas exchange eg Wmax testing;
  - shuttle tests; or
  - incremental step tests.
- The 6-minute walk test is recommended as part of pre-transplant assessment but its' use as an annual test cannot be recommended *(QoE – moderate)*.
- The 3-minute step test is not recommended for use as a measure of functional exercise capacity *(QoE – moderate)*.
- Tests such as the 1-minute sit to stand test may prove useful measures *(QoE – moderate)*.
- Emergency procedures will be accessible during all exercise testing *(QoE – moderate)*.
- Contraindications to testing will be assessed before each testing session *(QoE – high)*.
- Exercise test-specific standardised objective measurements should be recorded as appropriate and as a minimum HR, SpO_2 and indicators of effort and breathlessness should be performed before, during and after testing *(QoE – moderate)*.
- Other measures of fitness (eg strength, flexibility) and physical activity may be appropriate but should be assessed on an individual basis and follow recommended guidelines *(QoE – low)*.

Good practice points

- Exercise testing should be undertaken at least annually to evaluate the physical function and fitness levels of people CF.
- Where possible, comprehensive CPET with measures of pulmonary gas exchange and ventilation should be undertaken as the annual review test to provide a gold-standard measure of aerobic fitness.
- Where possible, tests of additional components of fitness (eg muscle strength) are also desirable.
- People with CF should be assessed for clinical stability prior to annual assessment of exercise testing (ie during a period where there is no evidence of pulmonary exacerbation) to ensure accurate and useful results.
- Age-appropriate subjective measures of perceived exertion, breathlessness or fatigue should be used to assess symptoms during exercise tests and to guide intensity of exercise training.
- Where possible, information obtained from exercise testing should be used to help guide more individualised exercise prescription.
- Where possible, exercise testing should be considered as an assessment tool to monitor other clinical interventions, eg new medications, exercise training programme.

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4. Physical activity and exercise

The importance of exercise in maintaining a healthy lifestyle is well-recognised in both health and disease. This chapter will provide a contemporary overview of the best practice recommendations for exercise counselling for people with CF, as well as the evidence that underpins its use which may facilitate patient education regarding the importance of exercise. Several key articles have been published to provide evidence-based guidelines for physical activity and exercise prescription for people with CF.[1,2]

In line with the published expert guidelines for people with CF,[2] the following definitions apply for this document:

- Habitual physical activity: bodily movement produced regularly by the contraction of skeletal muscles that result in a substantial increase over resting energy expenditure.
- Exercise: planned, structured, and repetitive bodily movement performed to improve or maintain one or more components of physical fitness.
- Sport(s): an activity involving physical exertion and skill in which an individual or team competes against another.

4.1 Exercise limitation in CF

In the era of increased life expectancy and new treatments, people with CF may have similar or greater exercise capacity than their healthy peers. However, a large number of individuals are not only affected by decreased cardiorespiratory fitness (ie aerobic), but also decreased muscle strength and endurance. Furthermore, poor posture and flexibility are common features in people with CF.[3,4]

Several factors may contribute to reduced fitness in people with CF. Ventilatory limitation is often not observed during exercise (even at maximal limits) in young children and adolescents who are physically active with good lung function. However, as lung disease severity progresses, ventilatory limitation during exercise is common. The individuals may present with increased lung dead space that worsens with lung disease severity, and which can be increased during exercise,[5] requiring a higher minute ventilation.[6] Additionally, airway obstruction due to mucus within the airways (+/- airway hyper-reactivity) may be present, requiring greater inspiratory airflows generated with greater respiratory muscle effort to achieve similar ventilation. In contrast to healthy individuals who have significant ventilatory reserve at maximal exercise, people with CF may have an exercise ventilation that reaches or exceeds their predicted maximum.[7] In short, those with more severe CF may have higher metabolic demands during exercise due to an increased work of breathing, as well as a higher ventilatory rate, due to increasing physiological deadspace. Such factors, coupled with an inability to increase minute ventilation during exercise due to lung disease, contribute to ventilatory limitation being the principal factor determining exercise capacity in these individuals.

But, there are non-pulmonary consequences of CF that may also affect the exercise capacity in people with CF. Peripheral muscle weakness is common in those with CF, particularly in the lower limbs,[8-10] and can have a significant impact on exercise tolerance and the capacity to undertake activities of daily living.[11,12] However, physical activity alone cannot explain these changes.[11] Other structural and functional changes in skeletal muscle are evident in people with CF,[9,13-15] for which several contributing factors have been proposed. CFTR is expressed in skeletal muscle cells[14] and lack of CFTR in skeletal muscle has been shown to predispose mice with CF to muscle wasting and diaphragm muscle pump failure.[16] Reduced antioxidant capacity, due to increased systemic inflammation and/or oxidative damage, may also lower mitochondrial efficiency.[17]

CFTR is also expressed in human vasculature and vascular endothelial dysfunction is associated with a poorer VO_{2max} in young people with CF[18,19] has been reported. Additionally, there is evidence of heart involvement in children and adults with CF,[20] which may be related to dysfunctional CFTR.[21]

4.2 Evidence for recommendation

In 2017 a systematic review[1] concluded that physical training has a positive effect on exercise capacity, pulmonary function and health-related quality of life based upon 13 randomised controlled trials. However, there remains a need for high-quality randomised controlled trials to comprehensively assess and clearly define the benefits of physical training in adults with CF.

Evidence from smaller studies has demonstrated both physical activity and exercise to be beneficial for people with CF, with high physical activity levels associated with improved aerobic fitness[22] – an important prognostic indicator in this patient group.[23-27] Being more active is associated with improved pulmonary function,[22] glycaemic control[28] and bone mineral density.[29,30] Structured exercise training has also been shown to slow the typical decline in lung function[31] or even result in an improvement in lung function in some cases.[32,33] There is also evidence that appropriate exercise training can improve exercise capacity,[33] quality of life[34,35] and mucociliary clearance.[36]

It is currently considered part of standard CF care to encourage a physically active lifestyle[1,2,37,38] and physical activity and exercise should be part of the routine management for people with CF at any age. Regular advice and education on frequency, intensity, duration and type of activity should be initiated from diagnosis in order to ensure fitness levels are maintained. This should, where possible, be informed by exercise testing (see Chapter 3 for more details).

4.3 Potential exercise-related risks

Exercise appears to be relatively safe for people with CF, with adverse events such as cardiac arrhythmias, pneumothorax and hypoglycaemia associated with exercise occurring in less than 1% of ~1,000 from a survey of 37 CF centres.[39] However, contraindications to exercise do exist and may be absolute or relative, and can depend on the patient's clinical status, ie more common in people with CF with more advanced disease and/or additional complications/comorbidities such as CF-related diabetes (CFRD). Other examples include CF liver disease (enlargement of liver and/or spleen) and risk from contact sports or martial arts, as well as risk of damage to/fracture of a portacath or other total implantable venous access device from contact sports or martial arts. Exercise type is an important consideration, with the following documented to present specific risks:

- Exercise at high-altitude (eg skiing) may increase the risk of desaturation and right heart failure.[40,41]
- Diving may increase the risk of pneumothorax especially in patients with more severe disease.[40]
- Contact sports (eg combat sports) should be avoided in patients with advanced lung disease, liver disease, portacath or those at risk of breaks/fractures, eg those with low bone density.[42]

As disease progresses, people with CF may be at increased risk of exercise induced oxygen desaturation and may require assessment for supplementary oxygen to ensure saturation levels are maintained > 90% during exercise.[43,44] This will improve performance and recovery and help prevent the development of pulmonary hypertension and/or cor pulmonale.[2] Whilst there is limited evidence of safety and efficacy of NIV during exercise, two small studies suggested that the use of NIV during exercise may result in improved ventilation and oxygenation in people with CF although impact on duration of exercise was varied.[45,46]

Despite concern regarding resistance training for young people, there is limited evidence on the incidence of injuries during strength training in children and adolescents. Rather, as outlined in the recent International Position Statement on Youth Resistance Training,[47] there is a compelling body of scientific evidence to support participation in appropriately designed youth resistance training programmes that are supervised and instructed by qualified professionals. Resistance training prescription should be based according to training age, motor skill competency, technical proficiency and existing strength levels and the biological age and psychosocial maturity level of the child/adolescent should be considered.[47] In line with international guidelines, youth resistance training should focus on developing the technical skill and competency to perform a variety of resistance training exercises at an appropriate intensity and volume, while providing young people with the chance to engage in programmes that are safe, effective and enjoyable.[47] Given the increased risk of osteopenia or osteoporosis in people with CF, the fracture history should be determined in each individual.

Care must also be taken with the use of muscle-building protein supplements, as the renal handling capabilities for these may be altered in CF. Furthermore, these renal handling capabilities may be challenged at times iatrogenically by the use of nephrotoxic drugs. Creatine may also pose renal-related risks to people with CF when taken alongside co-administration of intravenous aminoglycosides, with anecdotal cases of acute renal failure reported.

It is well known that people with CF are at an increased risk of sodium deficiency. Increased sweat production and salt losses in people with CF may increase the risk of dehydration and hyponatraemia, particularly during prolonged exercise and/or in warm or hot conditions. Low salt levels may also reduce thirst perception and reduce fluid intake during exercise. Since dehydration can cause tiredness, headaches, dizziness, muscle weakness and may contribute to thicker sputum making airway clearance more difficult; patient education on this topic is important before they begin or change an exercise programme. Pre-exercise assessments of hydration status (eg urine colour charts) should also be considered to help plan activity fluid and salt intakes. There is a lack of evidence available to guide individual sodium requirements for people with CF and no exercise-specific recommendations, however, this should be discussed with the dietician where possible. Individual needs may vary and should at present be guided by signs and symptoms of sodium depletion, dietary intake, exercise level and individual sweat rate.[48]

Hypoglycaemia during exercise is also a risk, particularly in combination with insufficient caloric intake. Education by the CF team is essential and self-monitoring of blood glucose should be encouraged where possible, as well as caloric intake for the activity planned.

In line with the guidance in the CF Trust Management of CFRD publication,[49] the following should be considered for individuals who are prescribed insulin (or some oral hypoglycaemic agents):

- Ensure that no more than 3 hours have elapsed since the preceding meal and that meal contained adequate carbohydrate.
- Ensure that the patient is adequately hydrated.
- Appropriate snacks and fast-acting glucose are on hand during and after exercise if required to correct hypoglycaemia.
- Where possible avoid injecting insulin in areas likely to be heavily involved in the exercise eg the thighs and gluteals.
- Blood glucose levels should be monitored and recorded before and after exercise, taking any necessary steps to avoid hypoglycaemia. Delayed hypoglycaemia can occur up to 24-36 hours post-exercise so monitoring should continue as such. Recording and sharing exercise blood glucose data can aid the patient with on-going self-management.
- Blood glucose must be $\geq$ 4 mmol prior to intense exercise and a 10 g pre-exercise snack (eg biscuit or banana) is recommended if blood sugar is below 7 mmol.
- Salt supplementation may be considered.

Exercise Training recommendations

All people with CF should have access to individually tailored exercise programmes that are frequently re-evaluated. Advice and counselling should be developed in conjunction with the individual and be directed by exercise capacity testing (see Appendix II), physical activity monitoring and appropriate physical activity counselling. The guidelines below aim to offer a practical guide to exercise training recommendations for people with CF.

Table 1

Type of activity	1-6 years	7-12 years	13-19 years	> 19 years
Habitual PA	60 min/day Developmentally appropriate activities	60 min/day Variety of activities enjoyed, preferably as a family	60 min/day Variety of activities enjoyed, especially with family and friends	150 min (preferably 300)/ week Variety of activities of choice
Aerobic exercise	No formal program recommended – but should perform full-body activities that increase breathlessness and heart rate	30-60 min MVPA/ day (at least 70% HR_{max}) Especially if using for airway clearance (must also huff/cough)	30-60 min MVPA/ day (at least 70% HR_{max}) Especially if using for airway clearance (must also huff/cough)	30-60 min MVPA/ day (at least 70% HR_{max}) Especially if using for airway clearance (must also huff/cough
Resistance training	No formal program recommended – but should perform actities using bodyweight to develop strength (eg calisthenics)	Exercise with own body weight aimed at strengthening muscles and bones (eg calisthenics) most days. If interested, begin formal weight training under good supervision, focusing on learning good technique first (2 times / week)	Formal RT 2-3 session/week per muscle group 1-3 sets 8-12 reps 70-85% 1-RM Incorporate limb and trunk muscles	Formal RT 2-3 session/week per muscle group 1-3 sets 8-12 reps 70-85% 1-RM Incorporate limb and trunk muscles
Other outcomes	Encourage normal motor development, including agility, balance and coordination	Encourage normal motor development, including agility, balance and coordination	Encourage muscle activities to help prevent/ minimise postural control	Adapt for disease-related complications (eg, CFRD, low bone density)

N.B. Information adapted from Swisher et al.[2] CFRD, cystic fibrosis-related diabetes; min, minutes; MVPA, moderate-to-vigorous physical activity; RT, reps, repetitions; resistance training; 1-RM, one repetition maximum.

Recommendations

Physical activity

- Young children with CF should perform regular, developmentally appropriate physical activity at least 60 minutes per day *(QoE – high)*.
- Older children and adolescents with CF should perform at least 60 minutes of moderate-to-vigorous physical activity per day *(QoE – high)*.
- Adults with CF should perform at least 150 minutes (2 ½ hours) per week (preferably 300 minutes – 5 hours) of moderate-to-vigorous physical activity and should seek to include a mix of aerobic + resistance training *(QoE – high)*.
- Those who are inactive and/or limited in their physical capacity should be encouraged to accumulate 10 minute bouts of physical activity throughout the day *(QoE - moderate)*.

Aerobic exercise

- Young children with CF should perform regular, developmentally appropriate physical activity at least 60 minutes per day *(QoE – high)*.
- Children and adolescents with CF should perform 30-60 minutes, 3 x week or more of aerobic exercise (at an intensity of at least 70% maximum heart rate) to improve fitness; this can also help to meet daily physical activity targets.
- Adults with CF should perform 30-60 minutes, 3 x week or more of aerobic exercise (at an intensity of at least 70% maximum heart rate) to improve fitness; this can also help to meet daily physical activity targets.
- Patients should be educated regarding the clinical importance of high aerobic fitness levels *(QoE - moderate)*.
- Patients should be educated on the difference between moderate and vigorous intensity physical activity and aerobic exercise and on the use of subjective measures of exertion, for example validated scales to assess exertion and/or breathless *(QoE - low)*.

Moderate-intensity physical activity equates to (or can be defined as):

- the individual working (exercising) at 40 to 59% of their peak aerobic capacity (VO_{2peak}) as measured during cardiopulmonary exercise test (CPET) *(QoE – moderate)*;
- the individual working (exercising) at self-reported perceived exertion rating between 11-13, as measured on the Borg perceived exertion scale. The Borg perceived exertion scale is a valid 15 item scale (ranges 6-20) for exercise prescription *(QoE – low)* Appendix IIa; or
- the individual working (exercising) at a rating of perceived breathlessness between 3-4 as measured using the modified Borg breathlessness scale (range 0-10) *(QoE – low)* Appendix IIa.

Vigorous-intensity physical activity equates to (or can be defined as):

- the individual working at 60 to 85% of their VO_{2peak} as measured during CPET *(QoE – moderate)*;
- the individual working (exercising) at a self–reported perceived exertion rating between 14-16, as measured on the Borg perceived exertion scale *(QoE – low)* Appendix IIg; or
- the individual working (exercising) at a rating of perceived breathlessness between 5-6, as measured using the modified Borg breathlessness scale (range 0- 10) *(QoE – low)* Appendix IIg.
- High-intensity interval training may be considered in patients who have achieved the recommended amount of physical activity for more than six months *(QoE – moderate)*.
- All patients who have expressed a desire to become more physically active should be offered support and advice *(QoE – low)*.
- Adults with CF may benefit from incorporating activities to maintain and/or improve posture and flexibility on most days of the week *(QoE – low)*.

Resistance exercise

- Adults with CF should undertake resistance exercise as a complement to and not a replacement for cardiorespiratory (aerobic) exercise *(QoE – moderate)*.
- Adults should be advised to undertake resistance exercise on two or more non–consecutive days of the week *(QoE – low)*.
- Weight training should be regarded as the preferred mode of resistance exercise to optimise the health benefits and monitor progression. Alternative modes of resistance training may be considered such as using body weight, resistance bands, free weights, medicine balls or weight machines *(QoE – low)*.

- Resistance training should incorporate both upper and lower limb exercises that target the major muscle groups *(QoE – moderate)*.
- A load should be selected that equates to 70-85% of the patient's one repetition maximum (1-RM) to improve muscular strength (1-3 sets, 8-2 reps for each exercise). To improve muscular endurance a load should be selected that equates to less than 70% of the patients 1-RM and more repetitions performed *(QoE – moderate)*.
- In the absence of the patient's 1-RM, a resistance (weight) should be selected that brings about local muscular fatigue after the desired number of repetitions for each exercise *(QoE – low)*.
- Respiratory muscle training may be considered *(QoE - low)*.

General

- Patients should be made aware of any increased medical risks associated with specific exercise or sporting activities *(QoE – moderate)*.
- Specific types of strength training (eg power lifting, body-building and maximal lifts) should be avoided until physical and skeletal maturity *(QoE – moderate)*.
- Specific guidance should be given on fluid-replacement and dietary/insulin requirements when appropriate *(QoE – moderate)*.
- Patients who exhibit desaturation will be assessed for supplementary oxygen during exercise *(QoE – moderate)*.

Good practice points

- Physical activity and exercise should be part of the routine management for people with CF at any age for health and a good quality of life.
- People with CF should be made aware of the health benefits of a physically active lifestyle and the physiological principles that underpin exercise training.
- A recommended exercise programme should be offered to all patients who may benefit and/or request one.
- Recommended exercise programmes must consider motivations and goal, current level of physical activity and ability, health status and circumstance, preferences and barriers to being physically active.
- Patients should be advised to minimise the time spent inactive for extended periods of time, particularly during periods of clinical stability.
- A structured exercise programme will be offered to patients who have musculoskeletal disorders that are likely to benefit from exercise training.

Other types of exercise

Yoga

Yoga is an ancient mind-body practice which has its origins in the Indus Valley. The physical practice of yoga (known as Hatha yoga) is one element of yoga practice, but it is what is commonly recognised as yoga in the West and therefore what is discussed here. Yoga combines breathing exercises (pranayama), physical postures (asanas) and relaxation/mindfulness techniques.

Although there is a growing body of evidence for yoga in the non-CF population, there have only been three pilot studies undertaken in people with CF. Two of these pilot studies have been presented in abstract form and have shown that yoga is safe and tolerated in adolescents and young people with CF,[50] and that it can lead to improvements in posture, chest wall excursion, lower extremity muscle performance and self-perceptions of body weight.[51] The final study was published and showed yoga reduced immediate anxiety and joint pain in people with CF between the ages of 7-20 years.[52]

Some physiotherapists in the UK are integrating yoga into their clinical practice and report benefits including improved low back pain, thoracic kyphosis, stress incontinence, ease of airway clearance, body image, body awareness, breath awareness, cardiovascular fitness, anxiety, sleep and disease mastery.

There are a wide range of different types of yoga practices including Anusara, Ashtanga, Bikram, Iyenga, Jivamukti, Kundalini, Restorative, Vinyasa, Yin, etc. Practices may vary in sequencing, asana, use of props, the duration of how long poses are held for, the temperature of the room and philosophical focus.

Pilates

Pilates is a series of carefully-controlled movements that aim to strengthen the body in an even way, with particular emphasis on strengthening the core muscles and using controlled breathing in time with the exercises. Pilates exercises can be performed in a 1:1 or group environment and are done on a mat or using special equipment, such as blocks and supports. The suggested benefits of Pilates include improved body awareness, postural alignment, tone, strength and flexibility. The principle of Pilates (building core strength) has been used in conventional physiotherapy for decades and many physiotherapists currently use Pilates based exercises in their own clinical practice alongside other techniques for the treatment of low back pain and neurological conditions. Upon review of the literature, there are no research trials which evaluate the benefits of purely a Pilates session for people with CF, however, in 2016 nine out of the 39 centres who responded to the CT questionnaire reported that they use Pilates in their clinical practice and find it beneficial for posture, fitness, musculoskeletal pain relief, airway clearance, breathing control and relaxation. In 2019 a qualitative study of UK CF MDTs regarding the promotion of physical activity for adolescence with CF noted Pilates was an example of exercise used in this group.[53] However, no further recommendations were given.

Good practice points

- Pilates may be considered in the management of people with CF and may be suitable throughout disease severity; however, it is important that a patient finds a qualified teacher who is able to adapt the class to the individual's needs.

Tai Chi

Tai Chi is a Chinese form of meditative movement which combines slow, choreographed movements with deep breathing and mindfulness. Research suggests Tai Chi can improve physical and emotional wellbeing for various chronic conditions including arthritis, low bone density, heart disease, hypertension and sleep problems; benefits include increased muscle strength, improved flexibility, pain and balance, and mild aerobic benefits (depending on the speed and size of the movements). Two studies have been conducted in the CF population to date.[54,55] The initial study by Lorenc was a small sample pilot feasibility study (*n*=7), which showed no adverse effects and suggested that Tai Chi may reduce CF treatment impact, improve respiratory symptoms, self-efficacy and sleep.[54] The second was the follow up to Lorenc's study and was a randomised comparative effectiveness trial. 40 adults (*n*=26) and children (*n*=14) with CF participated in eight lessons of Tai Chi over a three-month period, delivered either via videoconferencing or face-to-face. Tai Chi was found to be safe and well tolerated; it was feasible to deliver individual lessons via the internet and appeared to improve self-reported symptoms such as sleep, cough (both daytime and night-time), stomach ache and breathing.[55]

Good practice points

- Tai Chi has been found to be safe, well tolerated and may provide an alternative exercise for people with CF.
- Tai Chi is feasible to be delivered through individual lessons via the internet or face-to-face sessions.

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5. Airway clearance

Airway clearance is a mainstay of treatment for people with CF and is considered essential for all, ideally starting from diagnosis. These guidelines discuss the evidence for the different treatment options individually. However, since there is no strong evidence to show that any treatment technique is superior to another it is important that patient/carer preference should be highly regarded when deciding which treatment option to choose.[1] Adherence to airway clearance tends to be lower when the person with CF has a negative association with their treatment and this is associated with lower outcomes.

Whilst treatment options are discussed and generally researched individually, combining different treatments can make airway clearance more effective. It has been suggested that effective airway clearance has two components, a method to ventilate behind obstructed lung units and secondly, an expiratory airflow of greater than 30-60L/min with a peak expiratory flow/peak inspiratory flow of ratio of 1:4.[1]

No single treatment technique is suitable for all patients and the therapist delivering airway clearance must be well-educated in all aspects of airway clearance and associated therapy techniques.

5.1 The active cycle of breathing techniques

The Active Cycle of Breathing Techniques or ACBT consists of three components: breathing control; thoracic expansion exercises; and the Forced Expiration Technique (FET), also known as a 'Huff'.

In breathing control, the breathing pattern is addressed, the individual performs tidal breathing (gentle relaxed breathing) using the lower chest with a slower flow, but at his or her own rate.[2] Participants are encouraged to relax their shoulders and upper chest to encourage diaphragmatic breathing, and inspiration is ideally through the nose.[3] Breathing control is incorporated to allow rest periods and prevent wheeze in-between the more active parts of ACBT.[4]

Thoracic expansion exercises are deep active inspirations to full capacity with a passive unforced expiration which are repeated to a maximum of four breaths at a time.[4] The increased lung volume decreases air flow resistance via the collateral channels of the lung, which aids secretion mobilisation as air is able to pass through

these channels and get behind the mucus while at the same time forces exerted between adjacent alveoli aid lung re-expansion.[2] A three-second hold at full inspiration should be included to allow improved ventilation to all areas. A three-second hold at the top of the breath, aiming to keep the airway/glottis open before passively breathing out is encouraged. Increasing the lung volume above tidal breathing reduces collateral ventilatory resistance, allowing air to flow behind secretions aiding their mobilisation, while at the same time forces exerted between adjacent alveoli aid lung re-expansion.[5]

If secretions still need to be mobilised after thoracic expansion exercises, a further set of these deep breaths can be repeated after a period of breathing control before the FET. No more than four TEEs are recommended prior to BC to prevent patient fatigue and hyperventilation.[6]

The FET is an active forced expiration completed with a rounded mouth shape and open glottis, which is repeated once or twice with breathing control in-between.[4] The FET can be done at various lung volumes, starting with a mid-lung volume to low-lung volume breath, mobilising peripheral secretions, then a high-lung volume to mid-lung volume breath to move more proximal secretions to allow easy expectoration with minimal coughing.[7]

The FET has been reported in the literature as "probably the most effective part of chest physiotherapy"[8] and is now often independently incorporated into other airway clearance techniques or exercise regimes to ensure effective secretion clearance.[9-13]

ACBT can be adapted in terms of session length and position to individual need, but each component of the cycle should be clearly defined. It is a relatively simple technique which, once learnt, is not dependent on a device or on carer assistance, which minimises treatment burden.[5] It can be introduced as huffing games with children from around two years old[2] and can be taught to people with CF from as young as 4 years of age[9], depending upon the individual.

Studies looking at ACBT compared to postural drainage alone have described effective and efficient mobilisation and clearance of secretions[14] and improvements in lung function.[15] ACBT did not increase hypoxeamia[15] or air flow obstruction.[14]

It is possible to combine ACBT with a variety of adjuncts, postural drainage or manual techniques, and this may be beneficial to some individuals and should be considered and adapted as required.[16,20,21] Of note, the current evidence does not show that the effects of ACBT are enhanced by the addition of devices such as positive expiratory pressure (PEP)[17], the Flutter®[18,19] or high frequency chest wall oscillation (the Vest).[19] In severe infections or end-stage disease ACBT can be combined with non-invasive ventilation or other positive pressure support with setting modification as required to support deep and tidal breathing.[1,2] ACBT can also be utilised with the necessary advice, supervision and monitoring following haemoptysis or pneumothorax once the individual is medically stable.

Many of the studies investigating ACBT effect are short-term comparator cross-over studies against other airway clearance techniques such as PEP, autogenic drainage, high frequency chest oscillation and conventional chest physiotherapy. A recent Cochrane review concluded that from the available research there was insufficient evidence to support or reject the use of ACBT over any other airway clearance technique.[22] ACBT was comparable with other airway clearance techniques in terms of individual preference, pulmonary function, quality of life, exercise tolerance, oxygen saturations and occurrence of infective exacerbations.[22]

Two-long term studies over a year and two years respectively have compared ACBT or ACBT combined with postural drainage and percussion to other airway clearance techniques (autogenic drainage, oscillating PEP and PEP), concluding that ACBT is equivalent in effectiveness to the other techniques.[23,24] More long-term evidence is required to assess ACBT in terms of patient reported outcome measures and objective effect.[22,24]

Recommendations

- ACBT should be considered when recommending an airway clearance technique for all people with CF (as long as they are able to follow instruction) *(QoE – low)*.
- FET should be incorporated into airway clearance and exercise regimes to enhance airway clearance *(QoE – moderate)*.

Good practice points

- The use of ACBT should be adapted to the individual in terms of number of sets of each component completed and the length of breathing control rest periods.
- ACBT is a useful airway clearance technique at all stage of lung disease.
- ACBT promotes independence with airway clearance.
- ACBT has minimal contraindications for use and it is recommended to be a considered as a mainstay airway clearance technique.
- Combining ACBT with other adjuncts, taking into consideration patient disease severity, preferences, lifestyle, treatment burden, individual tailoring and effectiveness of treatment combinations can be advantageous.

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5.2 Autogenic drainage

Autogenic drainage (AD) is a controlled breathing technique, which aims to mobilise secretions from the peripheral airways into the central airways to aid expectoration and airway clearance.

At the start of a cycle of AD it is recommended to clear the nose to enable nose-breathing, particularly on inspiration.[1] The person is then instructed to complete a "diagnostic breath" consisting of a slow full inspiration, ideally through the nose, using the diaphragm and lower chest with a 3 second inspiratory pause at the top of inspiration keeping the glottis open. Expiration, ideally through the mouth, should be active, achieving the highest possible expiratory flow without causing airway compression or bronchospasm.[2,3]

Feedback from this diagnostic breath in terms of audible crepitations, tactile fremitus and proprioceptive sensations for the participant should then be used to target the next phase of the AD cycle.[1] Crepitations or fremitus detected at the start of the diagnostic breath out is said to represent secretions in the central airways, while crepitations or fremitus detected towards full exhalation are said to represent secretions in the peripheral airways.

The main part of the AD cycle has three possible phases of tidal volume sized breathing, carried out at differing lung volumes (low, mid or high), aiming to maximise expiratory flow at that particular generation of the bronchial tree to mobilise secretions from those parts of the airways.[4] At all lung volumes inspiratory flow rates are encouraged to be slow, quiet and gentle while expiratory flow should be as high as possible while avoiding airway closure.[2,3] Depending upon where secretions were detected in the diagnostic breath, the participant will breathe at that level to further mobilise secretions from that area, for example crepitation's heard at low lung volumes will lead to the participant exhaling fully to focus on "unsticking" secretions from the peripheral airways. Mid lung volume breathing can then be used to "collect" secretions moved to the middle airways, before high lung volume breathing (using full inspirations) works to "evacuate" secretions from the proximal central airways. Once secretions have been mobilised to the highest level they can be cleared with huffing and coughing. Ideally the AD cycles would be continued until the participants chest feels as clear as possible,[1,3] until fatigue prevents the completion of a good technique or as the individual's need defines.

AD can be performed in any position to assist regional ventilation. Thought should always be given to optimise and/or support a participant's posture in whichever position they prefer.

It is possible to combine AD with adjuncts such as PEP or, in end-stage disease or severe infections, non-invasive ventilation, to support the needs of the individual. While this may be beneficial to some individuals, the physiological basis of AD should be considered and settings adapted as required. Of note, there are no studies investigating the effect of the addition of adjuncts to AD. It is possible to utilise AD following haemoptysis or pneumothorax, once the individual is medically stable and with the necessary advice, supervision and monitoring.

It has been noted that children over the age of eight can be taught AD,[5] however, the individual should be assessed in terms of maturity and readiness to learn6 as some children older than eight may not have the focus and concentration required.[1,2]

It is possible to use the principles of AD with younger children or patients who are unable to complete independent techniques.[6] This is often called Assisted AD or AAD.[7-9] Breaths at differing lung volumes can be achieved by applying gentle manual pressure to the chest during inspiration, in expiration the breathing motion of the individual is followed.[1,7] As with AD, feedback from audible crepitation's or airway closure alongside tactile fremitus is important to target therapy.[1,10] The abdominal wall should be stabilised during AAD to avoid paradoxical movements.[1] Clearance is completed with a spontaneous cough.[1] AAD is often combined with therapeutic exercise such as bouncing on an exercise ball.[1,7] One trial investigated AAD and AAD with bouncing and concluded they did not induce or increase gastro-oesophageal reflux in infants under one year old.[7] A 2017 review concluded that trials are needed on AAD on the paediatric CF population, to assess the effects and "appropriateness" of this technique.[5]

There is minimal research investigating the effect of AD alone. One recent study has compared the effect of a single session of AD to period of rest in a small sample of CF patients. They reported a small statistical improvement in spirometry and a moderate improvement in global airway inspiratory resistance as measured by the forced oscillation technique, although distal airway resistance was unchanged.[11]

Most of the research into AD has compared its efficacy with other airway clearance techniques such as ACBT, oscillating PEP, PEP and Hi-PEP. A 2017 Cochrane review reported there were no statistically significant differences between AD and other airway clearance techniques in respect to changes in outcome measures such as FEV_1, quality of life, sputum weight, hospital admissions and intravenous antibiotic use.[12] One study reported patient preference for AD over postural drainage and percussion.[13] One trial suggested that AD did not affect the rheology of sputum, and so may not be an optimal ACT for people with viscous secretions,[14] while another trial suggested AD may be a preferable technique for individuals exhibiting airway hyperreactivity.[15] Two short-term studies have suggested that performing AD led to fewer episodes of oxygen desaturation.[15]

More research evidence is required for the short-term and long-term effects of AD and AAD, utilising more robust outcome measures, including patient reported outcomes, in both adult and paediatric populations.[5,12]

Recommendations

- Autogenic drainage should be considered when choosing an airway clearance technique for people with CF who are able to follow instruction (caution should be taken with children under the age of eight) *(QoE – low)*.
- There is evidence to suggest that autogenic drainage is as effective as other airway clearance techniques *(QoE – low)*.
- Consider AD in individuals with airway hyper-reactivity *(QoE – very low)*.
- Regular assessment of AD should be completed to ensure effectiveness of technique *(QoE – very low)*.
- The physiological principles of AD should be considered when combining AD with adjuncts or positive pressure support *(QoE – very low)*.

Good practice points

- Autogenic drainage should be taught by a trained physiotherapist who is able to adapt the technique to the individual patient's needs.
- Autogenic drainage can be considered for use as an independent airway clearance technique at all stages of lung disease, assessment of the patient should be carried out to ensure the patients ability to complete the different lung volumes required without shortness of breath.
- Autogenic drainage can be considered for use with patients over the age of eight, before that time assisted autogenic drainage may be helpful.
- Autogenic drainage may be helpful in treating patients with reactive or hypersensitive airways.
- Autogenic drainage has minimal contraindications for use and should be considered when selecting independent airway clearance techniques.
- Combining autogenic drainage with adjuncts such as PEP or non-invasive ventilation can be helpful for patients who need extra support. Physiotherapists should ensure the physiological principles of AD are complemented by the addition of the adjunct and assess the effect of the combination.

Research recommendation

- Long-term RCT studies comparing AD to other airway clearance therapies are needed to provide data for patient-important outcomes including quality of life.

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5.3 Positive expiratory pressure (PEP)

The use of resistance when breathing out creates a positive expiratory pressure (PEP), which can be used to enhance the mobilisation of bronchopulmonary secretions. PEP breathing generates a temporary increase in functional residual capacity (FRC) by breathing through a closed system, increasing interdependence between alveoli, facilitating collateral ventilation and therefore recruiting previously obstructed airways. It is useful in those with unstable airways, as it evens out ventilation and splints the airways avoiding collapse.[1] The PEFR/PIFR ratio with PEP is 0.47 so periods of PEP breathing are frequently combined with autogenic drainage, the forced expiration technique (FET) and cough to facilitate airway clearance.[1,2]

Low pressure positive expiratory pressure

Clinically, low pressure PEP is the most commonly used form of PEP and may be applied via a mouthpiece or mask. Treatment is usually undertaken in the sitting position[2] but may also be performed in positions to increase ventilation (eg supine or side lying).[3] Breathing through the device should be at tidal volume with only slightly active expiration (not prolonged or forced).[4] In order to select the appropriate level of expiratory resistance a manometer should be inserted between the expiratory valve and the resistor to measure mid-expiratory pressure.[5] The appropriate resistance is one which achieves a stable mid-expiratory pressure of 10-20cm H_2O.[4,6] 12-15 breaths are required per cycle to maintain FRC.[1]

Several studies have compared low pressure PEP with other methods of airway clearance both in the short term,[2,7-10] and long term (>1 year).[11-15] A systematic review of PEP in CF reported that in short or long-term studies no significant difference had been demonstrated between PEP and other airway clearance modalities with reference to pulmonary function, exercise capacity or quality of life.[16-19] Longer-term studies comparing PEP with other airway clearance techniques show equivocal or conflicting results in terms of FEV_1.[15,16,20-,22] A significant reduction in respiratory exacerbations requiring antibiotics was demonstrated in those who used PEP compared to high frequency chest wall oscillation (HFCWO) over a one-year period.[11,16,17] One study demonstrated that whole lung mucociliary clearance was greater when using PEP compared to treadmill exercise, but there was no difference in peripheral lung clearance between the two interventions.[7,17] Another study in children showed that airway clearance with PEP and AD prior to exercise led to improved ventilatory dynamics.[23] A systematic review showed larger sputum weight with PEP and FET compared to control but no change in mucus transport rate.[22]

High pressure positive expiratory pressure

High-pressure PEP involves forced expiratory manoeuvres against resistance, creating a high expiratory pressure, increasing FRC and end expiratory flow.[24] The same mask for low pressure PEP is used with a different manometer equipped to measure higher pressures (typically 40 – 100 cmH_20).[3,18]

The technique is performed in sitting where the patient is advised to perform approximately 8 – 10 breaths at moderate tidal volume then inhale to total lung capacity before performing a forced expiratory manoeuvre against the resistance to residual volume. This normally results in the patient coughing from low lung volumes and expectorating secretions. This is repeated until the cough is dry and no more secretions are produced.[3,25]

The appropriate resistance is calculated by connecting the outlet of the PEP mask to a spirometer and should be routinely assessed at clinics or more frequently on initiation of the technique. The patient is instructed to perform forced expiratory manoeuvres through different sized resistors where the resistor is chosen based on the maximal expiratory flow through all lung units which is demonstrated by interpretation of the flow-volume curve.[3]

A short-term study found high-pressure PEP yielded greater sputum volume when compared to autogenic drainage (AD). Improved lung function parameters were also found but did not exceed those achieved after AD and were associated with significantly lower sputum yield in those with airway hyperactivity, leading the authors to conclude high-pressure PEP may induce bronchospasm and should be preceded by the use of a bronchodilator or that another available airway clearance technique such as AD should be considered.[26,27] A long-term study[28] concluded high-pressure PEP resulted in improved lung

function, greater sputum yield, decreased airway stability and hyperinflation when compared to conventional physiotherapy.

Pryor & Prasad[25] advise this technique takes a considerable amount of effort and therefore would not be suitable for a patient who tires easily.

Baby positive expiratory pressure

The use of PEP has also been investigated in infants and is reported to be as effective as postural drainage and percussion.[29] This technique uses a soft face mask which is placed on the baby's face and gives a small amount of back pressure to the airways (PEP) when the baby breathes out, helping to open up the airways and clear any mucus. There is no specific guidance to resistor selection when using baby PEP therefore the assumption is that appropriate resistance is one which achieves an approximate mid-expiratory pressure of 10 – 20cm H_2O when a manometer is situated within the circuit.[4,6]

Bubble positive expiratory pressure

A bubble PEP circuit can be made up from a plastic bottle, tubing and water. The bottle is filled to 10-20 cm in depth. The tubing is placed into the water and as the individual breathes out against the resistance of the water, positive expiratory pressure is set up. Breathing out against the resistance of the water should be interspersed with FET and cough to encourage the clearance of secretions. The inner diameter of the tube should be 8mm to ensure the PEP threshold is the same as the water column pressure.[30]

There appears to be limited research on bubble PEP available. One study showed that some bubble PEP devices did not reach the recommended pressure of 10 cmH_2O and none reached 20 cmH_2O.[31]

Participant preference to PEP has been reported in several studies,[2,9,13,17,29] although the quality of many of these studies is reported as low.[21]

Recommendations

- PEP should be considered when recommending an airway clearance technique for all patients with CF *(QoE – low)*.
- There is insufficient evidence to support or refute the use of high-pressure PEP in CF *(QoE – low)*.

Good practice points

- No single treatment technique is suitable for all patients and the physiotherapist delivering airway clearance must be well-educated in all aspects of airway clearance and associated therapy techniques.
- PEP has not been proven to be more or less effective overall than other airway clearance techniques.
- Consider patient preference and their health beliefs when selecting an appropriate airway clearance technique for a patient with CF.
- Consider the age-appropriateness of specific airway clearance devices when recommending them for use as an airway clearance technique.
- The level of the expiratory resistor used should be regularly re-assessed and may need to be changed with alterations in clinical status.
- Patients must be instructed in appropriate cleaning regimens of PEP devices as per manufacturer guidelines.
- If used, treatment with high-pressure PEP must be assessed regularly, by a physiotherapist skilled in the technique, due to the high pressures used (40 – 100 cm H_2O).

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5.4 Oscillatory positive expiratory pressure in cystic fibrosis

Oscillatory positive expiratory pressure (OPEP) devices produce intra-thoracic oscillations, which are generated orally and created using variable resistances within the airways, by altering expiratory airflow. This produces controlled oscillating positive expiratory pressure which mobilises respiratory secretions.[1] Exhalation through these devices generate both oscillations of positive pressure in the airways and repeated accelerations of expiratory airflow that have been shown to result in improved sputum clearance.[2]

Oscillations or interruptions during expiratory airflow are considered to mechanically reduce the viscoelasticity of sputum and enhance mucociliary clearance.[3] Oscillations, both internally and externally, have also been considered to improve airway patency by preventing spontaneous compression through the introduction of alternating positive pressure where the consequent vibration loosens secretions allowing ease of expectoration.[4,5]

When the oscillation frequency approximates the resonance frequency of the pulmonary system, endobronchial pressure oscillations are amplified and result in vibrations of the airways.[6] These vibrations loosen mucus from the airway walls. The intermittent increases in endobronchial pressure reduce the collapsibility of the airways during exhalation, increasing the likelihood of clearing mucus from the tracheobronchial tract.[6] The airflow accelerations increase the velocity of the air being exhaled, facilitating the movement of mucus up the airways.[5] The devices frequently employed for this purpose are listed below:

- Flutter®: A small plastic device containing a large ball bearing, which repeatedly interrupts the outward flow of air.[5,7] It ventilates behind obstructed units by using a 3 second breath hold.[2] It has a PEFR of 68litres/minute, a PEFR/PIFR ratio of 1.15 and oscillates at 15-29Hz with a PEP of 5-19cmH_2O.[2]
- Acapella®: A flow-operated oscillatory PEP device, which uses a counterweighted plug and magnet to generate the oscillatory resistance.[8] It ventilates behind obstructed units by collateral ventilation.[2] It has a PEFR of 34litres/minute, a PEFR/PIFR ratio of 0.64 and oscillates at 13-30Hx with a PEP of 6-21cmH_20.[2]
- Cornet®: A horn-shaped tube, which houses a rubber inner tube. The degree of rotation of this inner tube reflects the resistance generated. As the individual exhales through the horn the inner tube unfurls generating a rhythmic bending and unbending of the inner tube within the horn throughout the expiration phase.[8]
- Aerobika (Trudell Medical International, London, Ontario, Canada)®: A flow-operated oscillatory PEP device, which uses a one-way valve to generate the oscillatory resistance.[6] The Aerobika may also be used simultaneously with nebulised aerosol drug delivery.
- Quake®: This device oscillates a column of air in both inspiratory and expiratory phases of respiration. It does not rely on an oscillating valve like the Flutter and Acapella, as it uses a manually turned cylinder that fits within another cylinder. Airflow occurs only when slots within the two cylinders line up. Therefore, the airflow is interrupted at regular intervals as the user turns the crank. The rate at which the device is cranked will determine the frequency of the flow interruption. Since the resulting vibration is not determined by the patients' rate of flow, the Quake theoretically may be more helpful for patients with severe obstructive lung disease who are unable to generate high peak expiratory flow rates.[6]

Numerous systematic reviews of oscillatory devices in cystic fibrosis reported no clear evidence that oscillatory devices were more or less effective than other forms of airway clearance and no evidence that one device was superior to another.[1,6,9-12] When oscillations are combined with DNase, there is a significant reduction in sputum rigidity and cough clearance index.[2] One study[6] comparing 4 OPEP devices in a simulated CF model found that each device functioned differently as more than one repetition of a series of exhalations are performed. They found that the Aerobika provided the most consistent pressure amplitude across resistance settings and produced the highest mean pressure amplitude at medium and high resistance.[13] In one RCT, flutter was shown to favourably alter respiratory flow bias compared to treadmill exercise.[14] Morrison and Innes also found some small but significant changes in sputum volume and weight and frequency of exacerbations, but these results were not wholly in favour of oscillating devices.[6]

Airway clearance techniques should be individualised to the patient.[9,15] If standardised instructions are given and not tailored to the individual poor technique can occur meaning

that therapeutic pressure ranges may not be achieved.[16] More than one airway clearance technique may be required in clinical practice and patient preference should be considered to improve adherence.[2]

Good practice points

- Oscillating PEP has not been proven to be more or less effective overall than other airway clearance techniques. There is no evidence that one device is superior to another.
- Consider patient preference and their health beliefs when selecting an appropriate airway clearance technique for a patient with CF.
- Consider the age-appropriateness of specific airway clearance devices when recommending them for use as an airway clearance technique.
- Patients must be instructed in appropriate cleaning regimens of oscillatory PEP devices as per manufacturer guidelines.

Recommendations

- Consider oscillatory devices when recommending an appropriate airway clearance technique for a patient with CF *(QoE – low)*.

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5.5 Extra-thoracic oscillations – High frequency chest wall oscillation (HFCWO/Vest)

Extra-thoracic oscillations are generated by forces external to the respiratory system, for example high frequency chest wall oscillation (HFCWO). HFCWO consists of an air-pulse generator connected to an inflatable jacket that fits over the chest.[1] Air pulses are transmitted to the vest, creating oscillations to the chest wall of 5-25Hz. Physiologically HFCWO enhances mucociliary transport by creating a cough-like expiratory flow bias that shears mucus from the airway walls[2], with the associated vibrations altering the rheological properties of mucus by decreasing the viscoelasticity and potentially rehydrating mucus.[3]

Evidence is variable when considering sputum clearance (wet or dry sputum weight). No consistent statistical difference between HFCWO and other airway clearance techniques have been demonstrated.[4,5-13] When respiratory function is the primary outcome, there is no evidence to suggest that HFCWO is superior to other airway clearance techniques.[4-6,14-19,26] One study demonstrated significant desaturation using HFCWO compared to PEP in patients with moderate to severe disease and recommended SaO_2 monitoring if used in this patient group.[14] There is now strong evidence illustrating an increase in pulmonary exacerbations and shorter time to next exacerbation when HFCWO is compared to PEP over a sustained period of time.[2] The HFCWO device does not provide any PEP,[25] therefore in order to ventilate behind secretions it has been advised that HFCWO should be combined with either deep inspiratory manoeuvres, 3 second breath hold, or a PEP device to achieve optimal outcomes.[3] A short-term improvement in LCI was demonstrated following 30 minutes of HFCWO compared to control of no chest physiotherapy. However, this supposed treatment effect was heterogeneous and not clinically relevant for the majority of the cohort.[20] Nebulisation during HFCWO does not affect peripheral drug deposition.[19]

Adherence to HFCWO was measured using a novel electronic device, recording daily timing and duration of use. Adherence was 82% in children, 69% in adolescents and 56% in adults. As prescribed therapy time increased, adherence decreased. Assistance with starting therapy was associated with significantly higher adherence.[21] Convenience, efficacy and comfort were the comparisons evaluated for patient satisfaction and again results were variable. In some studies, patients preferred the flexibility of alternative devices but others preferred HFCWO.[2,4-6,8-11,22,23] As a consequence of improved adherence to therapy, individual patient preference must be considered when formulating an airway clearance programme and consideration of the impact of a given device may have on a patient at particular stages of their disease.[24] The HFCWO compressor can be decontaminated after use as per local infection control guidelines. The Vest component is single patient use and must not be used for any other person.

Recommendation

- When considering frequency of exacerbation and time to next pulmonary exacerbation, an alternative treatment other than HFCWO should be considered. Cost of these devices may be prohibitive, especially in view of the lack of evidence of superiority over other airway clearance techniques *(QoE – high)*.

Good practice points

- HFCWO could be considered when adherence with other airway clearance techniques is problematic.
- HFCWO should be considered when patients are unable to carry out other airway clearance techniques for reasons such as autism, learning difficulties or severity of disease.
- HFCWO could be considered for use in conjunction with other airway clearance techniques eg ACBT, PEP.
- SaO_2 monitoring should be used for patients with moderate to severe disease using HFCWO.

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5.6 Intrapulmonary percussive ventilation (IPV)

Intrapulmonary percussive ventilation is a mechanical airway clearance device that combines internal thoracic percussion and inspiratory pressure through rapid mini bursts of air superimposed on a spontaneous breathing pattern. Expiration against the percussive element of the device leads to the maintenance of positive pressure within the airways.[1] Like other mechanical devices, IPV can be delivered either via mouthpiece or facemask.

The proposed methods of action include:

- maintenance of small airway patency, ventilation and prevention of airway closure and atelectasis;
- enhanced movement of secretions; and
- improved distribution of nebulised medications.

A number of studies have investigated the use of IPV in cystic fibrosis, however, the evidence is limited and is directed to patients with only mild or moderate disease severity.[2,3-5]

A comparative study of IPV and conventional chest physiotherapy (frequently considered in the literature to be manual techniques including postural drainage and percussion and/or vibrations) reported no differences between the techniques in terms of pulmonary function and expectorated sputum.[4,6-8] A single intervention study compared IPV with conventional physiotherapy and the Flutter® in a randomised cross-over design concluding that IPV and the Flutter® were equivalent to chest physiotherapy in terms of sputum cleared or change in pulmonary function measures from baseline.[3] Both studies included stable children and adults, however, the sample sizes were small and only the short-term effects of the interventions were studied. Similar findings have been found in stable CF patients in the outpatient setting.[9]

A short-term randomised crossover study compared the efficiency of IPV with CPT and high frequency chest wall compression (HFCWC).[2] All three treatment regimens had similar short-term efficacy in terms of sputum clearance with no positive or negative preference for comfort or convenience. Only one longer-term study compared IPV to 'conventional physiotherapy' over a six-month period and found no significant difference in hospitalisations or use of oral and intravenous antibiotic use.[9] All patients who used IPV for the duration of the study reported they would continue with the device if given the opportunity.

It is advised that every 48 hours the circuitry is dissembled and thoroughly cleaned and disinfected. There are disposable single patient circuits available, and the non-disposable parts must be ethylene oxide sterilised, pasteurised, or autoclaved between patients.

Recommendations

- Consider intrapulmonary percussive ventilation when recommending an airway clearance technique for adults with mild to moderate cystic fibrosis *(QoE – very low)*.

Good practice points

- IPV is a costly airway clearance device that requires ongoing purchase of consumables such as tubing, filters and interfaces and servicing of the device is recommended at regular intervals. As a result, these devices are not considered a convenient long-term airway clearance strategy, and this should be taken into account when considering this device.
- IPV could be considered when other airway clearance techniques have proved unsuccessful or fatiguing in patients with advanced or complex airways disease, there is presence of thick, tenacious secretions or for areas of unresolved consolidation despite conventional management strategies.
- Consider combining or alternating IPV with other airway clearance techniques to maximise effectiveness eg ACBT or AD.

- When using IPV, consider also using the device for the inhalation of mucoactive drugs to maximise effect or improve tolerance eg hypertonic saline.
- IPV settings should be tailored to the patient depending on clinical presentation and tolerance. Consider starting on low pressures for comfort and build up as tolerated until chest wall movement can be felt at the base of the thorax. Start with a high oscillating frequency (high cycles per minute) to break down mucus and shear secretions from the airway walls, then change to a low frequency (low cycles per minute) as the treatment progresses to promote migration of secretions centrally and enhance alveolar ventilation.

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5.7 Postural drainage and manual techniques

Postural drainage (PD) with the addition of manual techniques was the first airway clearance technique recommended for CF patients[1] and is still used by some people with CF today,[2] usually combined with other airway clearance techniques such as ACBT or PEP.

Postural drainage

PD involves placing an individual in different positions to drain specific sections of the lungs, with 12 specific positions identified.[3] The positions utilise the effect of gravity on enhancing mucocillary action thus mobilising peripheral secretions to the more central airways for easier clearance.[4,5] PD has been shown to improve regional ventilation[6] and can be a helpful adjunct to airway clearance in situations of lung abscesses or localised pathology.

While traditional postural drainage positions include a head-down tip to enhance drainage from the lower lobes,[3] more recent research highlighted that tipped postures can aggravate gastro-oesophageal reflux and lead to a risk of aspiration[7] so often now modified postural drainage positions are used with no head-down tip to limit this risk. The limited evidence for modified PD has shown equal efficacy to traditional PD positions, fewer risks of long-term respiratory complications and less episodes of dyspnoea.[8,9]

PD is a passive technique, reliant solely on gravity and regional ventilation changes from altered position. The addition of breathing exercises, huffing and coughing is key to utilising PD effectively.

Manual techniques

Percussion or clapping and expiratory vibrations or shaking over the chest wall can be added to PD to enhance the clearance of secretions.[1,6,10] Percussion consists of rhythmical clapping on the chest wall with a cupped hand usually during deep breathing[10], this can be completed by the individual or by a helper. Vibrations and shaking both involve oscillations of the chest wall in an inwards direction during expiration from a maximal inspiration, shaking being a larger movement, while vibrations involve a finer oscillatory motion.[10]

The exact physiological mechanism as to how manual techniques work has not been ascertained.[10] Murray[11] likened it to a ketchup bottle, in that by applying force to the outside of the bottle (ie the chest wall), it encourages the ketchup (ie the secretions) to be moved up the bottle to be expelled. This theory would also be enhanced by tipping the bottle (ie PD). It has also been suggested that percussion generates differing airflows, which create shearing forces within the airways beneath the percussed section, which loosen secretions and enhance mucocillary clearance.[10,12]

Utilising PD and manual techniques can take away an individual's independence with airway clearance, while being burdensome on carers to complete. Self-percussion is possible, however, completing this often distracts from the more important element of breathing exercises.

People with end-stage lung disease or severe infective exacerbations may find PD +/- manual techniques helpful in combination with ventilatory support such as non-invasive ventilation to help mobilise secretions while reducing individual effort. PD and manual techniques can also be considered for use with individuals who cannot actively participate in self-administered airway clearance techniques.

Research evidence for PD and MTs

The addition of percussion to PD has been shown to enhance the removal of secretions in small sample of patients who had copious secretions.[13] Vibrations have been shown to significantly increase peak expiratory flow rates over relaxed expiration,[14] and there is some evidence that high frequency oscillations can decrease the viscoelastic properties of mucus and enhance mucocillary clearance.[6,15] The addition of PD and percussion to the forced expiration technique (FET) has been shown to slow the annual rate of decline in lung function compared to FET only or no completed airway clearance.[16-17]

The literature highlights some potential detrimental effects of traditional PD and percussion, including hypoxic episodes, bronchospasm and increased gastro-oesophageal reflux.[18-20] Care needs to be taken treating people with raised intracranial pressures, cardiac rhythm changes, newborns and immature infants.[10]

Recommendations

- Consider modified postural drainage and percussion as an adjunct to other airway clearance techniques in patients with copious secretions *(QoE – very low)*.
- Consider modified postural drainage and percussion as an adjunct to other airway clearance techniques in patients with lung abscesses or specific regional pathology *(QoE – very low)*.
- Consider modified postural drainage and percussion as an adjunct to other airway clearance techniques with patients who are unable to complete effective self-administered airway clearance techniques either due to age, severity of disease or fatigue *(QoE – very low)*.

Good practice points

- When using PD, modified PD positions should be used as first line, with traditional head-down tilt positions used only if deemed necessary and not at all in infants or individuals with identified gastro-oesophageal reflux.
- PD or modified PD should be combined with an airway clearance technique.
- If the gravity assisted PD positions are not comfortable for the individual, consider alternative positioning such as sitting or high side lying.
- Postural drainage can be considered for patients who either because of their age or disease progression are not able to be as independent or as active a participant in their usual airway clearance regimen.
- Postural drainage can be considered in patients with lung abscesses or specific regional pathology.

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5.8 Intermittent positive pressure breathing (IPPB)

Intermittent positive pressure breathing (IPPB) is an established technique in physiotherapy airway clearance clinical practice.[1] Its clinical use was first described in the late 1940s; since then other systems have been developed, which can also deliver inspiratory positive airway pressure. Clinicians and patients are faced with increased treatment options but with no evidence from randomised controlled trails in CF to demonstrate superiority of one system over another.

IPPB is used in spontaneously breathing patients and involves patient triggered delivery of positive airway pressure during inspiration usually with a mouthpiece. Airway pressure then returns to atmospheric pressure during expiration. Flow rate can be adjusted to patient comfort, which may vary throughout active and rest phases of an airway clearance session.

IPPB requires either compressed oxygen or air as a driving gas making it a treatment unsuitable for home use. Careful consideration needs to be given to the most appropriate driving gas selection particularly in patients with established chronic hypercapnic respiratory failure (CHRF) given that the lowest oxygen concentration possible is approximately 45%.[2] Non-invasive ventilatory support may be a better option for these patients allowing longer duration of pressure support (if clinically indicated) and more precise titration of any additional oxygen requirement.

The dry compressed driving gas must be humidified via a nebuliser in the circuit. Clinical Practice Guidelines acknowledge that there is no evidence demonstrating superiority of IPPB to delivered bronchodilators over metered dose inhalers (MDI) or jet nebuliser systems. However, when all other validated systems have failed careful evaluation of IPPB delivery in individual patients may be considered.[3]

IPPB has been reported to increase tidal volume and therefore minute ventilation and reduce work of breathing. Expert patient assessment and instruction is required to ensure that the positive pressure is delivered to a relaxed patient who is not fighting the ventilator; allowing IPPB to be exploited to successfully augment the patient's usual airway clearance technique. Circuits are intended for single patient use and must be disposed of after patient has discontinued this treatment. All non-disposable parts of the equipment must be appropriately decontaminated in line with local infections control.[3]

Gates et al.[4] conducted a retrospective study of the use of IPPB in adults with CF who were admitted due to acute exacerbation over a period of 5 months. Out of the 39 patients that were admitted 12 received IPPB in combination with autogenic drainage. For some patients PEP and oscillating PEP devices were also combined with IPPB. The indications for use were impaired sputum clearance, increased work of breathing and lobar collapse. Whilst this study recognises the need for further prospective studies it highlights that this is a potential technique that may be useful for acute exacerbation management.

IPPB equipment is now no longer manufactured, which will make IPPB obsolete in the near future. As time progresses, although IPPB specific devices may not be as widely available, the principles of treatment can possibly be transferred and used with other devices. For example, cough assist machines or non-invasive ventilators can help with some elements of support, such as inspiratory effort management. There are also new machines being developed that may have effects similar to those of IPPB, such as the Alpha 300 (manufactured by Scientific Clinical Medical), although as yet there is no evidence for the use of these machines in CF.

Good practice points

- Due to the lack of published clinical trials investigating IPPB use in cystic fibrosis and so the clinical decision making of the physiotherapist must be informed by the pathophysiology, the clinical status and an in-depth knowledge of the advantages and disadvantage of the available equipment and operator competence.[1]
- Cleaning and appropriate decontamination must be done in conjunction with national and local infection control policies.
- Continue drug delivery through the pharmaceutically recommended systems and use 0.9% NaCl to provide humidity to the IPPB driving gas.
- An oscillating PEP device or positive end expiratory pressure (PEEP) valve may be added on to the expiratory port in the circuit, which may enhance mucociliary clearance.

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6. Sinus disease

The prevalence of sinonasal complications in cystic fibrosis has gradually increased as CF life expectancy increases, which may influence pulmonary exacerbations and have a negative effect on quality of life.[1]

There is still a substantial variation in the prevalence and reporting of symptoms with chronic rhinosinusitis affecting approximately 61% of patients.[2] It has also been identified that patients with high risk genotypes (those with Class I to III mutations) have more severe sinonasal findings than those with lower risk genotype (Class IV and V).[3,4]

There are emerging studies showing that some gene modulator drugs, particularly Ivacaftor, have reduced or reversed the severity of the sinus disease.[5,6]

6.1 Symptoms and investigations

There is little consensus as to the investigation and treatment of sinonasal disease in clinical practice. Common symptoms reported include facial pain/ pressure, loss of sense of smell or taste, nasal congestion and postnasal discharge.[7]

Multiple studies support the use of the validated SNOT-20 or 22 (see appendix IIIa) as a tool to identify patients with sinus disease, assess its severity, prompt appropriate referrals to ENT colleagues and as an outcome measure following treatment.[8-11] Two studies have found the SN-5 tool to be a valuable tool for use with children.[11,12]

Along with symptoms experienced, there has been a correlation between bacterial colonisation in the upper and lower airways,[13] and colonisation in the lower airways is associated with poor quality of life, poor clinical outcomes and high morbidity. For this reason and limited amounts of research, there is a need for continued research into sinonasal disease and prompt treatment.

6.2 Physiotherapy management

Sinonasal washout
Sometimes, rinsing your nasal passages with a salt water solution can be helpful. This is known as nasal irrigation or nasal douching and may help with symptomatic relief of chronic rhinosinusitis.[14,15]

Rinsing your nasal passages helps wash away any excess mucus or irritants inside your nose, which can reduce inflammation and relieve your symptoms.

Nasal irrigation can be done using either a homemade salt water solution or a solution made with sachets of ingredients bought from a pharmacy. Small syringes, squeezy bottles or pots (which often look like small horns or teapots) are also available to help flush the solution around the inside of your nose.

Sinonasal saline irrigation, alone or in conjunction with other adjunctive measures, may improve quality of life, decrease symptoms, and decrease medication use particularly in patients with frequent sinusitis.[14] Compared with normal (0.9%) saline, hypertonic saline (3% to 5%) may have a superior anti-inflammatory effect and better ability to thin mucous and transiently improve mucociliary clearance.[14]

It is beyond the scope of these guidelines to recommend a particular recipe for saline solution, however, various recipes and irrigation methods are available at https://www.healthline.com/health/sinus-flush#risks-and-side-effects.
See appendix IIIb.

Sinus Nebuliser Therapy
Sinonasal inhalation of vibrating aerosols is becoming a more common method of delivering mucolytics and antibiotics directly to the paranasal sinuses. Nebulisation with the PARI Sinus nebuliser aims to reduce pathogen colonisation and is well tolerated.[16]

Several studies have investigated the effects of mucolytics. Some have compared the effectiveness of 0.9% saline with 6% hypertonic saline and found improvements in SNOT-20 results in both groups, with no significantly better results from 6% hypertonic saline than 0.9% saline.[17] DNase had better results at reducing symptoms and improving SNOT scores.[17-19]

There are still limited studies investigating the effect of nebulised antibiotics and this has

highlighted the need for further studies into this treatment option.[15,19,20] 3% Tobramycin combined with 0.2% sodium hyaluronate in a nasal spray reduced secretions and improved sinus symptoms along with few side effects.[21]

Topical steroids are frequently recommended to help reduce symptoms and improve quality of life.[14,15,19]

Recommendations

- The SNOT-22 outcome measure is quick to administer, is inexpensive and is validated for use with adults *(QoE – moderate)*.
- Consider sinonasal inhalation of Dornase Alpha to help improve sinonasal symptoms *(QoE – high)*.
- Consider sinonasal inhalation of antibiotics such as Tobramycin to reduce bacterial colonisation, reduce exacerbations and symptom relief *(QoE – low)*.
- Nasal saline irrigation should be considered to improve symptoms and quality of life *(QoE – moderate)*.
- Topical steroids should be considered for symptom relief *(QoE – low)*.

Good practice points

- Patients should be screened for symptoms of sinonasal disease, at least annually or more frequently if symptoms persist or as an outcome following treatment.
- Physiotherapists should be aware of existing treatment regimens and enable patient choice to optimise adherence to treatment.
- Physiotherapists should be aware of sinonasal nebuliser equipment to be able to offer the most appropriate delivery system.

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7. Inhalation therapy

Delivering medication via the inhaled route (inhaled or nebulised) has potential advantages; medication is delivered straight to the target area of the lungs, a higher concentration is achieved at the site of action and there is less systemic exposure when compared to oral or intravenous treatment.[1,2] Some medications are only available in inhaled form (eg some mucolytics/hyperosmolar agents), and inhaled medication may be safer, more acceptable and more practical to deliver than other ways of delivering medication, such as intravenously, particularly for sustained use. There is also growing evidence that the direct targeting of some therapies to the site of action may be more effective.[2] A wide range of medications may be delivered by the inhaled route and various inhaler and nebuliser devices are available to do this.[3]

Managing the practicalities of inhaled therapy such as the choice of medication, drug response assessment, device selection, device provision, education and monitoring is frequently undertaken by physiotherapists.[4,5] This is logical given the timing needs of some medications which are often around airway clearance and given that many inhalation devices (inhalers and nebulisers) require breathing pattern training. With the advent of independent and supplementary prescribing for physiotherapists, prescriptions for inhaled medication are often completed and monitored by the physiotherapist.[5]

7.1 Medication

There are a number of documents which guide the use of inhaled therapy for people with CF. These include the National Institute for Health and Care Excellence (NICE) guideline for CF,[6] the NICE quality standards for CF,[7] the NICE specific medication guidance,[8,9] the NHS England clinical commissioning policies,[10-12] the Scottish medicines consortium policies[13] and other regional policies. Overall, it is accepted that there is good evidence that inhaled therapies are both clinically and cost effective.[6,7]

There is little guidance about the use of bronchodilators or inhaled corticosteroids for people with CF. Cochrane reviews suggest that short acting bronchodilators may be beneficial in individuals with demonstrable bronchodilator responsiveness or bronchial hyper responsiveness,[14] but there is poor evidence for the use of long-acting beta-2 agonists or long-acting muscarinic antagonist bronchodilators for people with cystic fibrosis.[15] The withdrawal of inhaled steroids evaluation study suggests that inhaled corticosteroids are best reserved for people with an additional diagnosis of asthma.[16]

There is clear guidance around mucolytics and hyperosmolar agents.[6,7,9,10,13] People with cystic fibrosis who have clinical evidence of lung disease should be prescribed Dornase Alfa as the first choice of mucoactive agent.[6,7,10] If clinical evaluation or lung function testing indicates an inadequate response to Dornase Alfa, both Dornase Alfa and hypertonic sodium chloride or hypertonic sodium chloride alone are recommended.[10] Mannitol dry powder for inhalation is recommended as an option for treating cystic fibrosis in adults; for those who cannot use Dornase Alfa because of ineligibility, intolerance or inadequate response to rhDNase and whose lung function is rapidly declining (forced expiratory volume in 1 second [FEV_1] decline greater than 2% annually) and for whom other osmotic agents are not considered appropriate.[9] It may also be considered for children and young people who cannot use Dornase Alfa and hypertonic sodium chloride because of ineligibility, intolerance or inadequate response.[9] Additionally, there is good evidence for the use of hypertonic sodium chloride for sputum induction and/or improving the quality of airway sampling.[17]

There is clear guidance around inhaled antibiotics. People should be prescribed inhaled antibiotics for the eradication of *Pseudomonas aeruginosa.*[6,10] People with cystic fibrosis who have chronic *Pseudomonas aeruginosa* infection should have sustained treatment with an inhaled antibiotic.[6,7,10] For people who have chronic *Burkholderia cepacia complex* infection and declining pulmonary status sustained treatment with an inhaled antibiotic should be considered to suppress the infection.[6,7,10] Inhaled antibiotic therapy is also recommended within certain treatment regimens for *non-tuberculous mycobacterium.*[18]

For specific details of recommendations please see the appropriate clinical commissioning policy for your area/region.

7.2 Bronchodilator trials

When using bronchodilators such as Salbutamol, Terbutaline Sulphate and Ipratropium Bromide, it is recommended that spirometry is used to assess the initial response to the medication[14] with regular reassessment to ensure this response is maintained.[19] Timing of post-dose spirometry is variable depending on the medication given. An increase of 15% in FEV_1 or FEF_{25-75}, 15-minutes following inhalation of a $Beta_2$ agonist and 30-minutes post-anti cholinergic agent, being suggested as significant.[20]

7.3 Drug response assessment

Inhaled antibiotics, Dornase Alfa and hyperosmolar agents such as mannitol dry powder for inhalation and hypertonic sodium chloride may cause bronchoconstriction.[21,22] The summary of product characteristics (SPC) of many of the commonly used inhaled antibiotics and mannitol dry powder for inhalation specify the need for a drug response assessment.[23-33] The need is not stated for Dornase Alfa[34] although there are case reports of bronchoconstriction and the NHSE inhaled commissioning policy advises a drug response assessment.[10] The need for a drug response assessment is also not stated for inhaled Levofloxacin although bronchoconstriction in listed as an uncommon side effect.[31] As hypertonic sodium chloride is classified as a medical device and not a medication, there is no SPC for it but there is evidence of the potential for bronchoconstriction so a drug response assessment is recomended.[35]

A decrease of ≥10-15% FEV_1 or FEF_{25-75} following inhalation defines significant bronchoconstriction.[3,4,7] Should this occur, a further test dose with pre-medication of a bronchodilator is advisable.[3,4,7,23-34] Appendix IV describes and provides a template and competencies for the drug response assessment procedure. There is the potential for bronchial hyper-reactivity to inhaled medication once long-term treatment is established. Processes should be in place to ensure ongoing monitoring for subjective and/or objective bronchoconstriction to inhaled medications.

7.4 Inhaler devices

There has been a great increase in the number of different types of inhaler devices available for bronchodilators, inhaled steroids and combinations of these medications. Different devices have different delivery characteristics and may require different inhalation techniques and inspiratory flow rates in order to effectively use the inhaler.[36] It is therefore important to understand the availability of particular medications through particular devices. An assessment must be made of the person's ability to use a device before prescribing a medication (for example prescribing terbutaline sulphate rather than salbutamol because a turbohaler would be preferable for an individual).[36]

The NHS business authority state that medication delivered via an inhaler must be prescribed by brand rather than generically.[37] It is also helpful to consider the number of different medications and devices that the person with CF requires and consider medication choices in order to limit the number of different types of devices where possible.

There have been great developments in dry powder inhaler delivery with the approval by NICE of dry powder Colistimethate sodium, Tobramycin and Mannitol.[8,9] It has been recognised that test dosing and education, particularly around technique, are key when commencing these medications in order to assess suitability and limit side effects such as coughing. Refer to Appendix IV.

7.5 Nebuliser devices

There are increasing types of nebuliser systems available. The most common types available are conventional nebulisation systems, ultrasonic nebuliser systems, adaptive aerosol delivery nebuliser systems (AAD) and/or vibrating mesh technology nebuliser systems (VMT). There is little evidence to recommend one type of nebuliser device over another in terms of randomised trials demonstrating improved clinical efficacy or patient preference. There is, however, an indication that new nebuliser technologies such as AAD and VMT have advantages over conventional systems. These include speed of nebuliser administration with AAD[38] and VMT devices being quieter. These devices may also provide better deposition[39] and more consistent dosing.[40] Further high-quality trials are needed to confirm these suggestions.[41]

Many new medications are licenced for administration only with a specific nebuliser system (for example Cayston® with the PARI eFlow and Altera® handset). It is important to note that different nebuliser systems have different delivery characteristics and therefore the delivered dose may vary depending on the device used[29] (See Appendix IV). Where a choice is made to deliver an inhaled medication through a device which isn't named on the summary of product characteristics, consideration must be given as to whether there is sufficient data to ensure a safe and effective dose is delivered. There should be an awareness that delivering medications through an alternative device is an off-label use and should be discussed with the prescriber (See Appendix IV).

It is helpful to consider the number of different medications and devices that the person with CF requires and consider medication choices in order to limit the number of different types of devices where possible. There are some possibilities around mixing medications in order to reduce burden, but consideration must be given around the legalities and appropriateness of doing so. Appendix IV provides a summary of medication compatibility.

7.6 Timing of medications

It is generally suggested that nebulised antibiotics should be taken after physiotherapy and after bronchodilators in order to ensure best deposition and protection from bronchoconstriction.[3,4]

Questions remain around the optimal timing of Dornase Alfa. Studies have suggested that inhalation either pre- or post-airway clearance is equally effective.[42,43] Others suggest that inhalation 30 minutes pre-airway clearance may improve small airway patency more than inhalation post-airway clearance.[44] The advised gap between administration of Dornase Alfa and inhaled antibiotics varies across the UK and is largely based on the strongly held beliefs of physiotherapists and tradition.[45] The gap advised may impact the complexity of people's treatment programme, their treatment burden and adherence.[45]

Hypertonic saline and Mannitol dry powder for inhalation should be taken immediately prior to or during airway clearance as they are thought to have an immediate mode of action. This may be directed by individual patient preference.

7.7 Combining inhaled medication with airway clearance techniques

It is possible to combine some nebuliser devices with an airway clearance device (eg PEP with eflow). Combining techniques is attractive as a strategy to decrease treatment burden and may also be driven by a wish to optimise deposition, but there isn't evidence to firmly demonstrate these outcomes. There is a suggestion that people may like combining airway clearance with nebulisation and find it less time consuming,[46] but it is important to note that there is a suggestion that combining airway clearance devices with nebulisation may decrease lung deposition.[47] The addition of an airway clearance device to a nebuliser is not identified in the summary of product characteristics of any nebulised medication and so this action creates an off-label use of the medication. Clinicians must consider whether there is sufficient data to ensure a safe and effective dose is delivered and discuss this with the prescriber. (See Appendix IV).

7.8 Cleaning and maintenance of equipment

Advice about cleaning of inhalers can be found within the medication summary of product characteristics or patient information leaflet. Advice about cleaning of nebuliser devices can be found in the manufacturer's information such as handbooks. Appropriate cleaning and maintenance of nebuliser equipment is essential to avoid bacterial contamination of the equipment, to decrease the risk of acquiring pathogens and to ensure efficiency of the delivery of inhaled medication.[48-50] Maintaining cleaning regimens can be particularly challenging in the hospital environment and thought should be given as to how appropriate regimens can be supported.[48,50] Please also see the section on infection control for more information.

Recommendations

- Inhaled medication (inhalers and nebulisers) must be prescribed by brand and not generically where possible *(QoE – moderate)*.
- Regular reassessment of the response to bronchodilators should be carried out where appropriate *(QoE – moderate)*.
- A drug response assessment will be performed in order to assess suitability and/or effectiveness of the inhaled medication for the individual *(QoE – moderate)*.
- Where bronchoconstriction is present on a drug response assessment, a further drug response assessment with pre-medication of a bronchodilator is advisable *(QoE – moderate)*.
- An assessment of the ability of the person to use an inhaler or nebuliser device will be made before commencing treatment *(QoE – low)*.
- Consideration should be given to using intelligent nebuliser technologies such as AAD and VMT *(QoE – low)*.
- Relaxed tidal volume breathing through the mouth and not the nose is recommended for people using nebulised antibiotics through a conventional nebuliser system *(QoE – very low)*.
- Expiratory filters should be used to avoid environmental contamination with exposure of others to the medication and also to avoid damage to property *(QoE – very low)*.

Good practice points

- Physiotherapists will remain up to date with regional commissioning policies related to inhaled therapy.
- Appropriate education for the use of inhalation devices and treatment strategy will be given to the person with CF/appropriate family and ongoing support provided.
- Physiotherapists should remain aware of inhaler and nebuliser developments in order to offer the most appropriate device for each medication.
- Physiotherapists must ensure that the medication and device issued to the person are compatible and will deliver a comparable dose to the medication and device combination stated within the summary of product characteristics.
- Off-label use of medication will be discussed with the prescriber.
- Cleaning and maintenance education must be an integral aspect of the provision of nebuliser equipment.
- A mouthpiece should be the preferred route of delivery for nebulisers.
- The device and appropriate parts are replaced appropriately and in accordance with the manufacturer's guidance.
- Ensure ongoing monitoring for subjective and/or objective bronchial hyper-reactivity to inhaled medications once long-term treatment is established.

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8. Oxygen

Oxygen therapy is commonly prescribed for the treatment of hypoxaemia in people with CF. Chronic and recurrent airway infection and inflammation, leading to progressive lung damage results in chronic hypoxaemia and can lead to cor pulmonale.[1] Episodic hypoxaemia can occur during sleep, exercise, air travel, at altitude, and during infective exacerbations of CF.[2] Individuals with respiratory disease are most at risk of compromised gas exchange during sleep and exercise, and the development of nocturnal hypoxaemia and hypercapnia are poor prognostic signs in CF.[3] It has also been postulated that chronic hypoxaemia may up-regulate airway inflammation, contribute to persistence of *Pseudomonas aeruginosa* infection and inhibit CFTR function.[2] There is no universally accepted method of measuring hypoxaemia in CF, leading to a lack of uniformity among published studies.[1] There are currently no CF specific guidelines to inform best practice regarding supplementary oxygen therapy in CF.

Oxygen therapy can be associated with some adverse effects, such as suppression of respiratory drive and decreased mobility due to tethering to a device.[1] There are also psychological implications, including issues with self-image and increased burden of care.[2] Adherence to oxygen therapy may be poor if no benefit is felt and often improves when oxygen therapy provides symptomatic relief.[3]

The practical use of oxygen in CF is complex.[4,5] Supplemental oxygen has a role in emergency care, respiratory exacerbation, chronic long-term use, sleep and exercise. It is also used with NIV, during air travel and at altitude. Oxygen requirement may differ during each of these situations and should therefore be assessed independently to ensure adequate oxygen prescription. Physiotherapists may be involved in the assessment, set-up and monitoring of oxygen therapy in CF.

Oxygen therapy in CF is complex and the optimal oxygen saturation in this group has not been investigated.[6] Further investigation into the role of oxygen in CF is required regarding the benefits of long-term oxygen therapy, administered continuously or during sleep or exercise, to inform when and how best to use oxygen therapy in the management of CF.[1,7]

Development of a local pathway based on available guidance can enable timely assessment and facilitate a more systematic and proactive approach to assessment and treatment planning along with greater patient involvement.[8]

8.1 Emergency oxygen

People with CF may become critically ill, requiring emergency oxygen therapy or may require supplemental oxygen during a hospital admission for an acute exacerbation. In CF adults, the time spent with oxygen saturations lower than 90% is greater during an infective exacerbation than in the stable state.[2] Those with advanced CF may suffer from exacerbations similar to advanced COPD exacerbations with associated hypoxaemia and hypercapnia.[6] There is limited CF specific guidance on the use of emergency oxygen so much of the information available is extrapolated from COPD guidelines.

All people with CF requiring emergency oxygen should be admitted to a regional centre.[6] If, due to geographical reasons, this is not possible, cases should be discussed and managed according to a protocol agreed by the regional centre.[6]

A target oxygen saturation range should be prescribed for all patients at time of admission.[6] It is recommended that emergency oxygen therapy is prescribed to achieve a normal or near-normal target saturation range of 94-98% for most acutely ill patients.[6] Oxygen can be delivered by nasal cannulae 2-6 Lpm or face mask 5-10 Lpm if hypoxaemic with no risk of hypercapnia exists in this group.[6] People with CF with advanced disease may demonstrate hypoxaemia and hypercapnia, those at risk of hypercapnic respiratory failure should be prescribed emergency oxygen with a target saturation range of 88-92%.[6] Oxygen should be delivered via venturi 28% at 4 Lpm or 24% at 2-3 Lpm or nasal cannulae at 1-2 Lpm in this group. If arterial blood gases then show a normal $paCO_2$, the target range can be adjusted to 94-98%[6]. For those on LTOT, a patient specific target range should be set.[6] As disease progression is variable, individuals with CF may need to be managed differently according to previous and current blood gas measurements.[6] There is a requirement to maintain adequate oxygenation and to avoid excessive hypercapnia and acidosis, and NIV may be useful in individual cases.[6,11,12]

In palliation, oxygen should be used for those with oxygen saturations <90% or for those who report significant relief of breathlessness with oxygen.[6]

Oxygen should be weaned in stable patients with satisfactory oxygen saturations in the target range and discontinued when SpO_2 is within the target range on room air, on two consecutive observations.[6]

Arterial blood gases are required when hypoxaemia is unexpected, oxygen saturations are deteriorating despite optimal management, there is increased breathlessness in previously stable hypoxaemia, or there are risk factors for hypercapnic respiratory failure.[6] For most people who require blood gas sampling, either arterial blood gases or arterialised earlobe blood gases may be used to obtain an accurate measure of pH and PCO_2. However, the arterial oxygen tension (PaO_2) is less accurate in earlobe blood gas samples (it underestimates the oxygen tension by 0.5–1 kPa), so oximetry should be monitored carefully if earlobe blood gas specimens are used.[6]

People with CF who have had previous episodes of hypercapnic respiratory failure should be given an oxygen alert card with recommendations for target saturation range and oxygen prescription based on previous blood gas measurements.[6]

Many people with CF may demonstrate high respiratory rates when critically ill or during an infective exacerbation. Those with a respiratory rate greater than 30 breaths per minute may benefit from oxygen supplied via venturi mask with the flow rate increased by 50% above the recommended level, to ensure gas flow rate exceeds inspiratory flow rate.[6]

There is little evidence to support the use of humidification, but it may be beneficial in those who require high flow oxygen for more than 24 hours, those who experience upper airway discomfort and dryness and those who have thick secretions that are difficult to expectorate. This can also be achieved with the use of nebulised normal saline.[6] A nasal high flow oxygen delivery system can deliver high flow rates with accurate FiO_2 and humidification; delivery of aerosol at high and low flow rates with nasal high flow in CF is efficient and reproducible.[11] High flow nasal oxygen has shown reduced respiratory rate and minute ventilation compared to NIV.[9] These systems are generally well tolerated.

Patients should be given an oxygen information sheet where possible.[6]

8.2 Long-term oxygen therapy

The progression of CF respiratory disease often results in chronic hypoxaemia and a myriad of complications associated with this. Long-term oxygen therapy (LTOT) is often prescribed to treat hypoxaemia and prevent these complications. Published studies regarding oxygen in CF primarily concern the effects of nocturnal and ambulatory oxygen.[1,11,13-17] There are no studies available that analyse the effects of LTOT in CF and recommendations for use are generally extrapolated from COPD guidelines.

In CF adults, LTOT should be ordered for those with a resting $PaO_2 \leq 7.3$ kPa. LTOT should also be ordered for those with CF with a resting $PaO_2 \leq 8$ kPa in the presence of peripheral oedema, polycythaemia, or evidence of pulmonary hypertension.[18] There is little evidence to guide when LTOT is indicated in CF children and it is generally thought that LTOT should be considered for hypoxaemic CF children to improve school attendance and for those who obtain symptomatic relief.[2,3] LTOT can also relieve dyspnoea when NIV is not tolerated in children with CF.[3]

Many people with CF develop hypoxaemia during sleep and exercise prior to the onset of daytime resting hypoxaemia.[3] Awake and exercise oxygen saturation levels do not accurately predict nocturnal oxygen saturation levels.[11] If long-term oxygen therapy (LTOT) is required, arterial blood gases are recommended to assess daytime resting PaO_2[18] along with nocturnal and ambulatory oximetry to allow accurate oxygen prescription for daytime, sleep and exercise.[3,5] It is recommended that non-hypercapnic patients initiated on LTOT should increase their flow rate by 1 litre/minute during sleep, but this recommendation is not specific to CF.[18]

In advanced disease, people with CF who are experiencing intractable breathlessness and are non-hypoxaemic ($SpO_2 \geq 92\%$) should receive a trial of opiates. Palliative oxygen therapy may be considered if breathlessness is unresponsive to all other treatments.[18]

Supplemental oxygen may cause hypercapnia, and close monitoring of $PaCO_2$ after commencing LTOT is essential in those at risk of developing hypercapnic respiratory failure.[1] A retrospective study cited a baseline $PaCO_2 > 6.5$ kPa at LTOT assessment strongly correlated with the development of progressive hypercapnia requiring NIV within 12 months of commencing LTOT.[11]

Formal LTOT assessment should be done after a period of stability, ideally eight weeks. If LTOT is ordered during an acute exacerbation, it should be limited to those with SpO_2<92% who are breathless and unable to manage off oxygen.[18] Suitability for LTOT is assessed by performing two arterial blood gases, usually three weeks apart.[18] When oxygen titration is complete, arterial blood gases should be reassessed to determine whether adequate oxygenation has been reached without precipitating hypercapnia.[18] Capillary blood gases and $TcCO_2$ can be used in place of arterial gases for monitoring.

The needs of the individual will be considered when selecting the delivery device and interface. Regular follow up by a healthcare professional experienced in oxygen therapy is required, either in hospital or at home.

Recommendations

- Emergency oxygen should be prescribed in the critically ill patient to achieve a target SpO_2 94-98% unless at risk of hypercapnic respiratory failure, in which case the target SpO_2 should be 88-92% *(QoE – high)*.
- LTOT should be ordered in CF adults with resting PaO_2 ≤7.3 kPa *(QoE – moderate)*.
- LTOT should be ordered in CF adults with resting PaO_2≤8 kPa in the presence of peripheral oedema, polycythaemia, or pulmonary hypertension *(QoE – moderate)*.

Good practice points

- Oxygen alert cards should be provided to those who have had previous episodes of hypercapnic respiratory failure, with recommendations for target SpO_2 range and oxygen prescription to ensure appropriate pre-hospital care.
- Oxygen supplied via venturi at a flow rate of 50% greater than the recommended flow rate may be beneficial in those with respiratory rates of greater than 30.
- Patients should be given an oxygen information sheet where possible.

8.3 Nocturnal oxygen therapy

Development of nocturnal hypoxaemia and hypercapnia are known to be poor prognostic indicators in CF.[18] However, there are no disease specific guidelines to suggest the optimum time for initiation of nocturnal or supplementary oxygen in the patient with CF.[18,19] Consequently, patients may be treated sub-optimally and should be regularly reviewed to ensure the most appropriate therapy.[21]

Sleep-related hypoxaemia is defined by the measurement of nocturnal SpO_2 <93.8 %.[22-24] Time spent below 93.8% can be between 5-30% of total sleep time before nocturnal hypoxaemia is considered of consequence.[2,24,25] Some literature considers hypoxaemia as SpO_2 of less than 90% for greater than 10% of the night.[19]

It is recognised that nocturnal desaturation is more prevalent in patients with worsening disease and in particular those with FEV_1 <65% predicted, even if they exhibit normal daytime oxygen saturations.[7,13,18,20,27,28] Additionally, those with baseline saturations between 93-94% are at risk of nocturnal hypoxaemia.[20]

Nocturnal desaturation has been associated with greater difficulty in performing treatment, increased exertional dyspnoea and impairment in neurocognitive performance, development of pulmonary hypertension and the inability to perform normal physical function.[2,24,20]

Nocturnal hypoxaemia can go undetected due to a lack of symptoms. However, a study found that patients who reported chronic pain due to headache from hypoxia/hypercapnia had disrupted sleep as a result, which can cause further detriment to the patient as poor sleep can be linked with cardiovascular, metabolic, immune and neurocognitive dysfunction.[20]

Although not yet studied in subjects with CF, chronic and intermittent hypoxaemia has been linked to low-grade systemic inflammation in other disorders and could worsen the already present airway inflammation and tissue destruction characteristic of CF lung disease.[25]

Before daytime resting hypoxaemia develops, many patients develop nocturnal or sleep time oxygen desaturation due to a combination of worsening V/Q mismatch in a supine posture, physiologic changes in the mechanics of respiration and derecruitment of ventilatory

muscles, especially during the rapid eye movement (REM) portion of sleep.[18,27,22,20] In the absence of daytime or exercise related hypoxaemia, it has been demonstrated that there was evidence of sleep-related desaturation, which may be clinically significant.[19,20,13,22] However, where exertional desaturation occurs it is prudent to assess for nocturnal desaturation.[1]

Monitoring evening PaO_2 and morning $PaCO_2$ were better predictors of nocturnal desaturation than measurements of lung function. Additionally, evening PaO_2 in those with moderate to severe disease (PaO_2 42-84 mmHg) contributed significantly to the prediction of a rise in transcutaneous carbon dioxide ($TcCO_2$) from non-REM to REM sleep.[13]

There is little evidence identifying significant benefit from the provision of supplemental nocturnal oxygen in advanced lung disease. There were no significant improvements in sleep arousal, sleep quality, total sleep time or indeed survival statistics.[7,19,14,18,29] Additionally, no change was identified in mood or social maintenance.[1] It did, however, improve non-REM and REM sleep, nocturnal oxygenation and participation in activities of daily living such as school and work attendance.[1,12,13,18,23,30]

There was evidence to suggest an increase in $TcCO_2$, particularly in those with severe lung disease eg FEV_1 < 29% predicted.[1,18,20] It is therefore recommended that the monitoring of transcutaneous CO_2 or capillary CO_2 (in the absence of more invasive arterial blood gas analysis) should be carried out to guide the clinician in the need for non-invasive ventilatory support to prevent CO_2 retention and consequent morbidity.[3,7,18]

8.4 Oxygen and non-invasive ventilation

In the presence of significant hypercapnia, non-invasive ventilation (NIV) may need to be considered in conjunction with oxygen supplementation.[3]

There are a number of reports of the use of NIV in patients with respiratory failure due to severe or end-stage CF lung disease. This topic will be covered in another section of these guidelines.

There are a number of studies also looking at the benefits of NIV use in sleep (with or without supplementary oxygen) and improvements in oxygenation.[7,13,30] In these studies, the use of nasal continuous positive airway pressure (CPAP) or bilevel pressure supported ventilation demonstrated an improvement in oxygen saturations during both non-REM and REM sleep. This was postulated to be due to prevention of airway closure, maintenance of end-expiratory lung volumes and reduction in the work of breathing with a possible reduction on oxygen cost of breathing.[7,13,30]

NIV was found to be effective in minimising the degree of hypoventilation occurring during sleep, as evidenced by arterial blood gas (ABG) samples showing an improvement in pH and a trend toward a lower $PaCO_2$ after a night of NIV compared with supplementary oxygen alone. The improvements in nocturnal oxygenation and reductions in CO_2 with NIV were achieved without modification of sleep quality or efficiency.[11,13,29] However, one study that compared NIV+/- oxygen to supplementary oxygen and air,[29] found no statistical difference in awake ABGs.

A recent study looking at the use of NIV +/- oxygen versus oxygen in patients with nocturnal hypoxaemia, in the absence of nocturnal hypercapnia, found that patients on NIV were less likely to develop hypercapnia, require a lung transplant or die at the end of 12 months, compared to the oxygen-only group.[31]

Further investigations into the role of oxygen in patients with CF, with regards to potentially improving daytime function and producing survival benefits are warranted in order to determine when and how oxygen therapy should best be used.[7] Despite the widespread use of nocturnal oxygen and the growing interest in NIV in patients with CF and nocturnal desaturation, many questions remain regarding the effectiveness of these therapies in positively modifying daytime function, as a bridge to transplantation in end-stage disease and long-term survival.[7,30]

Recommendations

- With those patients who have FEV_1 <65% predicted or a daytime SpO_2 of <94% overnight oximetry monitoring is advised to ensure nocturnal desaturation is not missed *(QoE – moderate)*.
- Monitoring of $TcCO_2$ is advantageous in guiding the application of supplementary oxygen and the initiation of non-invasive ventilation *(QoE – moderate)*.

- Spirometric parameters and measurements of awake resting oxygenation are of limited utility in predicting nocturnal desaturation. Nocturnal oximetry should be considered in patients with moderate to severe lung disease even with preserved awake resting SpO_2 *(QoE – low)*.
- Nocturnal oxygen should be prescribed with caution and further analysis of $TcCO_2$ should be undertaken to ensure no adverse effects occur, eg nocturnal hypercapnia. *(QoE – moderate)*.

Good practice points

- Monitor patients reporting headache for nocturnal desaturation.
- Polysomnography is useful for measuring sleep architecture.
- Simple overnight oximetry is widely available and provides clinically useful data.

8.5 Ambulatory oxygen

Ambulatory oxygen therapy (AOT) describes the use of supplemental oxygen during exercise or activity and can also be used to enable effective airway clearance in CF.[18] There are some studies considering the use of AOT in exercise but rarely during activities of daily living. People with advanced CF lung disease are likely to have reduced exercise tolerance.[32] AOT minimises desaturation during exercise and can aid episodes of desaturation during airway clearance and/or activities of daily living.[16] AOT has been shown to offer improvements in both intensity and endurance during exercise, and thus will maximise the benefit of exercise programmes.[1,15,18] Despite the improvement in oxygenation and exercise duration with oxygen supplementation, peak work capacity and oxygen uptake did not improve in exercise studies.[15-17] The use of supplemental oxygen has been shown to result in raised CO_2 levels,[1,17] and it is unclear what advice to give patients for whom AOT is impractical or declined.[33]

Desaturation on exertion may be identified during annual exercise tests and this is likely to develop before the need for LTOT.[16,18] Assessment should be considered if patients are experiencing breathlessness that is impacting on activity or exercise levels. It is appropriate to review the degree of desaturation and options for AOT with the patient, considering their views of AOT. A formal AOT assessment can then be carried out. Assessment for AOT is based on measurement of oxygen saturation (SpO_2) using a finger probe or the earlobe to determine if there is desaturation on exercise, defined as a drop in SpO_2 of ≥4% to <90%[2] and also to assess patient's response to AOT. Assessment should also consider the most appropriate device and setting to correct exercise desaturation. Where the respiratory rate is high, assessment using Venturi oxygen at a flow rate sufficient to exceed the patient's peak tidal (and exertional) inspiratory flow can offer advantages over oxygen therapy delivered by nasal cannulae. Patients with high respiratory rates should receive AOT at a flow rate via a Venturi mask, which exceeds their peak tidal and exertional inspiratory flow, and be supplied with home oxygen equipment which is able to deliver the required high-flow rates. It is worth considering that equipment delivering higher flow rates are likely to be heavier, supplying reduced hours of use, and that portability and duration of use declines considerably above 6 Lpm.[5,18] Assessment should consider daily activity and treatment programmes which may include exertion related to employment and sport[5]. If the patient already has an LTOT prescription, it is likely that they will require a different flow rate for activity and exercise.[5]

AOT requirements should be reviewed regularly, especially if commenced during an exacerbation or when unwell when an initial review at 4–6 weeks to consider if this therapy is still indicated. Home visits may be useful to identify problems with equipment or set-up and to further assess activities undertaken during daily activity. Further reviews should be carried out every 6 months when stable, or sooner if there are clinical changes. Supplemental oxygen should improve participation in and maximise the benefits of exercise.[15,17]

Recommendations

- AOT should be assessed by monitoring desaturation on exertion either using a formal exercise test or during specific activities *(QoE – low)*.
- Desaturation requiring consideration for AOT/ LTOT is defined as a drop in SpO_2 of ≥4% to <90% *(QoE – low)*.

Good practice points

- Patients should be routinely monitored for exertional desaturation, annually as a minimum and more frequently as necessitated.
- A venturi device may be considered where the respiratory rate is high.
- Consideration should be given to the type of equipment suitable for the patient and the types of activities they will undertake.

8.6 Oxygen for air travel

Air travel is common for patients with cystic fibrosis, but the guidance for air travel is vague as there is no threshold at resting sea level oxygen levels or FEV_1 that will reliably predict hypoxaemia or complications during air travel, thus there is no specific evidence for CF. All CF patients should be assessed by examination prior to flying.[34]

CF teams should consider the patient's previous flight experience, flight duration, destination and, if relevant, the time since the last exacerbation when giving advice to patients.[34]

Contraindications to commercial air travel include ongoing pneumothorax with persistent air leak, major haemoptysis and oxygen requirement at sea level with a flow rate exceeding 4 Lpm. Desaturation during flight or altitude is considered unlikely if FEV_1 is greater than 40% and resting saturations are greater than 92-94%.[4]

The hypoxic challenge test (HCT) is a method of assessing whether patients need in-flight oxygen. It involves a 15% normobaric oxygen challenge, which simulates the partial pressure of oxygen at altitude. In adults, if HCT results demonstrate PaO_2<6.6 kPa or SpO_2<85% in flight oxygen at 2 L is recommended. In children, if SpO_2 <90% during HCT in-flight oxygen is recommended.[34] Whilst the HCT can be a more accurate predictor of risk patients who are likely to desaturate during air travel, it is not available at all hospitals and does not replicate a 2-week holiday where the patient may return in poorer health than when they left. SpO_2, SaO_2 and PaO_2 during CPET have demonstrated a correlation with those measured during HCT, and since an exercise test is carried out at annual review, this can contribute to pre-flight screening for patients considering air travel.[35] Further research is needed to determine the value of HCT in assessing patients before air travel[34] and in determining reliable cut-off values for CPET which could then contribute to pre-flight screening.[35]

In children who are old enough for spirometry and whose FEV_1 is <50% predicted, HCT is recommended, and if SpO_2 falls below 90%, in-flight oxygen is advised. Infants and children who are oxygen-dependent at sea level will need their oxygen flow rate doubled at cruising altitude and should not need HCT, however, if they have had long-term oxygen within the last 6 months then HCT should be considered.[34] Infants under 1 year with a history of neonatal chronic respiratory problems should have HCT performed.

Advance planning is required, and patients are advised to seek advice before booking, to book extra services required with the airline such as in-flight oxygen and airport assistance. If oxygen is required at ground level, it will not be provided by the airlines within the airport. Patients should be advised to consider booking an aisle seat near the toilets to minimise further in-flight activity and consequent energy and oxygen expenditure.[34]

Airlines will generally require a medical form to be completed by the oxygen prescriber in order to supply in-flight oxygen but may also allow the patient to take onboard portable cylinders or concentrators. All arrangements and costs associated with in-flight oxygen will vary between airlines. Patients with medical needs who fly often can obtain a Frequent Traveller Medical Card (FREMEC), which represents temporary medical authorisation for passengers travelling on many airlines. It records important medical information and replaces forms otherwise needed for each flight. Once registered, assistance is available whenever the patient flies. FREMEC is issued by many airlines, with its validity period dependent on the medical condition.

Patients most at risk can be advised to avoid sleep and alcohol, to stay well hydrated and to have a small carbohydrate meal, all of which will prevent further desaturation.

Good practice points

- Patients should be advised to plan ahead and seek advice before booking, and patients should contact their considered airline for advice as well as their CF team.
- Patients at higher risk should be offered advice regarding sleep, alcohol, hydration and diet.
- An HCT may be helpful, but if this is unavailable then desaturation during flight or altitude is considered unlikely if FEV_1 is greater than 40% and resting saturations are greater than 92-94%.

8.7 Oxygen equipment

There are few published studies considering this topic and technological advances mean that the results are outdated quickly. Equipment used in the provision of oxygen can be divided into 3 categories as follows:

1. Source (concentrators, cylinders and liquid)
2. Delivery (cannula, masks, conservers and tracheal devices)
3. Supplementary (conservers, humidifiers and carrying bags/trolleys)

All sources of oxygen can be portable or static and decisions on the most appropriate type of device will be based on lifestyle, level of activity, flow rate required and patient preference. Equipment will be delivered directly to the patient by the oxygen contractor supplying the local area. Different contractors may source different types of equipment for their contract. This can result in slight variances in the specific equipment available to patients in different parts of the UK, but all will have availability of a range of flow rates and a variety of portable equipment. Some of the more portable equipment is likely to offer pulsed oxygen in order to minimise the size and weight of the device and higher flows of continuous oxygen are likely to be provided by liquid oxygen. Home concentrators are now available in some areas which enable the patient to fill small, portable cylinders that can then be used outdoors. Oxygen concentrators are available in more than one size and flow rate and will vary depending on supplier and location in the UK.

Controlled, fixed-flow oxygen can be provided by a venturi mask, but where a variable flow is acceptable, nasal cannulae are more discreet and have less impact on communication and eating or drinking. Psychological factors should also be considered such as the impact on self-image and burden of care.[4] Other devices such as the OxyArm™ have been developed, but have not been found to be preferred by patients. Oxygen-conserving devices can be integral or separately attached to the oxygen source, delivering pulsed oxygen on inspiration. Whilst some studies have agreed that these devices can reduce oxygen usage by around 50%, it has also been shown that demand flow oxygen is not as beneficial as continuous flow oxygen during exercise or activity. In addition, some patients, especially those who mouth breathe may have difficulty triggering the devices and therefore an ambulatory assessment should be carried out before it is recommended.[36] There is no evidence for the use of conservers overnight.

Backpacks and trolleys can be provided by the oxygen provider and are likely to improve compliance with ambulatory oxygen therapy, although many patients may prefer to source their own bag or carrier.[4]

Humidification devices are available for static sources of oxygen supply by bubbling oxygen through the sterile water. Despite the view that humidification will be helpful in the presence of excessive thick secretions, there is no evidence to support this other than when oxygen is supplied via a tracheostomy.[18]

Good practice points

- The oxygen equipment provided to the patient should be considered in order to meet the individual requirements of their prescription and to suit their lifestyle and preferences.
- Conserving devices should be considered in order to reduce the oxygen usage and extend cylinder life. The patient will require an assessment for this.
- Equipment to carry oxygen equipment should be provided and is likely to improve compliance.
- Humidification may not be helpful.

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9. Non-invasive ventilation

Non-invasive ventilation (NIV) refers to the mechanical augmentation of minute ventilation. It is a flexible form of ventilation, which can be used continuously, at night or intermittently for specific treatments in the day as indicated by clinical status. NIV use in CF was first described in the management of severe life-threatening respiratory failure as a bridge to transplantation.[1] Reports described its ability to achieve adequate oxygenation without exacerbation of hypercapnia, improvement in the symptoms related to hypercapnia and decrease in inpatient hospital days in those who can be discharged home with NIV.[1-3]

Consequently, NIV has become an accepted tool as a bridge to transplantation in CF clinical practice,[2,4] but increasingly its role has developed beyond this specific indication. British Thoracic Society/Intensive Care Society guidelines identify NIV as the treatment of choice for CF patients where ventilatory support is required[5] and there is observational data reporting the use of NIV to support ventilation in patients not listed for transplantation.[6,7] NIV can also be used beyond management of respiratory failure to augment airway clearance and exercise in CF patients.[8] A retrospective review of UK CF Registry data between 2007 and 2015 identified 1,077 patients who had a least 1 recorded use of NIV with an increasing trend towards use after 2012.[9]

Depending on local expertise, physiotherapists may be involved in the assessment, set-up of equipment and monitoring of NIV. If appropriate expertise is available, it can be provided on the CF ward and in the community.[5]

9.1 NIV for airway clearance

Non-invasive ventilation to support airway clearance has become recognised as a treatment option for cystic fibrosis patients and is considered in individuals with more severe lung disease,[10] during infective exacerbations[11] or in individuals having difficulty with expectoration.[8]

The use of NIV for ACT can be a good starting point to introduce ventilators to individuals who may benefit from nocturnal support in the future. Creating a good understanding of and relationship with NIV has been reported as important in being successful with NIV usage.[12] For those established on NIV resting settings may need to be altered, in partnership between the physiotherapist and patient, with an aim to augment airway clearance, for example to allow larger volumes or slower rates. Masks can be used for ACT or mouthpieces may be preferred for ease of expectoration.

The short-term effects (over one or two days) of using of NIV for ACT has been investigated in two studies with adult CF patients during infective exacerbations,[13,14] and in one adult[15] and one paediatric study[16] using stable CF patients. Slightly longer-term studies have been completed over a hospital admission[11] and a three-month period[17]. Results have included decreased patient fatigue[11,13,14,16] and lower respiratory rates during clearance,[13,14,16] while improvements in oxygenation,[13,15] respiratory muscle strength,[13] lung clearance index (LCI)[17] and FEV_1[11] have also been highlighted. None of the randomised controlled trials have shown a difference in sputum expectorated when using NIV-assisted ACT versus usual ACT, although published work based on semi-structured interviews with individuals established on NIV for ACT have reported improved ease of sputum clearance[12,18] alongside lower levels of fatigue[12] and lower levels of breathlessness during ACT.[18] Non-significant trends towards fewer hospital admissions and increased home intravenous antibiotic use for a cohort of 14 CF patients who had used NIV for ACT over a one-year period have also been reported.[18] The current literature shows a divide in preference for NIV-assisted ACT[11,13,18] and usual ACT,[15] while this may be due to differences in the study cohorts, it is essential to consider personal preference for all ACT interventions.

All the current publications have methodological limitations, such as small sample sizes, possible effects of concurrent treatments and non-standardised ACTs used with NIV or as the control. This, and the short-term nature of these studies, makes it difficult to draw robust conclusions to the effect NIV has when added to ACT or which patients may benefit most. No studies have compared the effect of NIV-assisted ACT to oxygen-supported clearance in those who desaturate. More robust research is needed into the use of NIV as an adjunct to ACT to fully identify short and long-term benefits and possibly guide patient selection.[8]

9.2 NIV for exercise

Clinically, NIV has been reported to be used during exercise to decrease dyspnoea, improve oxygenation and ultimately improve exercise tolerance in those patients with advanced respiratory disease.[5,19] One randomized control study involving 13 paediatric CF participants (aged 7-16), compares the effect of no NIV and use of NIV on 6-minute walking distance on a treadmill.[20] The results show some improvement in distance completed, improved pulmonary function results (FEV_1 and FVC) and less reduction in post-test peripheral oxygen saturation when NIV was used.

A preliminary cross over study involving 9 adult CF patients demonstrated significant improvement in peripheral oxygen saturations and some improvement in blood gases during submaximal cycle tests when NIV was combined with oxygen in comparison to oxygen alone. There was no difference in endurance shown in this study and patient satisfaction was higher when just oxygen was used.[21] Rodriguez et al[22] conducted a study looking at the effects on incremental treadmill test results comparing use of NIV with oxygen alone in 8 adults with CF. No significant differences in lung function, oxygen saturation or rate of perceived dyspnoea between the two groups was noted.

There is a need for further research into the benefits of NIV for people with CF with reduced exercise tolerance.

9.3 NIV for respiratory failure

Worsening hypercapnic respiratory failure, as a marker of pulmonary deterioration, has been strongly linked with reduced survival.[3,23,24] The prevention of the physiological, psychological and metabolic effects of sustained hypercapnia and acidosis[19] by the early application of bi-level ventilatory support may be beneficial. NIV has become established as part of clinical practice as a tool for bridge to transplantation in adult CF patients with severe life-threatening respiratory failure.[1,2,4] Reports also describe its use beyond a bridge to transplantation in those with established chronic hypercapnic respiratory failure.

A retrospective report of 20 years NIV clinical practice in 47 people with CF demonstrated that half of those treated with long-term NIV were not on the transplant list. The data suggested that in this severe CF population, NIV initiation and long-term use may have contributed to a slowing or reversal of lung function decline.[6]

A matched case control study in 12 adult CF participants with chronic hypercapnic respiratory failure demonstrated a survival benefit and a decrease in the number of exacerbations for those established on NIV, compared to those who continued with long-term oxygen therapy (LTOT).[25]

Reduction of pulmonary exacerbations in patients not transplant-listed was also seen in another small study of 11 CF patients. This study compared data one year before and after nocturnal NIV providing some support for early initiation of NIV.[7]

Whilst certain inferences on the effects of long-term NIV in chronic hypercapnic respiratory failure are impossible without control group comparisons, the continued emergence of observational data means that randomised placebo-controlled trials of long-term NIV in this group would have substantial ethical challenges. There are no studies exploring the use of short-term NIV during acute hypercapnic respiratory exacerbations.

A small qualitative study using semi-structured interviews with 9 CF adults using long-term NIV, 5 of whom were active on the transplant list, highlighted NIV provided positive relief from symptoms and improved QoL, suggesting this is an acceptable and valued treatment option to adult patients with CF.[26]

9.4 NIV for nocturnal hypoventilation

3 adult randomised controlled trials with a total of 27 participants assessed the use of NIV for nocturnal hypoventilation.[19,27,28] These show in single-night studies that both NIV and oxygen therapy can correct nocturnal desaturation. Compared to oxygen therapy NIV attenuates increases in hypercapnia during sleep.[19,27] When used over 6 weeks, NIV improved chest symptoms, exertional dyspnoea and peak exercise capacity compared with placebo.[28] There are variable reports on personal tolerance and preference for oxygen therapy or NIV.

NIV provision

A 2014 review of NIV in CF highlights important considerations around NIV use:[29]

- Skilled introduction, careful physiological monitoring and education of patient and nursing staff.
- Ongoing careful re-evaluation as the clinical condition changes, during initial admission and all subsequent admissions.
- Skilled personnel who are familiar with the different properties of the ventilators and interfaces available to them.
- The provision of 2 ventilators and battery support to those using NIV for more than 16 hours out of 24.
- The use of humidification.
- The availability of different ventilator and interface options.

People with CF should have access to comprehensive ventilatory support provided by skilled personnel, with access to various ventilator and interface systems keeping abreast of technology as developments occur. It is likely this may be a CF physiotherapist[30] but provision will vary locally. Remote monitoring of NIV has been shown to be feasible in a small group of CF patients using NIV at home for >3 months[31] and can help to guide manipulation of settings to optimise efficacy of ventilation in the individual patient. Introduction of CF specific local NIV pathways may help to promote elective rather than emergency set-up,[32] which may improve the individual patient experience.

There is no published evidence addressing infection control issues specifically in relation to NIV.[33] Nonetheless, equipment used in delivering NIV may be exposed to potentially infectious material during routine use through contact with the patient's skin, mucous membranes and respiratory secretions.[33] Where possible, single-use equipment is encouraged and appropriate decontamination of all other component parts taken between patients.

Recommendations

- NIV should be considered for all people with CF demonstrating nocturnal hypoventilation with a rise in PCO_2 despite optimal treatment *(QoE – moderate)*.
- NIV should be considered for those in ventilatory failure in terms of improved oxygenation, improved clinical stability or control of symptoms related to hypercapnia *(QoE – moderate)*.
- NIV should be considered if fatigue is limiting airway clearance *(QoE – low)*.
- NIV should be considered as an adjunct where desaturation is present during airway clearance *(QoE – low)*.
- NIV should be considered where there is difficulty clearing secretions with other techniques *(QoE – low)*.
- NIV-supported exercise could be considered in those with chronic hypercapnic respiratory failure established on long-term NIV to help increase exercise tolerance *(QoE – very low)*.

Good practice points

- To minimise risk of the use of positive pressure, especially in those with advanced lung disease, appropriate radiological investigations and medical review should be undertaken prior to commencement of therapy to ensure the presence of an undrained pneumothorax or other contraindications to NIV use are excluded.
- Appropriate monitoring and review will be carried out during the use of NIV to ensure optimal therapy is applied. Review may be within clinic, home visits or inpatient stays, frequency of review will be determined by the needs of the individual.
- A selection of ventilators, interfaces, mouthpieces, nasal pillows, nasal masks, full face masks and total face masks should be available and used appropriately according to individual assessment.

- Hospital policies to reduce the likelihood of cross-infection must be developed in conjunction with local infection-control teams.
- NIV may be used to facilitate airway clearance and for ventilatory support in both adults and children.
- If nocturnal ventilation is indicated, prior use of NIV for airway clearance may help reduce patient anxiety and ease the process of initiation due to patient familiarity with the device.
- NIV may be considered for use during exercise where dyspnoea or oxygenation limits activity despite optimal regimen and oxygen therapy. Use of NIV during exercise should be monitored carefully as little is known about the outcomes of this intervention.

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10. Musculoskeletal issues

With an aging CF population and increasing life expectancy, musculoskeletal (MSK) problems specific to the disease process occur in addition to those of the general age-matched population.[1] The combination of abnormal respiratory mechanics, CF-related bone disease (CFBD) and reduced muscle mass lead to a high incidence of MSK pain, fractures and postural changes.[1-8] These secondary complications can hinder an individual's ability to carry out activities of daily living, treatment and exercise and will contribute to the overall morbidity and mortality of the CF population.[3,5,9,10] It is essential that these secondary complications are investigated and optimally managed to help maintain the quality of life of people with CF.[11]

10.1 Posture and thoracic kyphosis

The muscles of the trunk have a dual role for respiration and posture[2,12,13] and will prioritise the needs of respiration.[3,14] In CF, this altered neuromuscular control may compromise spinal stability leaving the spine vulnerable to injury and lead to postural adaption[3,15] and MSK problems.[3,14-17]

Increased thoracic kyphosis is a common postural change in CF and occurs as a result of altered respiratory mechanics (altered neuromuscular control, increased work of breathing, hyperinflation and an excessive, prolonged cough) and low bone mineral density.[2,3,9,18] In addition, sitting in slouched postures, an inability to lie in thoracic extension, and pain, may further contribute to a muscle imbalance.[3,9,18,19] Postural changes and tightening of the pectoralis muscles have been noted in children from the age of seven[18,20] and MSK problems begin to present during the pre-pubescent years and are present by puberty.[3,18]

The association between worsening severity of CF lung disease and increasing thoracic kyphosis has been found in many studies, but is not universally agreed.[9,18,21-25]

Lack of clarity in the literature about thoracic kyphosis measurement taken in habitual or corrected postures and the method of assessment used, make studies difficult to compare.[26] The current gold standard method for measuring thoracic kyphosis is a standing lateral radiograph, which provides a Cobb angle. This method does have limitations of high cost and exposure of the patient to radiation, and often fails to represent the full contour of the thoracic spine.[26] Thoracic kyphosis can also be measured with the Flexicurve, which is inexpensive, easy to use, and in the general population has high levels of reliability and validity.[1,26]

A recent study concluded that school-aged children with CF (compared with healthy children) may require greater cardio-respiratory adaptations when carrying a backpack unilaterally during a moderate-effort walk.[18,27] This indicates the importance of maintaining 'good' posture in the CF population. Other studies have suggested that this is also important to prevent pain and to address the poor body image and reduced self-confidence that people report.[1,9]

10.2 CFBD and fracture

Optimising bone health is essential for the CF population and the most effective strategies have been found to be early recognition, prevention, and treatment.[28]

The reasons for CFBD are multifactorial[29-34] and include CFTR dysfunction, vitamin D, K and calcium deficiency, malnutrition, delayed puberty, hypogonadism, decreased physical activity, respiratory infection, systemic inflammation, exogenous glucocorticoids and CF diabetes.[35] Studies report the prevalence (in young adults with CF) of osteoporosis to be 23.5% and osteopenia to be 38%.[28]

Puberty is important for the development of bone density and is a time when there is both peak bone growth velocity and bone density accrual.[36] Therefore, during childhood and the pubertal growth spurt, regular weight-bearing exercises will enhance the building of a stronger skeleton through a higher peak bone mass and a larger bone size.[37] This type of exercise should continue throughout an individual's lifespan.

Fracture rates are higher in the CF population,[38,39] with an increased incidence of 20% for non-vertebral and 27% for vertebral fractures.[35] Vertebral fractures are most common at the thoracic level[38] and when present may contribute

to the development of an increased thoracic kyphosis. In the CF population, there is evidence of fracture under-reporting,[19,29] and a recent study of adults with CF found that 86% of vertebral fractures (found on Instant Vertebral Assessment during DEXA scanning) were asymptomatic.[40]

Rib and vertebral fractures can result in significant pain and individuals should receive adequate analgesia and physiotherapy advice as a priority, to enable chest expansion and airway clearance. Also, intravenous antibiotics and additional mucolytic therapies may be required.[36]

Optimising bone health needs to be managed by the MDT and physiotherapists should aim to input into this process.[37] Severity of pulmonary disease is related to BMD in people with CF and therefore it is suggested that screening guidelines for bone health in children with CF should target individuals with the poorest clinical status.[41]

10.3 Pain

Pain is a common problem in both children and adults with CF. It is associated with reduced quality of life, depression, anxiety, higher rates of pulmonary exacerbation and an increased risk for lung transplant.[42-44] Pain negatively impacts on the ability to participate in disease-related daily care[5,44] and, together with physical functioning, is the strongest predictor of survival in CF.[5] Clinical outcome (as a result of moderate to severe pain) appears to not be dependent on age, sex or lung function.[42]

There is a high incidence of undertreated pain in people with CF, with one study concluding that 59% of children and 89% of adults reported at least one episode of pain in the previous month.[28]

Studies show that the incidence of MSK pain ranges from 12% to 61% and back pain from 15% to 70%.[5] Spinal pain has been shown to be associated with a significant postural component.[6] A recent study of 400 adults with CF found that 79% reported pain in the back or other joints in the last year and 50% reported that activities of daily living were impacted by MSK pain.[45] The impact of MSK pain on an individual's ability to exercise was not discussed.

A recent systematic review suggested that further research exploring the measurement properties of instruments assessing pain in CF is required.[44]

Persistent (chronic) pain, including chronic back pain has been reported in the CF population.[23] A review of persistent pain is beyond the scope of these guidelines, but multidisciplinary team involvement or a referral to a specialist pain team should be considered best practice, to manage the multidimensional aspects of persistent pain.[46]

10.4 Inflammatory joint disease and scoliosis

Episodes of joint pain (arthralgia) are well-recognised in CF, usually starting after 10 years of age. Whilst much of this is mechanical in nature, it is reported that an inflammatory arthritis is present in 5-10% of patients.[47,48,49] Cystic fibrosis associated arthritis (CFA) and hypertrophic pulmonary osteoarthopathy (HPOA) are reported, but clinical manifestations are not consistently described in the literature. There is no formal definition of CFA or evidence base for treatment. The most clinically useful diagnostic summary for CFA remains that from Pertuiset et al in 1992.[50] They suggest that CFA should be diagnosed if there is an inflammatory arthritis without articular infection, without evidence of periosteal change on x-ray and after exclusion of another cause of inflammatory arthritis.[10]

Joint pain in CF requires a thorough diagnostic work-up as poor management of joint symptoms affects quality of life, an individual's ability to carry out activities of daily living and ability to exercise.[10] When inflammatory joint disease is suspected, a referral to a rheumatology specialist should be made to confirm the inflammatory nature of the symptoms, exclude other conditions (such as rheumatoid arthritis) and to consider treatment options.[4,46] All inflammatory joint conditions, including CFA, require multidisciplinary input from the CF team and the rheumatology team to ensure optimal patient care.[10]

Scoliosis is not common in young children with CF, but the incidence is significantly higher in adolescents than in the general population and is associated with a negative effect on lung function.[20,51-53]

10.5 Skeletal muscle function

Skeletal muscle atrophy, weakness and fatigue are common in people with CF and are associated with reduced aerobic capacity,[54] therefore increasing morbidity and mortality[55] and decreasing quality of life.[56] Causes of skeletal muscle dysfunction are multifactorial in persons with CF, and include malabsorption, physical inactivity[54] and the absence or dysfunction of CFTR in muscle.[8] Chronic respiratory disease also contributes to muscle wasting and weakness (cachexia).[57] Furthermore, as the life-expectancy of people with CF increases, the age-related loss of skeletal muscle (sarcopenia) also increases which may further exacerbate the risk of adverse events such as falls and fractures.[58] Interventions that improve skeletal muscle function or offset losses in muscle mass are therefore of considerable importance in people with CF and this is an area of ongoing research.

10.6 Screening and prevention of MSK dysfunction

Postural changes have been noted in children from the age of seven[3,60] and MSK problems by puberty.[3] It has been suggested that children as young as pre-school should receive regular screening for spinal or other postural abnormalities to minimise or potentially prevent secondary MSK impairments.[3]

MSK screening tools have been developed that aim to pro-actively identify problems and facilitate early intervention.[29,61-62] A thoracic spine movement screen, questions about pain and posture and a validated pain questionnaire, allow clinicians to select the appropriate care pathway for optimal patient management.[61-62,59]

A recent study suggested that the pGALS examination tool could be used to identify MSK problems in the paediatric population.[63] This study also identified that the question, 'do you experience difficulty going up and down the stairs?', can differentiate children with CF from typically developing children.

Posture assessment cannot be considered in isolation from movement and muscle activation[68] and should be individualised.

10.7 Treatment

Physiotherapy must emphasize the importance of physical exercise and postural care, as well as addressing the unique complications which occur as people with CF live longer.[11]

There is an increasing body of evidence demonstrating the role of physiotherapy MSK techniques for the prevention and management of non-inflammatory pain and postural changes, in both adults and children with CF.[1,3,19 64-66] MSK treatments include joint mobilisations, techniques to address muscle dysfunction/ tightness, postural awareness, education and strengthening exercises. A recent review of the literature concluded that larger studies are required to assess the effectiveness of manual therapy techniques.[67]

Studies in children with CF have found that the incidence of postural problems are directly related to the amount of regular exercise taken; 90% of children with postural issues reported doing little or no exercise. The studies conclude that to minimise postural issues, exercise should be incorporated into lifestyle from an early age.[18,65]

Changes in posture and thoracic kyphosis are achievable in patients with CF. However, a stretching programme of the muscles most commonly affected in CF may not be sufficient to address the multifactorial nature of altered posture.[9] In the general population there is also no consensus on the most effective treatment methods, but cognitive learning, manual techniques and exercise are recommended.[68]

Recommendations

- Regular weight-bearing activities should be encouraged to optimise bone mineral density *(QoE – moderate)*.
- MSK symptoms should be assessed and treated by MSK specialists at the CF centre and if this is not available, a referral to local MSK specialist should be made, to provide optimal and individually tailored management *(QoE – moderate)*.
- When required, referrals should be made to a rheumatology or pain specialist to provide optimal patient management *(QoE – high)*.
- Fracture history should be recorded and optimal physiotherapy care provided *(QoE – high)*.

Good practice points

- All patients should have an annual MSK screen from age seven (earlier if necessary) to proactively identify postural problems and to ask about pain (including MSK pain).

The Manchester Adult MSK screening tool (Appendix V) *provides a validated outcome measure for pain assessment and includes a matrix to signpost appropriate care pathways for those people with CF who have problems with pain or posture.*[53,59-60]

- Children and adults should be offered advice on how to develop postural awareness and encouraged to create habits that will maintain optimal muscle balance.
- Exercise should be encouraged to help improve posture and prevent the progression of postural problems.
- Individual ergonomic advice should be given to all patients and should encompass advice for home, school, the workplace and other daily activities.

Patients should be made aware that they can seek advice about posture, pain and MSK issues. When MSK problems or acute injuries occur, prompt assessment and treatment to enable a timely return to daily activities, sport and exercise should be given.

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11. Specific issues

11.1 Urinary and faecal incontinence

Urinary incontinence (UI)

UI is well recognised as being more prevalent in women and girls with CF than the healthy population.[1-11]

Onset of UI has been reported in girls as young as 11 years old.[6] Symptoms of UI in males with CF do occur, but to a lesser degree than in females.[12] One study reports increased incidence of UI in males with CF aged 18-50 when compared with age-matched controls. This was associated with higher levels of anxiety and depression.[13] Tolerance of symptoms may result in under-reporting of UI,[1,2] although the impact of UI on quality of life can be significant[14] and is reported to increase both with age and severity of symptoms.[8]

Vigilant and sensitive surveillance for UI is recommended to ensure that patients are able to access support and treatment as required.[1-3,11,14] The risk factors associated with UI in people with CF are multi-factorial and may include poor nutritional status in younger people,[7] imbalance of the muscles of respiration, posture and continence and increased intra-abdominal pressure associated with persistent cough and constipation.[15] Cough is the most commonly reported cause of UI and symptoms are associated with forced expiratory manoeuvres. Individuals with CF and UI may be reluctant to perform airway clearance treatment and lung function procedures effectively due to the increased risk of urinary incontinence.

The occurrence of UI seems to increase at times when cough is worse, such as during a chest exacerbation. The amount of leakage reported varies greatly and can be a few drops to emptying the full bladder.[3,11] The occurrence and severity of UI increases as disease progresses.[2,3] Analysis of scores from a musculoskeletal screening tool that uses validated questionnaires to assess pain and UI demonstrated an association between the presence of low back pain and symptoms of UI in females with CF.[16] Three studies have addressed the assessment and treatment of the pelvic floor muscles.[17-20]

An improvement in pelvic muscle endurance was reported following a three-month programme of pelvic floor exercises in a small self-selected group of CF female adults.[17] A three-month intervention of pelvic floor muscle training, electrical stimulation, biofeedback and bladder training resulted in reports of significantly fewer episodes of leakage (which was sustained following the treatment period) and an improvement in electromyography and ultrasound imaging measures.[19] Tension-free vaginal taping has also been reported as a safe and effective solution for stress incontinence in a very small sample of women with CF. An abstract report describes improvement in symptoms of both back pain and UI reported by adult females who were taught pelvic floor muscle exercises.[20]

Faecal Incontinence (FI)

Two studies report increased prevalence of faecal incontinence in patients with CF compared to the normal population.[11,21] Due to the extensive gastro-intestinal comorbidity in CF, the precise mechanism of bowel dysfunction and FI is unknown, and further specialist investigation is required to guide appropriate assessment and treatment.[11,22]

A lack of awareness of UI and FI treatment options and embarrassment linked to symptoms means physiotherapists must include urinary and faecal incontinence in their assessment to identify prevalence in all patients with CF.[1-3,23]

Care should be taken when teaching pelvic floor exercises as evidence suggests 40% of women with incontinence incorrectly perform a pelvic floor contraction with verbal education alone.[24]

Recommendations

- Physiotherapists should ask all patients about UI symptoms as part of their routine assessment, starting in paediatrics *(QoE – high)*.
- Both preventative and active strategies for the management of UI should be adopted *(QoE – low)*.
- Referral to a specialist physiotherapist should be considered in those with symptoms of UI *(QoE – very low)*.

- Undiagnosed or poorly-controlled diabetes may also contribute to UI through polydipsia and/or polyuria and therefore liaising with the multidisciplinary team about screening for CF-related diabetes is suggested *(QoE – very low)*.

Good practice points

- A sensitive and open approach with early recognition of symptoms will be adopted for both males and females with CF.
- People with CF should be taught controlled and effective coughing during airway clearance.
- The 'Knack' (a quick, voluntary contraction of pelvic muscles to help prevent urine leakage during a rise in intra-abdominal pressure) may be a useful technique to use before coughing or performing forced expiratory manoeuvres.
- The Manchester Adult MSK screening tool provides a validated outcome measure to assess symptoms of UI and includes a matrix to signpost appropriate care pathways for those people with CF in whom leakage is identified (Appendix V).

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11.2 Pregnancy and parenthood

CF teams as part of routine CF centre care are now more frequently required to support women with CF through one, if not multiple, pregnancies. Pregnancy is well-tolerated in women with CF with a good health status at baseline (FEV_1>60% predicted) and this is associated with a lower risk of developing complications during pregnancy, delivery and post-partum.[1-6] However, many women do experience difficulties in maintaining stability of their health during this time and pre-pregnancy risk factors for this include diabetes, inadequate nutrition and poor or declining lung function over the last year.[7] Due to the potential complications, wherever possible pregnancies should be carefully planned, with genetic counselling, optimisation of health pre-conception and close monitoring during and after pregnancy to detect any decline in health status.[2] Patients may discuss sexual activity and pregnancy intentions with physiotherapists and open communication and liaison with the wider CF multidisciplinary team is essential as family planning is complex.[8] Treatment for decline in lung function or nutrition should be proactive during and after pregnancy to ensure the best outcome for both mother and baby.[2]

Relatively little data exists regarding the outcome for mothers and almost none on the outcome of infants beyond the neonatal period.[3] One study examined the long-term effects on mothers up to 11 years after pregnancy and showed pregnancy and motherhood do not appear to accelerate disease progression, but lead to more illness-related visits, pulmonary exacerbations and a decrease in some domains of quality of life.[5] However, a retrospective review of pregnancies over 10 years at one UK CF centre showed moderate falls in lung function immediately after delivery, which persisted at 12 months postpartum.[9]

There are no prospective studies evaluating physiotherapy interventions during pregnancy. However, pregnancy has a significant impact on respiratory status and physiotherapy requirements are likely to change throughout the antenatal period.[1,10,11] It has been suggested that patients with an FEV_1<60% are more likely to need frequent changes in their airway clearance techniques and may require the addition of positive pressure during hospital admission to enhance airway clearance technique effectiveness and reduce work of breathing.[11] As the pregnancy progresses a reduction in functional residual capacity causes early airway closure into closing volumes and may lead to a risk of hypoxia and impaired secretion clearance due to atelectasis.[2] Proactive monitoring and escalation of treatment strategies with a low threshold for positive pressure (such as NIV and intermittent positive pressure breathing) may help to minimise these risks.

Additional nebulised medications are commonly utilised during pregnancy when the use of systemic preparations is limited by concerns about possible teratogenicity. Proactive use of mucoactive agents such as RhDNase, hypertonic saline and inhaled dry powder mannitol will help to optimise airway clearance when it is limited by physiological changes. The CF specialist physiotherapist is well-placed to advise the pregnant woman with CF in planning the support and care they will need post-delivery. Completing airway clearance and nebulised medication is essential to stabilise and improve pulmonary function once the baby has arrived. However, it can be the most challenging time as the CF mother will be divided between doing treatment and tending to her child.

Pregnant women should be advised to modify their exercise programmes to avoid contact sports and reduce overheating and dehydration that can occur with activity. Walking, swimming and prenatal yoga are recommended forms of exercise that can be utilised to maintain fitness levels during pregnancy.

So far little is known about the safely of CFTR modulators in pregnancy and breastfeeding.[12] There have been case reports of pregnancies on modulator therapy, but both ivacaftor and lumacaftor are excreted in milk of breastfeeding rats and ivacaftor is thought to cause cataracts in children, therefore both should be avoided in breastfeeding.[12]

With the development of assisted reproductive technology, more men with CF are becoming fathers.[13] Whilst fathers do not experience pregnancy, they are subject to many of the demands and challenges of managing young children.[13] One small study showed no significant change in disease trajectory, however, half of fathers with a FEV_1<40% at the time of the birth of their child had died or received a lung transplant before their child was 2 years old.[13]

Recommendations

- Airway clearance techniques will continue throughout pregnancy and be regularly reviewed and modified as pregnancy progresses with consideration to the degree of breathlessness and discomfort *(QoE – very low)*.
- Pregnant women should be familiar with using a fast and intelligent nebuliser system. This is good preparation for the postpartum period where time can be limited when caring for the new-born child *(QoE – very low)*.
- All patients should be given postural awareness advice, strengthening and stability exercises for the lumbosacral and pelvic floor regions. Onward referrals to musculoskeletal and women's health services for further input should be completed as appropriate *(QoE – very low)*.
- Proactive assessment for ambulatory oxygen desaturation is recommended and supplementary oxygen can be utilised to avoid drops (maintain SpO2 >90%) in foetal oxygen delivery *(QoE – very low)*.

Good practice points

- Airway clearance techniques and inhalation therapy will be reviewed regularly throughout pregnancy and modified as necessary.
- Several different techniques used alone or in combination may be introduced to maximise ventilation and utilise lung volumes that could be compromised by the growing baby.
- The abdominal muscles are progressively stretched during a pregnancy and can become separated down the midline (diastasis–rectus abdominus). If mechanical pain or muscular herniation occurs, a stabilising binder can be useful.[2]
- Positioning for airway clearance will require modifications potentially from an early stage in the pregnancy when nausea can impact on chest clearance, and sitting, standing and head-up positions should be considered. The supine position should be avoided during the 2nd and 3rd trimesters because of the pressure of the foetus on the inferior vena cava which can decrease venous return and cardiac output.
- Gastro-oesophageal reflux should be identified and treated if present.
- Proactive use of mucoactive agents such as RhDNase, hypertonic saline and inhaled dry powder mannitol will help to optimise airway clearance when it is limited by physiological changes.
- The importance of pelvic floor exercises should be stressed, and the 'knack' taught, to be used preceding any forced expiratory manoeuvres.
- If, on the rare occasion the patient becomes more unwell towards or during the delivery period, NIV can be used to support ventilation.
- Advice should be provided for managing treatments post-partum including structuring family assistance, combining treatments (eg hypertonic saline and PEP), using nap times for airway clearance and planning who can clean equipment.
- Physiological and mechanical changes encountered during pregnancy affect the breathing pattern, and some women may benefit from help to differentiate between the dyspnoea that occurs during respiratory exacerbations that require treatment and normal 'physiological' breathlessness of pregnancy, the management of which should be taught early.[2]
- Nasal obstruction may occur during pregnancy due to the increased amount of blood flowing through the body causing mouth breathing and/or snoring. Effective sinus management should be taught using saline spray or nasal lavage.[2]
- Pregnancy in people with CF post-transplant usually requires little physiotherapy input, but the physiotherapist will have a role in monitoring for signs of possible infection or rejection episodes and maintaining posture, mobility, pelvic floor and physical strength. The patient still has their own upper airways and nasal obstruction or sinus infections may occur.[2,14]

- Patients who stop CFTR modulator therapy during pregnancy and/or breastfeeding will require airway clearance and inhalation therapy review and close monitoring.
- New fathers with CF need to be aware of potential influence of fatherhood on their health and have airway clearance and inhalation therapies optimised to make adherence as easy as possible during this life-changing event.

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11.3 Physiotherapy in CF associated liver disease (CFLD)

It is estimated that between 20-40% of people with CF have cystic fibrosis-associated liver disease (CFLD). CFLD is an early complication of CF that occurs mostly in the first decade of life, particularly in those patients with a history of meconium ileus or pancreatic insufficiency and severe mutations.[1] The independent risk factors associated with cirrhosis in CFLD are male sex, *Pseudomonas aeruginosa* airway infection and CF-related diabetes.[2] CFLD is associated with a polymorphism in the alpha-1-antitrypsin gene.[3] The annual prevalence of CFLD has increased from 203.4 to 228.3 per 1000 patients from 2008-2013 in a UK nationwide prospective study.[2] CFLD may progress to chronic obstructive cholangiopathy, cirrhosis with associated Pulmonary Hypertension (PHT) with or without variceal bleeding and end-stage liver disease. This cirrhosis and PHT can negatively impact respiratory function due to organ-megaly, ascites, and intra-pulmonary shunting.[4] In adults, low BMI is significantly associated with cirrhotic progression and while this poor nutritional state may reflect the impact of progressive liver disease, it must also be factored into treatment goal-setting, as every effort to optimise nutrition in both CF and CFLD is essential to mitigate morbidity. Mortality of patients with CFLD is almost double those without and is recognised as the third largest cause of mortality in CF.

There remains no data examining the efficacy of physiotherapy interventions in patients with CFLD, however, it must be recognised that massive splenomegaly and the resulting abdominal distension, impaired nutritional intake due to gastric compression and impaired diaphragmatic function can cause dyspnoea.[5] Physiotherapy would therefore be focussed on symptom management and safety when considering airway clearance and exercise opportunities. Exercise programmes should be focused on prevention of sarcopenia, working closely with colleagues in dietetics to ensure adequate nutrition and glycaemic control.

Recommendations

- Patients with CFLD should have frequent review by physiotherapy to ensure adequate airway clearance, with quick escalation to use of positive pressure via PEP or NIV as adjuncts to airway clearance to aid good basal ventilation and secretion clearance in the presence of hepatomegaly *(QoE – moderate)*.
- Vigilance with monitoring haemoptysis and clotting factors with every treatment to prevent undue risk to the patient from bleeding (either intrapulmonary or variceal). Remembering that although platelet volume is often impaired chronically in this patient group, more important is large daily change in platelets or haemoglobin *(QoE – high)*.
- In the presence of such high nutritional demands, it is imperative that safe exercise and strengthening takes place within the context of adequate nutrition and diabetic control, so this patient group require close interdisciplinary review with Dietetics, Diabetes Nurse Specialist and Physiotherapy *(QoE – moderate)*.

Good practice points

- Abdominal distension due to hepatosplenomegaly or ascites may restrict diaphragm excursion and cause basal atelectasis. In these circumstances, supine positioning should be avoided; airway clearance techniques may be more comfortable and effective in an upright or side lying (head raised) position.
- Use of Positive Expiratory Pressure in the prevention of atelectasis should be considered.
- Contact sports should be avoided in those with hepatosplenomegaly.
- Physiotherapists should work closely with dietitians to optimise nutritional status and glycaemic control where required to allow the patient to remain as active as possible and to exercise effectively and prevent sarcopenia.

- In the presence of abnormal clotting, manual techniques should be avoided. Potential of these patients to have haemoptysis is increased also, therefore physiotherapists should be vigilant regarding same and refer to haemoptysis guidelines should this occur.
- Deficiency in regulatory mechanisms result in derangement in the extracellular fluid volume and may lead to ascites, oedema or pleural effusion. Careful attention to positioning for airway clearance and during exercise is important.
- In the presence of active variceal bleeding, physiotherapy may need to be discontinued or carried out with extreme caution.
- Intensification of airway clearance (including treatment during anaesthesia) may be required if repeated anaesthetics are required for monitoring and management of oesophageal varices.
- Anaemia should be considered as a cause of breathlessness when carrying out respiratory assessment, and anaemia may affect ability to exercise.
- In those with hepato-pulmonary syndrome, monitoring of oxygen saturations SpO_2 during exercise and any physiotherapy interventions is important, with frequent assessment of nocturnal oxygenation and oxygen requirements during exercise.

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11.4 Haemoptysis in cystic fibrosis

Haemoptysis is the expectoration of blood from the lower airways, which can range from a minor streaking of blood in the sputum to massive bleeding that can have life-threatening consequences due to airway obstruction, hypoxaemia and haemodynamic instability.

Although haemoptysis is thought to be a common complication of CF, there is huge variation in the literature on incidence. It is thought to occur in approximately 9% of the CF population[1], but there is some reporting of mild haemoptysis to be as high as 60%.[2,3] UK CF Registry data reports annual incidence as 4.5% (0.5% <16 years, 7.2% >16 years)[4]. Adults are nearly 4 times more likely to experience haemoptysis than children,[5] with the median age of first episode occurring between 18 and 30 years of age.[2,3] Massive haemoptysis occurs in approximately 1-4.1% of all patients with CF and is rarely seen in children younger than 10 years.[2,3]

The bleeding site usually arises from a bronchial artery, but many reports have also suggested aberrant origin of the haemorrhage from non-bronchial collateral vessels or from anastomosis between bronchial and non-bronchial circulation.[6] Knowledge of the precise pathogenesis of haemoptysis is limited, but has been attributed to the persistent inflammation of the airways and vascular growth, which results in hypertrophied bronchial arteries.[7,8] Chronic and acute inflammation weakens the vessel walls and often leads to episodic or persistent bleeding into the bronchial lumen. Risk factors shown to be associated with haemoptysis in CF are older age, more advanced lung disease and the presence of *Pseudomonas aeruginosa,*[5] with massive haemoptysis more likely to be associated with the presence of *Staphylococcus aureus* in sputum cultures.[7]

Diagnostic investigation of haemoptysis includes history taking, clinical chemistry, chest radiography and in the case of moderate to large volume haemoptysis, contrast enhanced computed tomography with pulmonary angiography (CTPA). This is used to identify hypertrophied vessels, localising the source of bleeding as an aid to planning subsequent treatment intervention such as bronchial arterial embolisation (BAE). Rigid bronchoscopy can be performed as a diagnostic measure in identification of the bleeding vessel, however, there are some limitations to this and unless the vessel is bleeding at the time of bronchoscopy it is often difficult to localise. CTPA has been shown to have higher sensitivity and specificity when compared to bronchoscopy for diagnosing bronchial arterial abnormalities.[9]

Differentiation of severity of haemoptysis is necessary as treatment differs. This is based on volume of blood expectorated. Estimation of this can be challenging and is often under- or over-estimated[10]. Much of the literature considers the definitions of haemoptysis as follows:[8,10]

- Scant haemoptysis <5 ml
- Mild haemoptysis >5 ml <50 ml in 24 hours
- Moderate haemoptysis >50 ml <250 ml in 24 hours
- Massive haemoptysis >250 ml in 24 hours

Mild or moderate haemoptysis is commonplace and often associated with pulmonary exacerbation. Generally, this is self-limiting and is managed conservatively, usually responding to a course of antibiotic therapy. Other medical treatments which may be considered alongside antibiotics are vitamin K, blood replacement and tranexamic acid.[3,11,12]

In the event of a massive haemoptysis the aim of initial management is maintenance of gas exchange by maintaining the airway, administering oxygen and positioning with the bleeding side down (if known). Nebulised adrenalin may be administered where frank haemoptysis does not settle spontaneously. Once stabilised, BAE is an accepted and effective method of controlling the bleeding[6], but reoccurrence rates can be high.[1]

There are no published studies regarding the physiotherapeutic management of haemoptysis. North American guidelines[12] based on a Delphi consensus provide some guidance. Whilst there was no representation from physiotherapy on the expert panel, these guidelines do include recommendations regarding physiotherapeutic strategies for managing haemoptysis.

For scant, mild haemoptysis, there is no evidence to indicate that alteration in treatment strategies is necessary, and there is good consensus to suggest that stopping airway clearance and all inhaled therapies is inappropriate.[12] It has been suggested that enhanced airway clearance to aid the removal of purulent secretions contributing to the pulmonary exacerbation may be beneficial.[11]

In the management of moderate haemoptysis, modification of physiotherapy is prudent. In theory, positive pressure treatments may aggravate friable vessels and consideration should be given to discontinuing these in favour of more controlled breathing techniques such as ACBT or AD. Percussive devices and oscillatory devices should also be used with caution. Whilst there are concerns that airway clearance therapies may dislodge a clot and exacerbate bleeding, this is unlikely and if bleeding is related to the underlying infection and inflammation, clearance of airway secretions is an important component of care.[12] For patients with mild to moderate haemoptysis, the expert panel felt the benefits of continuing all inhaled therapies outweighed the risks and suggest that therapy should be withheld only if it seemed to exaggerate or provoke bleeding.[12]

In the event of massive haemoptysis, there should be consideration for temporarily ceasing all airway clearance[12] with continual assessment and review being maintained. There is also strong consensus regarding the recommendation to withhold NIV in the event of massive haemoptysis in many circumstances.[12] The use of hypertonic saline and rhDNase has been suggested to present a risk, although this remains unproven. Hypertonic saline might be considered more of a risk due to potential to irritate the airways, induce cough and therefore possibly provoke bleeding; there is strong recommendation to consider stopping this in the event of massive haemoptysis.[12] There is no guidance regarding modification of inhaled mannitol in the event of haemoptysis as the consensus guidelines pre-date its licence. However, as it has a similar mode of action as hypertonic saline and has the potential to provoke uncontrolled coughing it should follow the same recommendations. There is also suggestion that the benefit of continuing all other inhaled therapies outweighs the risks and therefore should only be withheld if they seem to exaggerate or provoke bleeding.[12] Flume[11] found a decreased incidence of haemoptysis in patients who were using rhDNase long-term.

There is a lack of published studies regarding exercise following haemoptysis. Exercise and habitual physical activity guidelines[13] based on consensus opinion of physiotherapy experts worldwide, recommend ceasing exercise following moderate or massive haemoptysis, resuming a gradual exercise programme following 24-48 hours of no new bleed.

Patients may experience recurrent haemoptysis despite BAE. There are no published studies, however, there is emerging evidence through individual case reporting, that physical activities or triggers (such as salbutamol, caffeine-based drinks or anxiety) which increase heart rate (HR) can provoke episodes of haemoptysis. The proposed mechanism is not clear, but it is suggested that the increase in pulmonary artery blood flow and blood pressures, as a result of the increase in HR, causes break through bleeding in small blood vessels around areas of infection. Inhaled medications have also been shown to provoke recurrent bleeding in some individuals. Where there is clear association, the risks versus the benefits of withdrawing the inhaled therapy might be considered. More studies are required to gain clearer understanding of factors that may be associated with recurrent haemoptysis and how to manage this in the long-term.

Recommendations

- For mild haemoptysis there should be no immediate change to airway clearance, exercise, NIV or inhalation therapies *(QoE – low)*.
- For moderate haemoptysis vigorous exercise should be ceased for 24-48 hours *(QoE – low)*.
- For massive haemoptysis airway clearance, vigorous exercise and NIV should be temporarily ceased *(QoE – low)*.
- Consider stopping hypertonic saline *(QoE – low)*.
- Continue other inhaled therapies unless they appear to aggravate or provoke bleeding then they should be temporarily ceased and then reassessed once bleeding settles *(QoE – low)*.

Good practice points

Mild haemoptysis

- Continue airway clearance, inhaled therapies and exercise, but with close monitoring of symptoms combined with medical management to treat underlying infection.

Moderate haemoptysis

- Physiotherapy interventions should be modified following clinical assessment. This should include careful consideration of the benefits against the risks of altering treatments regimes, recognising that maintaining

effective airway clearance is an important component of ongoing treatment of underlying infection. Treatment modifications should include the following:

- Avoiding the use of positive pressure techniques (internal, external or oscillatory) for 24-48 hours post-bleed. Consider airway clearance techniques such as ACBT or AD which utilise controlled coughing.
- Minimising vigorous or excessive coughing.
- Continuing all inhaled therapies, but consider stopping on an individual basis if identified as potential trigger to uncontrolled coughing or further bleeding.
- Ceasing physical exercise for 24-48 hours post-bleed.
- Maintaining physical activity with careful monitoring of physiological status.
- Temporarily ceasing NIV or, where considered too great a risk, consider temporarily reducing inspiratory pressures until bleeding settles.

Massive haemoptysis

- Acute management should prioritise assessment and maintenance of airway and physiological status utilising NICE guidance on recognising and responding to the patient deteriorating or at risk of deterioration.[14]
- Optimise oxygenation and humidification.
- Careful positioning (high side lying, bleeding side down). Cease all physiotherapy treatments and exercise.
- Following embolisation, in liaison with interventional radiologist, resume normal airway clearance and a graduated exercise programme.
- Ensure adequate analgesia if chest pain limits effective airway clearance.
- Psychological support and reassurance in resuming normal activity and treatments may be required.

Recurrent haemoptysis

- Where patients experience ongoing hemoptysis despite BAE, identification and modification of potential triggers may be required while taking into consideration individual needs.
- Where exercise has been identified as a trigger, avoid increasing HR more than 20-30 bpm above resting HR and/or <120-130 bpm maximum HR and/or where resting HR >100 bpm limit to physical activity only keeping increase HR to a minimum during acute phase of recurrent hemoptysis.
- Avoid or reduce caffeinated drinks.
- If tachycardia associated with salbutamol is identified as a trigger, consider reducing the dose or an alternative bronchodilator.

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11.5 Pneumothorax in cystic fibrosis

Spontaneous pneumothorax is defined as the presence of air in the pleural cavity and is frequently considered a poor prognostic indicator in CF, with an average survival rate of 24-30 months following the initial episode.[1-5] A small paediatric study suggested survival rate to be slightly better at 48 months.[6]

2018 UK CF Registry data reports annual incidence of pneumothorax (requiring chest drain) to be 0.4%, with no reported incidence in people with CF <16 years of age.[7] This is similar to the evidence in the literature which reports annual incidence of spontaneous pneumothorax to be approximately 0.64% (1 in 167 people with CF),[1,2,8,9] with the median age of incidence 23 years.[8]

A recently published review suggests anatomical risk factors such as cysts, sub-pleural blebs and bullae, all commonly identified in the lungs of people with CF, to be associated with pneumothoraces.[9] These areas are prone to distention as a result of gas trapping due to small airway obstruction. There is supporting evidence associating severe airflow obstruction with pneumothorax, with 75% of patients experiencing a pneumothorax having an FEV_1 measured as <40% predicted[1] and high residual volumes in people with CF experiencing pneumothorax.[10] Specific pathogens and nebulised therapies have been linked to an increase in risk of pneumothorax, however, it is more likely that their presence reflects the severity of airways disease and airflow limitation.[3,11]

Clinical presentation of pneumothorax in CF may occasionally be asymptomatic, but more often presents with sudden onset of chest pain and breathlessness. It has the potential to result in respiratory failure, particularly in patients with severe disease manifestation. Diagnostic investigation can be challenging with chest X-rays having the potential to be misleading particularly in advanced disease. There should be low justification for a chest CT scan as this accurately assesses pneumothorax size and supports clinical decision making for ongoing medical management.

The primary goal for medical management strategies is to re-expand the lung. Small asymptomatic pneumothoraces may be managed conservatively and resolve spontaneously, however, as recurrence rates are high (20-75% of patients), more aggressive management is justified in this population.[2,12-15] Management strategies include high flow oxygen therapy and chest drain placement; the latter having an additional advantage of facilitating interventions aimed at preventing recurrence, such as pleurodesis. Surgical pleurodesis or pleural abrasion using video assisted thoracoscopic surgery (VATS) appears to be the most effective management option.[1,2,4] Pleural procedures, including pleurodesis do not have a significant adverse effect on the outcome of later lung transplantation.[5]

It is suggested that supplemental oxygen at high flow rates generates a partial pressure gradient between the pleural cavity and end capillary blood by decreasing the partial pressure contribution of nitrogen, theoretically increasing the reabsorption of gas from the pleural cavity. Increased rates of reabsorption whilst on oxygen were demonstrated in a small prospective study of 10 patients, which extended into the paediatric age range.[6]

It is recognised that patients remain at risk of respiratory deterioration, despite medical management with insertion of intercostal drain. Lord et al[9] identify several contributing factors which include pleural pain, immobility and underlying lung volume loss. They stress the need for prompt, early management which should include intravenous antibiotics and adequate analgesia to allow effective airway clearance and early mobilisation under the supervision of experienced CF physiotherapists.

There are no published studies advocating the physiotherapy adaptations required when managing a CF patient with a pneumothorax, although there are two consensus guidelines available that provide some recommendations regarding physiotherapy interventions. These have been based on results of a worldwide informal survey regarding exercise management[16] and expert opinion by a Delphi consensus regarding airway clearance techniques, NIV, inhaled therapies and general activities,[17] however, it should be noted that the latter did not have physiotherapy representatives on the expert panel.

Flume et al[17] highlight that it is generally considered appropriate to continue airway clearance as reducing airway obstruction by clearing mucus may aid resolution and/or prevent any worsening of the pneumothorax. There is little

guidance recommending the most appropriate airway clearance technique, but techniques that are based on controlled breathing such as active cycle of breathing techniques (ACBT) or autogenic drainage (AD) may be considered more favourable.[18] Flume et al[17] strongly recommend withholding positive pressure techniques due to the risk of increasing intrapleural pressure and thus potential to cause progression of the pneumothorax. Whilst it did not reach good consensus, there is suggestion that when a chest drain is in situ, it may not be necessary in all circumstances to withhold positive pressure. There is no guidance on when to resume positive pressure techniques following resolution of pneumothorax; it may be suggested that local guidelines should be adhered to, with individual risk benefit assessments being undertaken. The point at which spirometry is resumed may be extrapolated and provide some guidance, but again this remains contentious in the absence of supporting evidence. Confirmation of radiological resolution is key to reducing risk with such procedures, and it is advised that patients may undertake manoeuvres that increase intrapleural pressure at 2–3 weeks following successful pleurodesis.[3,19] Where pneumothoraces have been managed conservatively it may be necessary to extend this period up to 3 months, in order to reduce the risk of recurrence.[9]

Patients with respiratory failure who develop pneumothorax should be admitted and monitored closely.[9] There is strong recommendation to withhold NIV in most circumstances,[17] although there are individual case reports where a chest drain has been sited and non-invasive ventilatory support remaining a necessity.[20] Recommendations state that this should be undertaken in an appropriate high-level care setting.[17]

There is no published evidence on the use of inhaled therapies with pneumothorax. There is, however, strong recommendation to maintain all aerosol therapies,[17] which should be reviewed and optimised by the CF team to ensure ease of airway clearance.[9,18]

There is a lack of available evidence regarding exercise management whilst pneumothorax remains evident but there is some guidance for the acute recovery period, ie two weeks post resolution. Flume et al[17] highlight good consensus on avoiding activities, such as weightlifting, that may increase intrathoracic pressure. Swisher et al[16] are more specific and recommend the need to avoid lifting weights that are greater than 5lb and/or activities that produce the Valsalva manoeuvre. Gradual upper body exercise should be resumed following removal of chest drain over 2-4 weeks.[16] Consensus was not sufficient to make a definitive recommendation on when to resume exercise at higher intensities,[17] although there is guidance for the general population, where it is felt reasonable to advise that sports that involve extreme exertion and physical contact should be deferred until full resolution and that activities involving scuba diving should be discouraged permanently.[3] For the CF population there is suggestion that exercise intensity should be reduced initially with low-grade activity being encouraged,[18] to ensure airway clearance prior to carrying out physical exercise in order to minimise vigorous coughing during exertion,[16] with the aim to gradually return to normal physical exercise activities.

Recommendations

- Airway clearance should be continued, with avoidance of techniques that increase positive pressure in favour of more controlled techniques (eg ACBT, AD) *(QoE – low)*.
- NIV should be withheld or in circumstances where ventilatory requirements are such that it cannot be withheld, close monitoring in high level care settings should take place *(QoE – low)*.
- Upper limb weightlifting (>5lb) should be avoided for two weeks post resolution and airway clearance is advisable prior to exercise to minimise the risk of coughing during exertion *(QoE – low)*.
- Inhaled therapies should be continued, in particular mucolytics to optimise airway clearance *(QoE – low)*.

Good practice points

- Patients should be advised and taught how to avoid paroxysms of coughing.
- Ensure appropriate and adequate hydration and maintain use of inhaled therapies to ensure ease of airway clearance.
- Ensure appropriate analgesia to enable the patient to participate in airway clearance, maintain thoracic expansion and commence early mobilisation.

- Encourage cardio-vascular exercise at lower intensity, gradually increasing post-resolution with the aim of resuming normal activities.
- Avoid upper limb resistance exercises until at least 2 weeks post-resolution.
- Gradual re-introduction of therapy techniques using positive pressure when manoeuvres such as respiratory function testing is resumed.
- Scuba diving should be avoided permanently and there should be caution around high-altitude activities following a pneumothorax.

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11.6 Critical care

Admission to the critical care or intensive care unit is associated with a poor prognosis in CF. Factors associated with a poor outcome include prior colonisation with *Burkholderia cepacia* complex, rapid decline in FEV_1 and severe exacerbation.[1] Positive outcomes are associated with potentially reversible conditions, such as the acute management of haemoptysis or pneumothorax[2] and post-operative management. Endotracheal intubation (mechanical ventilation) is associated with a poor prognosis.[3,4] However, the outcome of treatment with non-invasive ventilation is good[4,5] and many centres may manage non-invasive ventilation in high dependency or ward areas. Extracorporeal membrane oxygenation (ECMO) is used on critical care as a salvage strategy in patients with CF with respiratory failure and is being increasingly used as a bridge to lung transplantation.[6,7] The use of ECMO has emerged as a promising intervention that can avoid invasive ventilation and allows patients to eat, ambulate and undertake airway clearance while awaiting lung transplantation.[8-10] Ambulation whilst on ECMO has been shown to be an independent predictor of successful bridge to transplant.[12]

There are no published studies of physiotherapy management of the intubated and ventilated patient with CF. However, the NICE guideline, 'Rehabilitation after critical illness in adults', should be adhered to as appropriate.[11] These national guidelines should also be applied to those patients receiving ECMO.[13] Rehabilitation on ECMO requires a careful, multidisciplinary approach, including involvement of staff with experience of moving patients on ECMO.[13]

Recommendations

- Ensure regular airway clearance is continued and optimise humidification *(QoE – low)*.
- Ensure good positioning for optimal ventilation and drainage of secretions *(QoE – low)*.
- During the patient's critical care stay and as early as clinically possible, perform a short clinical assessment to determine the patient's risk of developing physical and non-physical morbidity (NICE guidelines [CG83]) *(QoE – moderate)*.
- For patients at risk of physical and non-physical morbidity, perform a comprehensive clinical assessment to identify their current rehabilitation needs. This should include assessments by healthcare professionals experienced in critical care and rehabilitation (NICE guidelines [CG83]) *(QoE – moderate)*.
- For patients at risk, agree short-term and medium-term rehabilitation goals, based on the comprehensive clinical assessment. The patient's family and/or carer should also be involved (NICE guidelines [CG83]) *(QoE – moderate)*.
- The comprehensive clinical assessment and rehabilitation goals should be collated and documented in the patient's clinical records (NICE guidelines [CG83]) *(QoE – moderate)*.
- For patients at risk, start rehabilitation as early as clinically possible, based on the comprehensive clinical assessment and the rehabilitation goals. Rehabilitation should include:
  - measures to prevent avoidable physical and non-physical morbidity, including a review of previous and current medication *(QoE – moderate)*; and
  - an individualised, structured rehabilitation programme with frequent follow-up reviews. The details of the structured rehabilitation programme and the reviews should be collated and documented in the patient's clinical records (NICE guidelines [CG83]) *(QoE – moderate)*.
- For patients on extracorporeal membrane oxygenation, ambulation and rehabilitation should be completed as able by physiotherapists trained in managing patients on ECMO *(QoE – low)*.

Good practice points

- To ensure optimal management there needs to be excellent communication and liaison between both the critical care and CF physiotherapy teams and the wider multidisciplinary teams.
- The use of timetables to protect airway clearance and rehabilitation time for patients may be beneficial.

Research recommendations

- The heterogeneity and the low number of patients with CF admitted to critical care may explain the reason why there have been no published studies of physiotherapy and/or rehabilitation interventions in this patient cohort. To overcome these methodological challenges, a case series approach (single- or multi-centre) would be useful to explore the effectiveness of airway clearance and rehabilitation interventions in patients with CF admitted to critical care.

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11.7 Pre-transplant rehabilitation (prehab)

The physiotherapy intervention before lung transplant can be a complex balance of airway clearance, inhalation therapy and rehabilitation. The goal of physiotherapy prior to lung transplant is to maintain people with CF in as clinically optimal condition for surgery as is possible, while optimising quality of life.[1] There are currently no published studies on prehab in people with CF. One study examined pulmonary rehabilitation in people awaiting lung transplant and showed regular exercise is feasible in this low lung function population, however, there was only one person with CF included.[2] Pulmonary rehabilitation classes are not possible in CF due to infection control. However, individually tailored exercise programmes to maintain/improve functional capacity, including strength training and flexibility exercises, should be provided to all patients awaiting lung transplant. Interval training and strength training are often better tolerated than continuous aerobic exercise that is limited by breathlessness. Although the evidence is limited, supplemental oxygen therapy and non-invasive ventilation may facilitate exercise training and allow a better exercise response in patients with severely affected respiratory function.[1,2] The use of short- and long-term goal setting with patients is encouraged by clinical experts, but there is currently no evidence in CF.

Good practice points

- All people with CF on the lung transplant waiting list should be educated about the benefits of prehab.
- People with CF should have individually tailored exercise programmes that include interval training, strength training and flexibility and these should be reviewed regularly by a physiotherapist or exercise practitioner (as pre-exercise prescription guideline).
- Ambulatory oxygen therapy may be used during exercise following a formal assessment by a physiotherapist demonstrating improvement in exercise performance and or symptoms.
- Non-invasive ventilation can be used to support exercise, but settings should be adjusted from baseline settings.
- Short- and long-term goals will be completed with people with CF to facilitate and motivate prehab.

Research recommendations

- Define the rehabilitation needs of people with CF awaiting transplant.
- Define the efficacy of exercise interventions in people with CF awaiting transplant, with regards to the type (endurance, strengthen or combined), intensity, duration and mode of delivery (hospital, community, virtual).
- Evaluate the acceptability and effectiveness of non-invasive ventilation as an adjunct to exercise in people with CF.

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11.8 Physiotherapy intervention following bilateral lung transplant

The physiotherapy input following lung transplantation can be extremely varied and diverse and includes the management of the individual in the intensive care unit, on the ward and as an outpatient. Physiotherapy intervention includes treatments to improve functional capacity, muscle strength, joint range of movement and postural alignment.[1] Other musculoskeletal issues may also need to be addressed, along with appropriate short-term and long-term goal setting. Physiotherapy input may also involve respiratory weaning (weaning from a tracheostomy, non-invasive ventilation and oxygen support), liaison with gyms and pulmonary rehabilitation centres, organisation of nebuliser units and preparation for employment or for a major life goal.[1]

The majority of studies investigate the effects of exercise/activity of daily living post-lung transplant and have a mixed patient population, including patients with chronic obstructive pulmonary disease, emphysema, interstitial lung disease, pulmonary hypertension and alpha-1 antitrypsin deficiency.[3-9] These studies included participants with both single and bilateral lung transplant.

A systematic review investigating the effects of exercise training in adults after lung transplantation[6] found 7 studies that fulfilled the inclusion criteria, 2 of which were randomised controlled trials, 4 prospective cohort studies and 1 controlled trial with healthy subjects.[6-8] The majority of the studies investigated aerobic exercise training with 2 studies including resistance exercise and 2 studies investigating the effect of resistance exercise on lumber bone mineral density. Exercise training showed positive effects on maximal and functional exercise capacity, skeletal muscle function and bone mineral density. Aerobic exercise training methods that produced positive effects included treadmill, cycle, arm ergometry and stairs. The review shows evidence that structured exercise training post-transplant could improve maximal and functional outcomes but due to the variety of protocols and outcomes used it is impossible to provide specific exercise training recommendations following lung transplant.[6]

A study investigating exercise performance in people with CF before and after bilateral lung transplant showed exercise capacity improved post-transplant but remained below the aged matched healthy controls.[7] An increase was shown between peak exercise arterial-venous oxygen difference pre- and post-transplantation but was not of statistical significance. The investigators conclude that an impaired oxygen extraction was suggested to be the predominant mechanism limiting exercise capacity after transplantation and that this abnormality could not be solely explained by deconditioning or anaemia.

Recommendations

- All people with CF should receive a structured exercise programme following discharge from hospital after lung transplant *(QoE – very low)*.

Good practice points

- Non-invasive ventilation may be needed post extubation, particularly in those who have used it as a bridge to transplant.
- Liaison with the pain management team may be necessary to ensure effective airway clearance and participation in an exercise regimen.
- Due to vagal nerve denervation and impaired cough reflex post-transplant, appropriate airway clearance techniques should be used.
- The use of any positive/negative pressure adjuncts will be discussed with the surgeons before use due to the effect on the bronchial anastomosis.
- An individually tailored exercise programme including cardiovascular and resistance work to improve functional capacity should be introduced in line with the patient's goals. Resistance exercise is important to help combat the effects of the long-term steroids required with the immunosuppression regimen.

- High dose steroid therapy following a rejection episode can increase the risk of tendonitis, tendon rupture and osteoporotic changes. Care must be taken when advising on exercise programmes.
- Liaison with the dietitian to ensure that the exercise programme prescribed does not exceed calorific intake.

Research recommendations

- Define the acute and long-term rehabilitation needs of people with CF post-transplant.
- Evaluate the presence of long-term secondary effects of transplant on peripheral muscle function/dysfunction in people with CF.
- Define the efficacy of exercise interventions in people with CF post-transplant, with regards to the type (endurance, strengthen or combined) intensity, duration and mode of delivery (hospital, community, virtual).
- Explore perceived benefits and barriers to exercise in people with CF post-transplant.

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11.9 Palliative and end of life care

People with CF experience a slow deterioration of lung function coupled with numerous disease complications and increased symptom burden, which may continue for many years. This long, chronic 'terminal phase' of their disease trajectory is associated with intensive daily therapy regimen, making it difficult to predict prognosis.[1-4]

People with CF often experiencing multiple 'near misses' making the timing of death difficult to predict.[4,5] Active and palliative treatment run in parallel, as both therapeutic models help to improve and relieve symptoms in end-stage disease.[4-6] The majority of people with CF die in hospital and this is likely due to the intensity of treatments and the complexity in predicting the terminal stage. With the aging population of people with CF, it is becoming more common for patients to be supported at home or in a hospice at end of life with support from community palliative care teams. Advance care planning (ACP) is particularly important as predicting time of death is so difficult, it should start early and be part of usual care.[4] Research shows the majority (92%) of people with CF were comfortable talking about ACP with their CF team.[7] These conversations should ideally be completed early, in outpatient settings and with a familiar member of the team, which may be an experienced physiotherapist.[7-9]

Although most people with CF die from respiratory failure, technological advances, eg non-invasive ventilation and extracorporeal membrane oxygenation, have provided alternative treatment choices for the very sick person. Lung transplantation is a potential option for people with advanced disease, although it must be acknowledged that not all individuals are eligible or choose this option. In addition, organ availability remains an issue in the United Kingdom with 40% of patients dying on the waiting list.[4,6,10-12] Patients awaiting lung transplant can further complicate end of life care as the patients' families and multidisciplinary team have to balance the hope of possible transplantation alongside the reality of possible death.[2,4]

The World Health Organisation (WHO) defines palliative care for both adults and children as follows: "Palliative care is an approach that improves the quality of life of patients and their families facing problems associated with a life-threatening illness. This is provided through the prevention and relief of suffering by means of early identification, accurate assessment and treatment of pain and other problems, physical, psychosocial and spiritual".[13]

Palliative care:

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten nor to postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death; and
- offers a support system to help the family cope during the patient's illness and in their own bereavement.

Physiotherapists have a key role in end-stage disease management. Physiotherapists focus on maximising functional ability and comfort in order to enhance quality of life and this does not change during end-stage disease management and end of life care.[14,15] Many of the symptoms experienced at end of life (eg breathlessness, anxiety, fear, secretions and pain) can be alleviated by a variety of physiotherapy techniques in conjunction with multidisciplinary and medication strategies. Interventions need to be adapted to consider many different factors, and while it is important to appreciate the benefit it may give, it is also important to appreciate the possible burden it imposes.[14]

Few studies have directly addressed the input of physiotherapy during end of life care. In a retrospective analysis[14] common treatments included airway clearance with active cycle of breathing techniques, intermittent positive pressure breathing, non-invasive ventilation, exercise, anxiety management and relaxation techniques, with a reduction in the use of adjuncts such as positive expiratory pressure and oscillating positive expiratory pressure. It is important to note that many individuals continued with airway clearance techniques to within 24 hours of death.[14]

Early integrated palliative care input is essential in the management of these complex, often untreated symptoms, and to allow patients to establish relationships and build trust with the palliative care team.[4,16-18]

Recommendations

- Consider referral or seek advice from palliative care services with regards to patients with high symptom burden such as pain, breathlessness which limited the efficacy of physiotherapy treatments *(QoE – low)*.
- Physiotherapy treatment should focus on optimising quality of life and symptom control in advanced disease *(QoE – low)*.
- Physiotherapy airway clearance interventions need to be tailored to the individual needs of the patient *(QoE – low)*.
- Consider intermittent positive pressure breathing and non-invasive ventilation as physiotherapy adjunction to reduced treatment burden *(QoE – low)*.
- Patients should be offered physiotherapy input/support in the last stages of life *(QoE – low)*.

Good practice points

- Good communication between the CF team, the person with CF and their family is paramount during all aspects of the terminal stages. The CF team must take into account the person with CF and their family's level of understanding, concern and fear of the unknown when discussing any treatment changes and be prepared to answer questions.
- Early discussions around preferred place of death should be completed by the multidisciplinary team, and if appropriate physiotherapist can lead on these conversations.
- If an individual's preferred place of death is home or hospice, physiotherapy input needs to be provided and/or supported in this setting, and if necessary training should be provided by the physiotherapy team to hospice staff, community palliative care team or the individual's family around non-invasive ventilation and physiotherapy treatment.
- Frequent short treatment sessions may be required to maximise symptomatic relief but minimise burden.
- Consider positive pressure such as non-invasive ventilation to reduce work of breathing and provide symptomatic relief during airway clearance treatments, exercise or to support breathlessness management pre- and post-activities of daily living such as washing or dressing.
- People with CF using non-invasive ventilation may choose to remove their non-invasive ventilation in the terminal stages. Physiotherapists should be prepared to discuss with individuals and families what may happen when they remove their non-invasive ventilation and liaise with the wider multidisciplinary team to optimise symptom control medications if this is the patient's wish.
- Individuals who are 24-hour non-invasive ventilator dependent will have two machines to alternate (day and night) and should have more than one face interface to alternate to reduce the risk of pressure areas.
- The use of nasal masks or mouthpiece interfaces for short periods may enable individuals to speak to relatives and drink/eat more easily.
- To optimise individual independence, if they are non-invasive ventilation-dependant, consider setting up their non-invasive ventilator on a trolley to enable them to mobilise more easily.
- Physiotherapists need to consider how to support their colleagues and manage their own emotions when managing people with CF at end of life. The opportunity to reflect as a team or individually should be available for all staff and teams should promote positive coping strategies.[19]

Research recommendations

- Explore physiotherapists experiences and challenges of providing physiotherapy interventions towards the end of life in people with CF.
- Explore what the role of physiotherapy is in supporting people with CF who choose to die at home.

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12. Complementary therapies

Complementary therapy (CT) and alternative medicine are terms often used to describe treatments outside the usual medical treatment remit. The evidence base pertaining to the UK use of complementary therapies in CF is limited and based on a questionnaire sent to all adult and paediatric CF centres in the UK in 2016. Of the 39 centres who responded to the survey, 24 stated CTs are integrated into their management of people with CF and are applied by either the physiotherapist, an external 'complementary therapist', or another member of the multidisciplinary team. Some of the most common therapies described under this umbrella include acupuncture, aromatherapy, art therapy, massage, music therapy, Pilates, reflexology, relaxation techniques, singing, tai chi and yoga. Salt cave and salt lamps (halotherapy) are not currently utilised as a treatment by the CF clinicians, however, they have been reported in the 2016 questionnaire responses to be of interest to people with CF.

Although there may be evidence for some CTs (such as acupuncture for chronic tension headaches)[1] in the non-CF population, research relating to many of these treatments in people with CF is lacking and there is insufficient evidence to support or refute their use. Many physiotherapists have an interest in CTs and some techniques such as therapeutic massage and relaxation, form core training at an undergraduate level with further courses (such as acupuncture/pressure) are available and targeted at experienced physiotherapists.

It is beyond the scope of these guidelines to produce a full systematic review of all CTs, however, some guidance is offered below.

12.1 Acupuncture

Acupuncture is considered an alternative medical therapy that is gaining increasing popularity in the Western world. Although there is insufficient high-grade evidence to support a recommendation for the use of acupuncture in respiratory disorders, acupuncture has been an integral part of Traditional Chinese Medicine (TCM) for a considerable time.[1] There is a growing use of acupuncture in respiratory conditions and anecdotal evidence that patients are requesting acupuncture as a treatment modality.[3-5] TCM provides a holistic approach when formulating an individual therapeutic strategy. With consideration to the multi-system impacts of CF, acupuncture or acupressure points are selected to regulate and strengthen diseased "organs" as well as suggestions made to change diet and lifestyle.[3] Acupuncture uses needles whereas acupressure uses the application of physical pressure. Both are applied on acupoints positioned along the meridians. Meridians are the channels within the human body where vital energy (Qi) circulates.

In 2010, Carrolan et al[2] mapped the treatment of adults with CF by physiotherapists (from 20/23 specialist adult CF centres in the UK) using acupuncture. Four adult CF centres were providing acupuncture treatment by physiotherapists, most commonly treating back pain, breathlessness, headaches, joint pain, anxiety, sinus pain and pleuritic chest pain. There are studies in people with CF, which have demonstrated improvements in parameters such as quality of life, exercise capacity, decreased anxiety and dyspnoea scores using acupuncture techniques.[4-8]

It has been reported that "acupuncture is not widely available in UK adult CF centres mainly due to lack of trained professionals available to provide a service". Some centres have funded non-NHS acupuncturists to provide a service to patients, but this is not a consistent offering nationally as funding varies from centre to centre. Carrolan's[2] study demonstrates that of the surveyed physiotherapist respondents, 71% felt that acupuncture treatment should be carried out by a physiotherapist with acupuncture training, rather than a fully qualified (but non-health professional trained) acupuncturist.

Acupuncture is considered relatively safe, but as it is an invasive procedure it carries undeniable risk with pneumothorax being a rare but dangerous potential complication. The incidence of serious events like pneumothorax could differ depending on the style of acupuncture and the training of therapists. However, there are a growing number of case studies from different countries highlighting the risks associated.[9-13] Whilst these are only single institution case studies, they all raise the importance of individuals having access to an accredited and registered acupuncturist and clinicians having a high index of suspicion for pneumothorax if a patient complains of chest pain following acupuncture.

Good practice points

- Consider a professionally trained acupuncturist as an alternative if no physiotherapist qualified in acupuncture is available; visit the British Acupuncture Council website www.acupuncture.org.uk for guidance.
- There is no age limit for when acupuncture or acupressure can be performed, however, children may have a more acute response to acupuncture and it is therefore advisable to trial acupressure first.
- Much of the research available on acupuncture is methodologically weak including small sample sizes, lack of proper controls and poor statistical analysis.[5] These are all flaws that can also be attributed to much of the research within CF care. Although results should be considered with caution, patients' reporting of subjective improvements should be noted and used to determine continuing treatment.
- In the absence of physiotherapists trained in practicing Western-style acupuncture, patients may be referred to a fully qualified Traditional Chinese Medicine/Five Element acupuncturist (details available from BAcC) in order to benefit fully from this holistic treatment approach.
- Alternative therapies such as acupuncture must not replace standard CF treatment.
- The person with CF should be encouraged to discuss use of alternative therapies with the CF team before commencing.
- Clinicians must have a high index of suspicion if a patient complains of chest pain after acupuncture, since pneumothorax is a serious adverse event.[9]

12.2 Halotherapy (salt caves and salt lamps)

For centuries, especially in Eastern Europe, people have visited natural salt caves for the healing and therapeutic properties of the air. Halotherapy (HT) can be delivered in artificially constructed 'salt caves' that stimulate the conditions of a natural cave by dispensing dry aerosol micro particles of salt. Other modes of HT delivery are via salt inhalers or 'salt pipes'. Suggested mechanisms of action are mucolytic, antibacterial, anti-inflammatory, immunomodulating and hyposensitizing.[14]

Evidence to support HT use is limited and primarily for COPD or asthma patients. One study carried out a randomised double blind study into the use of halotherapy as a treatment for children aged between 5-13 years with mild asthma.[15] The study had small numbers (29 treatment group and 26 control) but found a statistical significant improvement in bronchial hyper- responsiveness and in most parameters of quality of life questionnaires. They found no improvement in spirometry or Fractional exhaled Nitric Oxide (FeNO) levels following treatment. FeNO levels can be measured through a simple test where you exhale into a machine. This machine measures the level of exhaled nitric oxide. Nitric oxide, a substance that is produced throughout the body can be found in high levels in those with inflamed airways.[15] Both the control and treatment group had treatment twice weekly 45-minute sessions for seven weeks. The treatment group received salt aerosols produced by a halogenerator. A halogenerator brings a flow of clean, dry air that is saturated with highly dispersed negatively charged particles of sodium chloride into the chamber. The halogenerator is also supplied with a microprocessor in order to monitor temperature, relative humidity and mass concentrations of aerosols.[14]

Another study explored the efficacy of salt cave HT in 139 chronic respiratory patients, among whom only five had CF.[16] Improvements in flow-volume loop parameters and decreased bronchial resistance measured by plethysmography were reported after 10-20 daily one-hour sessions. Two smaller studies have also shown benefit. Six CF subjects had five salt cave HT sessions (45 minutes on five consecutive days) and showed improvement in lung function and sputum production.[17] Whereas, the second study with 13 CF patients showed no significant change in lung

function, but improvements in Borg dyspnoea index scores, SNOT-20 scores and subjective health perception levels with no adverse effects.[18] It is well recognised that hypertonic saline (even in the lowest concentration) can provoke bronchospasm in susceptible individuals; none of the participants in the study reported such symptoms.[18]

More recently a paper has highlighted a list of contraindications for HT, which include hyperthyroidism, active tuberculosis, high-grade hypertension, cardiovascular and respiratory failure, acute-stage blood disorders, contagious diseases, fever, open wounds and malignant diseases.[14] Giangioppo et al[19] refer to the risk of cross-infection in relation to HT as associated with "sitting in a salt room for extended periods with other respiratory patients can also promote the spread of infection".

There is minimal evidence available evaluating the efficacy of salt spray inhalers or salt pipe use in CF patients. Rabbani et al[20] explored the use of salt spray inhalers in 20 non-CF bronchiectatic patients (inhalation through the inhaler for 25 minutes per day for two months). After a two-month treatment course no significant improvements were identified in lung function tests, 6-minute walk test results or quality of life questionnaires. However, there were no significant adverse effects. There is also no evidence available to suggest salt lamps might have a physiological beneficial impact on the respiratory health of patients with CF. There have, however, been no reports of adverse side effects as a result of its use in any studies. The benefits to emotional health and well-being provided by salt lamps have been extensively documented (though not in CF), if not scientifically supported.[17, 21]

The evidence supporting the use of HT is weak due to poor quality of study design, methodology and data collection. Furthermore, with HT having more popularity in Eastern Europe many of the papers were not available in English. Exploratory studies have demonstrated that HT may have some benefit in CF patients, however, many of the studies have looked at COPD or asthma populations.

Longer-term studies using larger sample sizes and randomised controlled study design are necessary to be able to add strength to support recommendation of use.

Good practice points

- Where people demonstrate an interest in salt therapy, physiotherapists should offer inhaled hypertonic saline as a safe and known alternative where appropriate.
- There is no information regarding the management and control of infection when using HT and therefore physiotherapists should advise people with CF accordingly.

12.3 Relaxation techniques (including massage, aromatherapy and reflexology)

A recent Cochrane review[23] considered the impact of psychological interventions which were largely concerned with adherence to treatment, emotional and social adaptation and health-related quality of life. Whilst there were no concrete recommendations there is some evidence that behavioural interventions targeting specific illness-related symptoms and behaviours can work. There is clearly some multidisciplinary crossover in this area with many of the multidisciplinary team being appropriately trained in aspects of relaxation, cognitive behavioural therapy (CBT) and massage.

Massage has been used as a therapy for its benefits such as improving circulation, decreasing some forms of oedema, reducing musculoskeletal pain and tension.[24] Zink et al in 2019 conducted a pilot study in 24 8-21 year olds with CF over a 10-12 week period. Their purpose was to evaluate massage therapy on quality of life (QoL). They concluded that massage therapy was found to significantly reduce muscle tightness, marginally reduce pain and aid relaxation and thoracic excursion in participants with CF. There was no statistically significant improvement in QoL scores.[25] Short-term benefits of massage and musculoskeletal physiotherapy on pain reduction in adults with CF have also been documented,[29] but longer-term, large-scale studies are needed. Common symptoms of chronic illness such as anxiety and depression may be alleviated by massage.[24] A small RCT study in children with CF noted subjective improvements in both anxiety levels and mood of parents and children using

parent-administered massage therapy.[26] Abstracts highlighting the importance of massage therapy to adults with CF during inpatient admissions have also been documented.[27,28] Massage therapy can help relieve stress and pain, as well as promote well-being and relaxation, however, data analysis is ongoing.[28] Benefits of massage therapy are documented, but contraindications must be noted, and massage should not be performed over pitting oedema, areas of impaired tissue integrity and fractures. Caution should be exercised in patients with prolonged bleeding times.[24] Use of aromatherapy massage (the therapeutic use of plant-derived, aromatic essential oils combined with massage to promote physical and psychological well-being) in CF has limited documentation and is currently only cited in pilot studies in abstract form, subjectively all 6 adult patients with CF reported improvement in anxiety and possible ease in airway clearance.[29]

Research for the use of reflexology (a system of massaging specific areas of the foot or sometimes the hand in order to promote healing or relieve stress in other parts of the body) in cystic fibrosis was found lacking so no recommendations are available.

Research for the use of art therapy (a form of psychotherapy involving the encouragement of free self-expression through painting, drawing or modeling used as a remedial or diagnostic activity – definition may vary) in CF was found lacking so no recommendations are available.

Good practice points

- Consideration of massage therapy for the relief of musculoskeletal pain.
- Consideration of massage therapy to decrease anxiety in parents and patients with CF.
- Contraindications to massage therapy must be noted.
- CF teams should consider who takes a lead on introducing relaxation techniques and who can carry them out within the team so that there is a coherent and consistent approach.

Research recommendations

- Lack of trials and high-powered evidence for massage/aromatherapy massage and its use in the management of patients with CF indicate further areas for good quality studies are required.
- There is insufficient evidence to recommend any specific frequency, type or duration of massage therapy over another.

12.4 Singing

Many families feel singing is a good form of treatment for children with CF. A Cochrane review in 2014 reported there is insufficient evidence to recommend singing as an effective adjunct treatment in individuals with CF, however, they should be encouraged to participate but not replace current modalities.[32] More recently in Scotland, the Breath Cycle project evaluated the benefits of classical singing techniques and breathing control on respiratory health in adults with CF. Only 14 patients completed the pilot study reducing the authors ability to find statistically significant differences, however, improvements were suggested in tidal breathing during exercise, FEV_1 and lung clearance index.[33] A literature review in 2018[34] regarding singing lessons for respiratory health, reviewed 17 studies in a variety of pathologies, 3 in CF and all with small numbers. It concluded generally that singing may be used as an adjunctive treatment for respiratory disease. However, as mentioned above, this should not replace current airway clearance modalities in CF.

12.5 Other complementary therapies

There are many other areas that fall under the complementary therapies umbrella and those included in this guideline are not exhaustive. It is worth noting that from our survey of CF centres that complementary therapies, on the whole, are liked by patients, however, funding and staffing are among the limiting factors around provision. There appear to be no standardised outcome measures. Adequately-powered, well designed RCT are needed with precise methodology recorded for the future.

Whilst CTs are considered to be a useful adjunct to standard therapies for the management of holistic CF care, it should be acknowledged that standard therapies must not be discontinued or modified without close consultation with the CF team. It is also advisable that physiotherapists, like with any form of treatment, consider the potential risks to the patient should they choose to embark on complementary therapies, eg the possibility of infection control within salt caves and the risks associated with osteoporosis and yoga as highlighted above. It should also be recognised that some alternative therapists, although specialists in their chosen fields, may not have the rigorous regulations and clinical governance that state registered physiotherapists work within and may have little experience of working with the complexities of CF.

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13. Adherence

Adherence is defined as "The extent to which the patient's behaviour matches agreed recommendations from the prescriber".[1] It has been recognised that this term is preferable to compliance, defined as "The extent to which the patient's behaviour matches the prescriber's recommendations".[1] Concordance is a wider concept that doesn't only refer to the taking of treatment but focuses on the interaction between clinician and person. It is based on the idea that consultations are a negotiation between equals and recognises the rights of people to decide whether or not to take prescribed medicines.[2] Adherence is considered the preferred term for medication-taking or treatment behaviours.[1,3]

People with CF may require multiple medications to control symptoms and slow disease progression.[4] Studies suggest the median number of daily medications prescribed for those with CF is seven.[5] Administering these treatments takes a mean time of 108 minutes a day[5] posing significant challenges in terms of scheduling treatment around education, work and families.[6] People with CF also need to undertake many daily non-medication based treatments, including airway clearance, activity and structured exercise, dietary supplements and monitoring dietary intake. In view of this treatment burden, poor adherence has been identified as the greatest cause of treatment failure[7] and monitoring adherence to prescribed therapy identified as a priority.[8]

Many influences and barriers to adherence are reported in the literature, including lack of knowledge,[9] communication,[10] self-efficacy (the belief that the individual can perform the behaviour),[11] perceived illness severity,[12] coping styles,[13] depression,[14] family factors,[15] support,[16] parental supervision,[17] characteristics of the treatment regimen,[15] problems with fitting treatment into lifestyle, a perception that treatment doesn't help or may be harmful itself and the physical consequences or side-effects of the treatment.[18]

Adherence is recognised as variable depending on the treatment;[10] eg good adherence to pancreatic enzymes does not predict good adherence to nebulised medications. It may also vary for a single treatment in an individual at different times.[19] Adherence levels in people with CF have been found to decline into adolescence and young adulthood,[20] which may reflect the transition from family administration of treatment to independence. Adherence may also be influenced by changes in the prescribed regimen or by intervention to enhance one aspect of the regimen where a drop in other aspects may be seen.[21] This would suggest that ongoing comprehensive assessment of adherence patterns is needed.

13.1 Measuring adherence

Methods of measuring adherence vary in objectivity and validity. The most common methods of assessment are self-reported. When compared to more objective measures, these strategies have been shown to over-estimate adherence.[22,23] The reasons for this are multifactorial and may include inaccurate recall and a reluctance to admit behaviour that is not in-keeping with the agreed treatment plan.[10] This social desirability bias may be particularly important for people with CF where decisions on life-saving procedures such as lung transplants are potentially influenced by adherence reports/data.

Daily diary methods have been shown to be more accurate[10] but are time- and resource-consuming and so not appropriate for long-term clinical use. Prescription filling is more objective, however, studies have shown this method also over-estimates adherence as there is no guarantee all dispensed medication is taken.[7] Other direct measurements such as blood levels are also used, but these are limited in accuracy and in practicality for long-term use[24] as well as being unsuitable for the measurement of many physiotherapy treatments such as airway clearance. Electronic data capture is the most objective adherence measure and its use in adherence trials is increasing. Pill bottles, nebulisers, inhalers and some methods of airway clearance can be electronically monitored to log the exact date and time of use. This data can be fed back to individuals to aim to improve future adherence. Early devices had high rates of malfunction, but as technology advances, they are now more reliable.[7] For some applications of this technology such as pill bottles, there is still no guarantee the medication is taken, which prevents this method from being seen as the gold standard.[7]

13.2 Adherence to airway clearance

Most studies assessing adherence to airway clearance have used questionnaires or telephone diaries to assess adherence. They assess adherence to airway clearance overall rather than providing individual data for different techniques. Reported adherence rates to airway clearance range from 33.3 ± 43.15% to 91.2%.[25] A pilot study using electronic data capture suggested adherence rates to oscillating PEP of 45% as compared to self-reported adherence of 100%.[21]

Larger-scale studies of adherence to airway clearance as measured by electronic data capture in people with CF are underway. Project Fizzyo[26,27] have worked together with engineers and designers to develop electronically chipped airway clearance devices and wearable activity trackers. Newly developed computer games driven by breathing aim to enhance treatment enjoyment and adherence. The devices are enabled to send longitudinal data to the clinician and person with CF throughout the study comparing adherence with and without the games and to provide data to answer key questions about adherence to airway clearance in people with CF.[26]

13.3 Adherence to exercise and activity

Despite exercise and activity being widely advocated as beneficial, there are little adherence data. Adherence levels to exercise have been assessed as higher than adherence to airway clearance.[28] Overall, people with cystic fibrosis report a preference for exercise as compared to other treatments.[29-31] Exercise is regarded as socially acceptable[32] and an area over which people feel they have control.[33] Studies are in process which utilise electronic data capture to assess adherence to exercise and activity.[26,27]

13.4 Adherence to inhaled medication

Monitoring adherence to inhaled medication has become easier and more accurate using adaptive aerosol delivery technology, which provides detailed monitoring including date, time, completeness of dose and time taken to nebulise, and with chipped vibrating mesh devices. This electronic data capture suggests that adherence to nebulised medications can be low and/or variable.[34-36] Monitoring allows greatly improved accuracy in identifying adherence levels and is acceptable in the CF population.[34,36] When measured objectively using electronic data capture, long-term adherence rates to nebulised treatments are 36% in adults[22] and 67% in children.[35]

A significant study utilising electronic data capture is ACtiF: development and evaluation of an intervention to support adherence to treatment in adults with cystic fibrosis.[37] This project involves the development of a behaviour change intervention which includes the development of a web portal, CFHealthHub, to capture adherence data from patients' nebulisers and display this to clinicians and people with CF. CFHealthHub facilitates a range of evidence-based interventions including problem-solving and setting implementation plans to increase treatment adherence. The randomised controlled trial has now completed, and final results are awaited. A data observatory phase is ongoing and involves quality-improvement cycles, guided by the learning from the randomised controlled trial aiming to integrate CFHealthHub into clinical practice as a resource accessible to all of the MDT.[37]

13.5 Why is adherence important?

Adherence research has been highlighted as a high priority by policy makers and the WHO.[38] Poor adherence has implications for the person with CF, their family, the CF team and society as a whole, leading to unnecessary exacerbations resulting in additional antibiotics and hospitalisations. This is expensive, undermines quality of life, can lead to antibiotic-related adverse events and may reduce life expectancy.[24,39] People with CF who collect less medication are more likely to be admitted to hospital for a pulmonary exacerbation and incur higher healthcare costs.[40] Studies have also demonstrated the importance of adherence to inhaled treatments on health outcomes, with people collecting four or more courses per year of nebulised tobramycin being 60% less likely to be admitted to hospital than those collecting one,[41] and greater adherence to Dornase alfa being associated with shorter inpatient stays.[42]

13.6 Strategies to impact on adherence

A Cochrane systematic review identified evidence for psychological interventions to impact on adherence.[8] Positive effects were seen predominantly with behavioural and educational interventions but with an impact on dietary intake and nutritional status rather than on other aspects of treatment and are therefore less applicable to physiotherapy-related treatments.[8]

Self-management strategies such as educational approaches have also been assessed.[43] The trials included used self-reported outcomes to assess adherence and gave conflicting and unclear results. One study assessed a wide-ranging programme aimed at self-management of CF demonstrated no differences in adherence to physiotherapy-related treatments such as airway clearance, exercise and inhalation therapy,[44] whereas an airway clearance and inhalation therapy-specific programme demonstrated improved adherence outcomes but with wide confidence intervals.[45]

There are some small-scale pilot studies looking at strategies to impact on adherence. These have included 'token economy',[46] which found variable improvements in adherence to exercise which may have been related to the type of reward. Motivational interviewing is also an area of interest to researchers, but little evidence of significant impact on adherence has yet been demonstrated.

The use of interventions to support habit formation is showing promise with high adherers reporting stronger habit compared with low adherers. Habit may be a promising target for self-management interventions.[47] There are ongoing studies that will enhance future understanding of strategies to impact on adherence.

A Cochrane review assessing interventions for enhancing medication adherence found that outcomes are inconsistent from study to study.[48] It identified that interventions are mostly complex and not very effective, so that the full benefits of treatment cannot be realised. It highlighted that research in this area needs advances, including improved design of feasible long-term interventions, objective adherence measures, and sufficient study power to detect improvements on clinical outcomes.[48]

Recommendations

- Consideration should be given, where possible, to using devices which utilise electronic data capture to record adherence in order to tailor provision of treatments and adherence interventions to the individual *(QoE – moderate)*.
- Where adherence levels are measured, this should, where possible, be to different treatments and over time *(QoE – moderate)*.
- When adherence to inhaled therapy is suboptimal, clinicians should aim to use the quickest and simplest device possible for each medication *(QoE – low)*.
- Habit formation, self-management and educational strategies should be considered when addressing adherence patterns *(QoE – moderate)*.

Good practice points

- Physiotherapists should spend time during consultations aiming to understand the person's adherence patterns.
- Treatments should be rationalised or combined, where possible and appropriate, in order for the person with CF to have the simplest and quickest treatment regimen possible.
- People with CF and their families should be supported to monitor and enhance adherence to treatment.

Research recommendations

- There is a need for studies assessing long-term adherence to airway clearance and exercise/activity using objective data capture methods.
- There is a need to assess the variation in adherence to different airway clearance techniques.

There is a need for high-quality studies to assess the impact of strategies aiming to enhance adherence to airway clearance, exercise/activity and inhaled therapies.

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14. Infection prevention and control

Chronic pulmonary infection remains the most important indicator of morbidity and mortality in a person with CF.

In the UK CF Registry 2018 Annual Data Report there were 10,509 registered patients with CF. Of these 7.1% cultured *non-tuberculosis mycobacteria* (NTM), chronic *Pseudomonas aeruginosa (PSA)* was identified in 5.9% of patients <16 years of age and 41.4% >16 years of age, and *Staphylococcus aureus* was identified in 8.6% <16 years and 20.5% in the >16 years age bracket.

There had been an increase in the prevalence of NTM over the preceding 3 years of Registry data from 5.8% in 2016 to 7.1% in 2018.

There are several infection control guidance documents in existence (NICE, CFF, Cystic Fibrosis Trust) and they provide specific guidance around segregation, cross-infection and surveillance. There is, however, a lack of physiotherapy specific guidance.

We will use this chapter to highlight the current and recommended IPC practices identified both nationally and internationally. Whilst this information and associated advice is based on the current evidence, it should also be taken in combination with local IPC policies, as additional and not instead of.

It should be noted that it is beyond the scope of this guidance to discuss settings beyond the hospital environment or comment on other infection control risks.

14.1 Segregation

Infection in the airways of people with CF drives inflammation associated bronchiectatic changes and respiratory decline. Primary prevention of these infections through effective IPC is an important management strategy.[1] Much of the literature alludes to the segregation of specific pathogens, based on respiratory tract culture results, including *Burkholderia cepacia complex* (*BCC)* (including epidemic strains of *B. cenocepacia* ET12), transmissible strains of *PSA* (for example, Liverpool Epidemic strain LES and Australian Epidemic strain AES-1,[2,3] MRSA, non-*PSA* and more recently NTM (*more specifically Mycobacterium abscessus* [M. abscessus]).

There is clear evidence that increased incidence of bacterial infection occurs when cohort segregation is not implemented.[4,5] Doe 2010[4] highlighted factors that increased risk of MRSA acquisition including transferring from a centre without segregation policies, where the patient was nursed on a general ward and where the individual worked as or lived with a health care provider. Conway 2008[6] reported that there is overwhelming evidence that cross-infection with several respiratory pathogens occurs in CF units when patients can mix with each other.

Cohort segregation appears to interrupt the spread of infection, thus reducing the morbidity and mortality associated with chronic infection.[7] However, cohort isolation alone will not provide enough protection against the acquisition of dominant strains of specific pathogens.[8-10] Studies utilising bacterial genotyping have demonstrated that person-to-person spread of different strains of the same species of particular pathogens and there is clear evidence of the emergence of dominant strains.[11] For example, *BCC* ET12 although identified over 2 decades ago, still maintains its dominance and as a consequence of its multi-resistance and consequent limited therapeutic options has led to the widely accepted agreement to separate all people with CF who culture *BCC* from each other and all other people with CF.[1,8-10,12-15]

Elborn (2009),[12] following the publication of the ECFS Consensus guidelines,[12] conducted a survey of 547 European centres between 2005 and 2006, examining the management for prevention and treatment of infection. More than 70% of centres segregated those categorised as non-*PSA* from those colonised with *PSA* but only 50% of centres were segregating at a species level during inpatient stays and <30% in the outpatient setting. This meant that those people with CF colonised with *PSA* were exposed to more epidemic or dominant and potentially deleterious strains. It is recognised that people with epidemic strains of *PSA* require more hospitalisations, have an associated increased resistance to antibiotics and therefore have a faster rate of clinical decline.[7] It is therefore logical to assume that all people with CF pose a significant risk to each other and that segregation will only work if minimal contact and optimal IPC strategies are employed.[16]

Epidemiological studies have identified that nosocomial transmission of CF-specific pathogens (*PSA*, M. abscessus, *BCC*) during synchronous

hospital clinic attendances is a more likely route of transmission than social contact outside the hospital environment,[6,17] suggesting that indirect transmission is a likely factor in acquisition.

Rowbotham 2019[1] reports the findings of an extension of a randomised control trial[18] where the first acquisition of *PSA* following segregation was 289 weeks as compared to 52 weeks in the non-segregated arm. This strongly suggests that cohort segregation is indeed a worthy endeavour.

14.2 Aerosols

Many of the pathogens that affect people with CF can be found in the natural environment. Most initial acquisitions of these infections are thought to be from the environment but the significance of the relationship between these environmental pathogens and those found in CF patients remains unclear.[14,19-27]

In the hospital setting, there is evidence to suggest that patient to patient cross-infection can occur[21,24-31] and this potentially could happen through:[25,26,30-32]

- contact transmission (direct and indirect (fomite));
- droplet transmission (infectious respiratory droplets >5μm); or
- airborne transmission (droplet nuclei <5μm).

Respiratory secretions, in the form of droplets and droplet nuclei are expectorated from people with CF during cough manoeuvres. These have been shown to have high yields of viable pathogens within them.[9,21,33-39] *PSA* and *BCC* can survive for long periods in water; *PSA* can persist suspended in sputum on dried surfaces for up to 8 days[20,22,25,40] and Clifton et al[21] suggested that mucoid strains of *PSA* have a longer half-life and therefore have an increased survival advantage, surviving in droplet nuclei for up to 45 minutes. M. abscessus has also been shown to be viable for 24 hours after cough aerosolisation.[27]

Transmission of CF pathogens is considered to be via the airborne route and is responsible for the patient to patient spread of epidemic strains of *PSA* and *BCC* during identified outbreaks, recognising that cross-infection continued to occur despite segregation, rigorous contact-based precautions and decontamination of environments.[40]

Respiratory activities such as breathing, talking, sneezing and coughing influence the volume of airborne particles potentially carrying pathogens.[35] Higher-velocity activities such as sneezing and coughing further enhance transmission of any respiratory infections. Wood[38] and Zuckerman[41] identified higher risk of infectious aerosol particle production during periods of exacerbation when coughing was more prevalent and when respiratory function or airway clearance occurred. *PSA* droplets were identifiable at 1-2 metres following conversation,[37] highlighting the potential risk for cross-infection within waiting rooms and the associated difficulty in maintaining a safe distance between people with CF.

Particle size distribution of aerosols is a key determinant for both deposition in the respiratory tract and for the ability of particles to remain airborne. Andersen Cascade Impactors are used in research to identify distance travelled and size of particles dispersed.

Clifton et al[21] looked at the aerosolisation of 3 strains of *PSA* expressing a mucoid phenotype using nebulisation into an aerobiological chamber. The 3 strains of *PSA* and non-mucoid environmental strain were detectable for 35 minutes following completion of the nebulisation. Wainwright et al[34] reported that therapies including physiotherapy and inhalation of nebulised mucoactive agents which induce coughing are likely to result in similar cough-induced aerosols seen with voluntary cough and greater than that detected in tidal breathing. This suggests that enhanced infection control practices should be employed during periods of nebulisation and airway clearance.

During cough manoeuvres droplets, described as >5 μm, have been shown to travel up to 3m from the source, but are unable to stay airborne for long. Droplet nuclei, described as <5 μm, are of respirable range, can travel further (up to 5-10m) and stay airborne for longer (up to 3 hours).[22,24,34,36,38,40,42,43] Airborne contamination has been detected in CF clinics, wards, corridors and pulmonary function testing rooms.[13,14,22,40,42-44] The highest rates of airborne contamination were shown to occur after airway clearance and pulmonary function tests, and persist in confined spaces.[13,22,44] Air contamination after spirometry only reduced to extremely low levels 30 minutes after the patient left the room.[31,32,41] However, increasing the air exchange/room ventilation rate in clinical areas allows for more removal of pathogens from the air and in theory reduces the risk of airborne transmission of pathogens.[21] Modifying the flow of people with CF through

clinics by avoiding people waiting in communal areas and enhancing infection control procedures within the clinic setting has reduced the rates of transmission.[28,31,32.45,46]

There is growing concern that these studies have shown the potential for airborne transmission although definitive evidence of this remains limited.[21,27,29,41,42] The infective dose for each organism is also unknown and research into this aspect is limited by ethical considerations. It has been suggested that the use of enhanced air exchange/ventilation or negative pressure rooms will reduce the risk of airborne transmission, but needs further research.[21,32,38,47,48] When sputum samples are required it may be worth obtaining sputum samples prior to clinic attendance to minimise cough aerosols in the environment.[38]

Surgical masks, worn by people with CF during cough manoeuvres, are effective at reducing airborne *PSA* load by ~90% and it has been surmised that by reducing droplet and droplet nuclei spread, this reduces the risk of surface contamination and airborne transmission,[38,49] although this remains controversial.[30-32,41] Masks may be poorly tolerated in young children and those with respiratory distress, in these circumstances both Wood[38] and Zuckerman[41] proposed that good cough etiquette, enhanced air exchanges in the clinical environment, longer wash out periods between patients or negative pressure rooms should be considered. Rowbotham,[1] Wood[38] and Yan[50] suggest that face masks should be worn by patients in high-risk/ communal areas (for example in transit through the hospital corridors, in the X-ray department or when visiting pharmacy), but that face masks were not required in individual hospital rooms during examination or admission. Chen[11] demonstrated a fall in incidence of *BCC* with the implementation of masks and gloves worn by patients outside of individual rooms. One study found there to be no difference in examination room air contamination when patients were masked or not.[41] It was observed that patients tended to touch or remove masks during the study period thus influencing the degree of environmental contamination.

Saiman 2013[51] suggested that healthcare workers did not require masks to be worn **unless** the patient was under droplet containments precautions (eg for influenza, TB, COVID-19 etc).

14.3 Transmission

Both direct and indirect patient to patient transmission of infection should be considered when identifying the source of new infection. Direct patient to patient transmission via droplets is less likely as a result of individual and cohort segregation, therefore indirect transmission via environmental contamination or fomite spread should be considered.[50] Clinical strains of *PSA*, *BCC* and more recently M. abscessus have been recovered from hospital water supplies and surrounding surfaces, eg drains and showers. It is unclear what the original route of contamination was (environmental or patient contamination).[22,23,26,30,52,53] CF pathogens have been detected in CF clinic settings, on surfaces of instruments and furniture.[44] *M. abscessus* has been shown to be potentially spread by surface contamination of an inpatient room.[27]

Whole genome sequencing has enabled species identification of pathogens, specifically M. abscessus isolates. Yan[50] analysed the M. abscessus isolates of 14 patients and found clusters of genomically similar isolates. When epidemiological analysis was performed the patients had multiple cross-over periods of outpatient clinic attendance, suggesting that it was at these clinic attendances when cross-contamination occurred.[50,54]

Rowbotham[1] identified that *PSA* and *BCC* was evident on the hands of healthcare workers and could be transmitted for up to 180 minutes. Skin and fingernails of healthcare workers and the use of false nails encouraged bacterial contamination, therefore diligent hand hygiene and wearing of gloves when engaged in clinical care is recommended.[14]

A recent published audit of healthcare workers (HCWs) caring for patients under droplet or contact isolation found viruses on 31% of glove samples, 21% of gown samples, and 12% of face mask samples. In addition, 21% of bare hand samples, 11% of scrub samples, and 7% of face samples tested positive for respiratory viruses.[55]

"Our findings of viral contamination on PPE, clothes, and skin of HCWs emphasize the significance of appropriate PPE use, PPE doffing practices, and hand hygiene in infectious transmission prevention via the contact route," the study states.[55]

There was an association between the number of self-contacts by HCWs with their gloves, gowns, or masks and the concentration of virus on those pieces: the more self-contacts, the more virus.[55] "The strongest correlation identified was between self-contact with the gown (torso) and virus concentrations on a personal stethoscope, which is often draped around the neck".[55]

Bacterial contamination of person with CF's hands was common[44] and the bacteria identified at the beginning of the clinic visit was not the same as that identified at the end. Possible routes for contamination, either via aerosols, droplets or fomites were:

- contaminated patient equipment including respiratory devices;
- high touch surfaces;
- hand shaking;
- door handles;
- table surfaces;
- soap dispensers;
- chairs;
- hand wash basins; and
- bed linen.[9,40,44,50,51,54,56]

Epidemic strains were found to be more prevalent, possibly surviving longer due to the longer half-life.[21]

Alcohol gel was sufficient at removal of surface bacteria and recommended more regularly during the clinic visit.[44,57]

Several different cleaning products have been cited in room cleaning regimens, but these differ from study to study. Chlorine-based products and vaporised hydrogen peroxide have been used as part of final cleaning regimen of rooms that have been occupied by patients with M. abscessus.[50] Chlorine-based products have also been used for surface cleaning in rooms of patients who have *PSA.*[22] Bleach has been used in drains where *PSA* has been isolated.[22] UV light shown to be effective at killing *PSA*, *BCC* and *Stenotrophomonas maltophilia.*[21] Others recommend using EPA-registered hospital disinfectant/detergent.[30]

Although grade quality was considered low or very low on much of the evidence, RCTs into infection control issues are not considered ethical.[1] There is however a wealth of evidence to support the benefit of segregation.

With the increased use of digital technology, face to face contact with the MDT and the person with CF could be less frequent. With a reduction in frequency of clinics the likelihood of cross-infection could be reduced.[1] Although each hospital has its own challenges and physical resource limitations, a unified approach to infection control practices is needed across hospitals managing CF patients.[50]

Recommendations

- Develop a robust local IPC strategy which recognises the requirement for individual and cohort segregation *(QoE – moderate)*.
- Use microbiological data to segregate people with *PSA*, *BCC* or M. abscessus infections, eg by using separate outpatient clinics, this should also extend to physiotherapy sessions and use of treatment rooms and gym spaces *(QoE – moderate)*.
- The local IPC policy should include recommendations for cleaning and decontaminating rooms and equipment used between people with CF and the use agents with activity against CF pathogens including M. abscessus *(QoE – high)*.
- During inpatient care, ensure all physiotherapy manoeuvres and exercise are conducted in individual rooms. If a physiotherapy gym is to be used it should be by no more than one person with CF at a time with appropriate surface cleaning and decontamination. The time between people with CF using the gym should be optimised according to air exchanges/room ventilation *(QoE – moderate)*.
- Ensure appropriate cleaning and decontamination of all multiuse physiotherapy and exercise equipment between people with CF *(QoE – moderate)*.
- Stethoscopes or pulsoximeters should be for individual patient use where possible and appropriately decontaminated after use and between patients *(QoE – low)*.
- Covered sputum pots should be used for respiratory secretion containment and appropriate disposal *(QoE – moderate)*.
- The use of water repellent gowns and gloves should be used when performing airway clearance or direct clinical care to prevent the possibility of fomite cross transmission both for in and outpatients. This is in line with contact and transmission-based precautions *(QoE – moderate)*.

- Patients should be encouraged to practise hand washing or use alcohol-based hand gel frequently and especially in the outpatient environment before use of a spirometer or other handheld apparatus *(QoE – moderate)*.
- Consider the use of surgical masks for CF patients in communal areas of the hospital to reduce the risk of environmental contamination and airborne transmission of potential pathogens *(QoE – low)*.
- When carrying out spirometry in standard airflow rooms consider allowing a washout period between patients *(QoE – low)*.
- Consider specification of room ventilation (number of air changes per hour) when planning new CF facilities to reduce the risk of airborne transmission of CF pathogens *(QoE – moderate)*.

Good practice points

- Consider allowing time after spirometry, to allow droplets to settle before cleaning and disinfecting the room (unless tests carried out in a room with enhanced ventilation).
- The fingernails of healthcare workers should be kept trimmed and artificial nails are not advised.
- Audit and enhance staff adherence to cleaning and hand hygiene.
- Consider minimising cough-inducing and aerosol-generating procedures in outpatient rooms by collecting sputum and cough swab specimens at home prior to appointment.
- Appropriate cough etiquette should be encouraged (cough or sneeze into a tissue or your elbow not your hands. Discard any tissues into an appropriate bin. Wash hands after using a tissue).
- Optimise infection control practices and processes in physiotherapy and Pulmonary Function Laboratory.

For inpatient episodes

- Patients should be accommodated in single rooms with an en-suite basin, toilet and shower.

For outpatient episodes

- Patients should avoid using communal waiting areas, instead patients should be placed in an individual clinic room on arrival to clinic.
- Patients should be encouraged to wear a surgical mask when in the outpatient environment and in transit through the hospital to reduce droplet nuclei generation and environmental contamination.
- Increase usage of telehealth consultations where possible.

14.4 Nebulisers and Airway Clearance Devices

There is an ever-increasing variety of medical devices available for nebulised therapy and airway clearance, and subsequently, a variety of devices may be used over time by a single patient.

Nebuliser

Nebuliser contamination by various clinically significant pathogens, including *BCC*, *Stenotrophomonas maltophilia* and *PSA* have been well documented.[58-63] In addition, yeast and moulds have also been cultured in high prevalence from nebulisers, even after washing and drying.[64] There is little evidence to support correlation between the organisms cultured from nebulisers and patients own respiratory samples.[58-61] Nonetheless, these findings highlight the need for rigorous nebuliser cleaning and disinfection, as a contaminated nebuliser could potentially result in re-infection of the airways or represent a source of new infection.

Airway Clearance Devices

There are few studies investigating the contamination of airway clearance devices, but a recent study found that 28/30 devices tested were contaminated with bacteria; these were mainly environmental bacteria, but five samples were positive for pathogenic bacteria.[65] Cleaning, defined as soaking in hot soapy water, rinsing and air-drying resulted in complete eradication in half of the samples, partial eradication in 30% and failure to eradicate in the remainder.

Current guidelines

The CF Foundation (CFF) IPC guideline[51] gives recommendations for nebuliser maintenance both in hospital and at home. The use of disposable nebulisers in hospital is advocated. After each use, any residual medication should be rinsed out with sterile water and the components replaced after 24 hours. At home they recommend cleaning with dish detergent followed by disinfection with one of multiple methods (boiling in water, dishwasher, steam, 70% alcohol soak, 3% hydrogen peroxide soak). Both cold methods of disinfection require rinsing with sterile water. The final step is complete air-drying. These steps should be carried out after each use.

Until recently, recommendations for nebuliser care in the UK were borne out of manufacturers' guidelines and local IPC policies. Manufacturers' recommendations are highly variable and inconsistent and can change frequently resulting in confusion and reported variation of practice between centres,[66] between healthcare staff responsible for nebuliser care[67] and between patients at the same centre.[68] These studies highlighted everyday practical limitations such as the cost implications of using disposable nebulisers in hospital, the practical challenges around disinfecting in hospital and lack of facilities to carry out good nebuliser hygiene.

A comprehensive review on nebuliser hygiene in CF has been recently published[69] and offers recommendations on cleaning and disinfection practises for nebulisers in hospital and at home (VI, VII).

Key points regarding nebulisers are listed below.

- Nebulisers should be washed with detergent after each use.
- Nebulisers should be disinfected immediately using thermal disinfection.
- Following disinfection, parts can be stored in the disinfector unit until used the next time (within 24 hours). This recommendation supports the findings of two studies investigating steam disinfection of nebulisers and airway clearance devices in a baby bottle disinfector.[70,71] Steam was found to be a safe, effective, simple method of disinfection for nebulisers inoculated with common pathogens including *Staphylococcus aureus*, *PSA*, *Burkholderia multivorans* and M. abscessus. Furthermore, Hohenwarter[70] found that active drying of components was found to be a source of recontamination and that components could be safely left undisturbed in the disinfector until required.
- Leaving parts to air dry is not definitive as the review cites two recent papers showing how NTM and Staphylococcus Aureus (MSSA and MRSA) can survive on plastic surfaces for 24 hours during the air drying process.

These guidelines can be used in conjunction with manufacturers' instructions to drive local policy and inform advice given to patients.

To date there are no such guidelines for airway clearance devices, although each manufacturer provides information with the devices (See Appendix VIII). However, good practice would suggest that the procedures for the nebuliser should apply for hygiene of airway clearance devices. Similarly, there is little from the literature to guide the frequency of changing bacterial filters and patient tubing from devices such as the IPPB. The AARC clinical practice guideline for the IPPB recommends that IPPB circuits should be changed between patients, when visibly soiled, or according to institutional infection control policy.[72]

A simple, clear, consistent approach to the maintenance of these devices is a significant step in overcoming the barriers to this part of a patient's daily routine.

Good practice points

- Nebuliser components and airway clearance devices should be washed with detergent after each use.
- Washing the components is essential to remove residual medication or debris.
- Steam disinfection represents an effective, safe and simple method of disinfection.
- Sterile water should be used for the final rinse if disinfection is not possible.
- Air drying is effective in most cases.

Research recommendations

- Literature review to formulate universal guidelines for the cleaning and hygiene of airway devices and adjuncts.

14.5 Education and adherence to IPC recommendations

Healthcare professionals

Despite increased evidence and recognition that the implementation of strict IPC procedures decreases the spread of pathogenic bacteria in CF there is continued evidence of healthcare professionals, patients and their families are inadequately fulfilling recommendations put in place to improve IPC practice.[1,14,74,78,81]

A large multi-centre US study looked at the possible barriers to healthcare professional adherence to IPC guidelines in CF centres. The main barrier to adherence identified was a lack of awareness of, or access to IPC guidelines. Other barriers to adherence identified were the complex attitudes of some healthcare professionals towards some aspects of the guidelines, some reporting that they did not see the value of adherence, in particular to guidelines relating to socialisation between people with CF and the cleaning and disinfection of nebulisers and some reporting a lack of confidence in their own ability to prevent socialisation between people with CF and to clean rooms between patients.[74]

Local audits and then targeted healthcare professional education and skills programmes have been shown to improve adherence to IPC on a local level.[1,75] Educational IPC posters visible in clinical areas are thought to both improve patient and also healthcare professional accountability.[75] The education of patients and staff regarding the requirement of personal protective equipment (PPE) such as gowns and gloves enhanced adherence to infection control measures. One novel method was the implementation of 'safe zone' decals 2.5 ft (75 cm) from the doorway, beyond this zone all healthcare personnel were required to wear the appropriate PPE.[1,75]

Barriers to healthcare professional implementation and adherence to IPC recommendations have been identified as:

- reduced access to available recommendations;[14,74]
- reduced knowledge of the content of the recommendations;[14,74]
- reduced time available or support to adhere to recommendations;[14,74]
- healthcare professional's low confidence in their ability to change patient behaviours;[14] and
- healthcare professional's lack of confidence in their own ability to adequately fulfil the recommendations.[14,74]

The following good practice points are strategies suggested to overcome these barriers to adherence.

Good practice points

- Improved awareness and access to IPC guidelines for healthcare professionals.
- Enhanced IPC education and skills workshops/training for healthcare professionals.
- Sharing successful interventions between CF centres.
- IPC educational posters in clinical areas.
- Local audits of IPC adherence can inform strategies to reduce local barriers to staff adherence to recommendations.
- More work is needed to link adherence to infection prevention and control guideline adherence with improved patient outcomes.

14.6 People with CF and their families

Poor adherence behaviours are well documented in people with chronic disease and specifically people with chronic respiratory disease.[76] The treatment burden associated with airway clearance and nebuliser therapy has been well documented and it has been shown that adherence to these therapies has been variable.[73] Unsurprisingly then, the importance of, and subsequent adherence to, the cleaning and maintenance of nebulisers and airway clearance devices is also often neglected.[58,59] The care of respiratory equipment may be considered a mundane and insignificant practise to people with CF. A positive relationship has been shown between knowledge

and adherence of IPC in families with children with CF.[77] Della Zuana et al[63] showed that the incidence of nebuliser contamination improved after a single education session, to include written and oral instructions. In a large multicentre US study people with CF and their families who had more frequent contact with their CF centre had increased knowledge and awareness of the principles of IPC, increased confidence in their own ability to perform IPC practices and a higher perception of the health benefits of adherence to the recommendations. Families of younger children with CF had better adherence to IPC practices, such as cleaning and disinfecting of nebuliser equipment, than adolescents and adults with CF. It was proposed that this could be because relatively new recommendations have been better integrated into the care of younger patients, families may have heightened concerns regarding the impact of these practices on their child's health, and that older patients with advancing disease may need increased support in order to adhere to recommendations.[81]

A number of studies have found that a high proportion of people with CF are unaware or unconcerned with the risks of physical contact with other people with CF.[1,51,75,78,81] Many people with CF have been found to place a high value on the specific support and friendships that face to face contact with other people with CF can bring and feel that these benefits outweigh the potential risks of contact.[76,78]

Barriers to patient and family implementation and adherence to infection prevention and control recommendations have been identified as:

- inadequate awareness of IPC recommendations;[1,76,78,81]
- reduced understanding of risks and therefore the benefits of adhering to IPC recommendations;[1,51,78,81]
- length of exposure to the recommendations (newer recommendations vs older recommendations with engrained behaviours);[51,76]
- lack of belief in the evidence underpinning the recommendations (possibly because of the lag time between risky behaviours, ie contact with other people with CF, infection then symptoms);[1,51,76,78,81]
- perceived benefit of friendships, contact and support offered by other people with CF outweigh perceived risks of cross-infection;[76,78]
- time constraints;[76] and
- impact of deteriorating health on ability to perform recommended IPC practices (such as cleaning and disinfecting physiotherapy and nebuliser equipment).[81]

The following good practice points are strategies suggested to overcome these barriers.

Recommendations

- Physiotherapists working in CF should have full awareness and understanding of the local and national IPC recommendations *(QoE – moderate)*.
- Physiotherapists working in CF must also have an awareness and understanding of the manufacturers recommendations for cleaning and disinfecting specific physiotherapy and nebuliser equipment *(QoE – low)*.
- Physiotherapists working in CF have a pivotal role in educating and supporting families of people with CF and people with CF in specific strategies in IPC recommendations including:
  - performing hand hygiene;
  - containing and disposing of sputum;
  - cleaning and disinfection of physiotherapy and nebuliser equipment;
  - cough etiquette; and
  - avoiding contact with other people with CF *(QoE – moderate)*.

Good practice points

- Education is an essential tool to improve acceptance and adherence to hygiene protocols and to drive positive outcome.
- Enhanced regular patient and family IPC education and skill training.
- Specific education and training on nebuliser and physiotherapy equipment cleaning and disinfection.
- Increased frequency of discussions around IPC recommendations.
- Intervention/education on how to improve adherence to IPC recommendations and balance other socioeconomic demands.

- Improved IPC learning materials.
- Promotion of strategies for people with CF to find social support from others with CF in creative ways that do not violate IPC recommendations (eg websites/chat rooms/forums, social networking sites, telephone and texting).
- Offer increased support to those with deteriorating health to perform recommended IPC practices (such as cleaning and disinfecting nebuliser equipment).
- Consider peer to peer education using the internet as a vehicle for communication.

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15. Non-medical prescribing

Physiotherapists have been non-medical prescribers (NMP) since 2015 and are required to undertake CPD appropriate to maintain their competence. A physiotherapist independent prescriber may prescribe any licensed medicine from the BNF, within national and local guidelines (including a restricted list of controlled drugs as set out in Regulations)[1] for any condition within the practitioner's area of expertise and competence within the overarching framework of human movement, performance and function. They may also mix medicines prior to administration.

Regulation of NMP practice

Physiotherapist Prescribers must only prescribe once they have successfully completed an HCPC approved prescribing programme and had their entry on the HCPC register annotated to show their prescribing status.

The HCPC 'Standards for Prescribing' outline the standards of prescribing proficiency required for physiotherapists annotated as prescribers on the HCPC register. These are in addition to the general standards of proficiency for physiotherapists that apply to all registrants.[2]

The Royal Pharmaceutical Society 'A Competency Framework for Prescribers' and the CSP 'Practice Guidance for physiotherapist supplementary and independent prescribers' provide details of prescribing competencies and practice guidance that must be maintained to ensure safe and effective prescribing, including information on the assessment, consultation and prescribing governance.[3,4]

Physiotherapist Prescribers must meet the requirements of HCPC, CSP and their employer in order to ensure they are prescribing safely in line with best practice local and national guidance. Physiotherapist Prescribers must also ensure that they have adequate indemnity for their prescribing practice and that their practice has been endorsed by their employer (which may require an addition to their job description).

Recommendations

- All CF MDTs should review whether the addition of a physiotherapist prescriber may enhance the service they offer to patients *(QoE – low)*.
- Principal and advanced CF physiotherapy practitioners within a CF service should consider NMP training as part of their annual CPD and/or job planning review to support patients and services *(QoE – moderate)*.
- Physiotherapist Prescribers working in CF must undertake CPD specific to CF and prescribing. This can be achieved through attendance to ACPCF NMP group events. Additional CPD activities may include CF conferences, peer supervision, local medicine reviews and journal clubs *(QoE – moderate)*.
- Physiotherapist Prescribers working in CF should be part of any local clinical governance teams/programmes monitoring quality improvement in CF care *(QoE – low)*.

Good practice points

- Physiotherapist Prescribers working in CF should be endorsed by the CF centre MDT and improve the patient experience without compromising safety or access to quality care.
- Physiotherapist Prescribers working in CF must remain up to date with CF medication guidance relevant to their prescribing practice which may include local guidelines, Cystic Fibrosis Trust guidance, Commissioning guidance and NICE appraisals.
- Physiotherapist Prescribers working in CF should help people with CF make informed decisions about their treatment and support patient's use of appropriately prescribed medicines to best effect.[5,6]
- Physiotherapist Prescribers working in CF should have access to a local NMP prescribing forum to support long-term CPD and development needs.

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16. Glossary of abbreviations

AAD	Adaptive aerosol delivery
ACBT	Active cycle of breathing techniques
ACPCF	Association of Chartered Physiotherapists in Cystic Fibrosis
ACT	Airway clearance techniques
AD	Autogenic drainage
BAE	Bronchial artery embolisation
BTS	British Thoracic Society
CF	Cystic fibrosis
CFLD	Cystic fibrosis associated liver disease
CFQ-R	Cystic fibrosis questionnaire – respiratory
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed tomography
FEF25-75	Forced expiratory flow (25-75)
FET	Forced expiration technique
FEV_1	Forced expiratory volume in 1 second
FRC	Functional residual capacity
FVC	Forced Vital Capacity
GORD	Gastro-oesophageal reflux disease
GRADE	Grading of Recommendations Assessment, Development & Evaluation
HFCWC	High frequency chest wall compression
HFCWO	High frequency chest wall oscillation
HRCT	High resolution CT imaging
IPPB	Intermittent positive pressure breathing
IPV	Intrapulmonary percussive ventilation
MRSA	Methycillin Resistant Staphylococcus Aureus
NIV	Non-invasive ventilation
PD	Postural drainage
PEEP	Positive end expiratory pressure
PEP	Positive expiratory pressure
QoE	Quality of evidence
SIGN	Scottish Intercollegiate Guidelines Network
UI	Urinary incontinence
VAS	Visual analogue scale
VATS	Video-assisted thoracoscopic surgery
VMT	Vibrating Mesh Technology

Appendix I

Clinical Guidance for the Physiotherapy Management of Screened Infants with Cystic Fibrosis and Screen Positive Inconclusive Diagnosis

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Introduction

Babies born with cystic fibrosis (CF) have essentially normal lungs, but within various timescales, develop chronic respiratory disease. Since the introduction of newborn screening throughout the UK, babies are diagnosed with CF soon after birth, often before they develop any symptoms or lung pathology. Additionally, a new group of patients has emerged named cystic fibrosis screen positive inconclusive diagnosis (CFSPID). This refers to children who have either a normal sweat test in the presence of two mutations, at least one of which is of uncertain significance (Group A) or a borderline sweat test in the presence of zero or one mutation (Group B).[1]

The majority of newborn-screened infants present to CF centres with no signs or symptoms of disease. The importance of early intervention is well recognised, and most CF centres have adopted a policy of close monitoring and aggressive treatment of early lung disease.[2,3] A significant number of children with CF now have normal lung function well into early adulthood even though they are very likely to have underlying lung pathology.[4] The advent of newborn screening raised questions about the role of traditional, routine airway clearance in asymptomatic babies. While specialist physiotherapists agreed unanimously that physiotherapy interventions were appropriate once respiratory symptoms were apparent, the place of routine daily airway clearance prior to this was less clear.[5,6] It was also recognised that while infants may be asymptomatic at diagnosis, over time they will swing along a spectrum of being asymptomatic at times and symptomatic at others. The ideal solution would have been to undertake a prospective randomised controlled trial comparing twice-daily routine airway clearance with a regimen of close monitoring and airway clearance as required. As this proved not to be a possibility, a Delphi consensus was undertaken by the Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF) amongst specialist physiotherapists in the UK, in order to formulate guidelines for the management of infants with CF diagnosed by newborn screening.[7] Consensus was reached on the majority of statements and although most physiotherapists agreed that routine twice-daily airway clearance was no longer needed, it was not possible to reach a full consensus. An amendment allowed practitioners to rationalise their treatment intervention on an individual patient basis. Physiotherapists have a duty to provide safe and effective care and daily treatment regimens need to be tailored to individual needs, lifestyle and symptoms, particularly as long-term routine airway clearance is seen as a substantial burden for patients and families.

Arguments for early commencement of airway clearance in symptom-free infants are three-fold. Firstly, there is good evidence that early lung disease precedes the development of overt symptoms in children with CF.[2,8-17] Secondly, anatomical and physiological differences, which result from immaturity of the respiratory system, in combination with CF, render the CF infant more vulnerable than the older child to respiratory complications and infection. Finally, establishing daily routines early in a life-long illness may facilitate acceptance of the need for treatment and adherence on the part of both the child and family. It may also enable parents to maintain their competency in airway clearance techniques (ACTs).[18-20] Conversely, the presence of bacterial infection and raised inflammatory markers reported from bronchoalveolar lavage (BAL) is not always associated with excessive sputum production or symptoms that respond to airway clearance. There is no physiological argument or scientific proof that physiotherapy is helpful in

alleviating the inflammatory process within the airways. It is well known that adherence to routine therapy in chronic disease poses a significant problem and that when the benefit of a treatment is not immediately apparent, adherence is often poorest.[21-24] Taking into consideration the above salient points, it is clear that there is no absolute clear approach. This notion was reinforced by the ECFS neonatal screening group who developed a consensus on the management of newborn screened infants.[25] They stated that infants must receive care by a CF specialist physiotherapist; techniques to facilitate airway clearance should be undertaken on a regular basis, however, debate exists as to the best strategy in managing asymptomatic infants. Physiotherapy should be completed more frequently in the symptomatic infant.

A new dynamic to CF management following the introduction of newborn screening is the identification of CFSPID infants. Many of these infants are completely asymptomatic with normal or borderline sweat test results, and it is unclear as to what their disease presentation/progression and long-term outcomes will be. This poses a further dilemma for specialist CF physiotherapists. To date there is only one study prospectively evaluating infants with CFSPID.[26] 82 CFSPID and 80 CF infants from 7 CF centres in Canada were followed up for 3 years. 11% of the CFSPID infants subsequently progressed to CF. Reassignment of diagnosis was based on abnormal sweat test results and updated functional analysis of mutations on CFTR2, rather than on clinical symptoms. Respiratory symptoms of wheeze and cough were common in subjects with CFSPID, but were less frequent than in the CF group. There was a higher frequency of *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* compared to healthy children, but not of *Haemophilus influenza* and *Staphylococcus aureus*. The authors concluded that CFSPID infants are at risk of positive cultures for CF associated bacteria, as well as fulfilling diagnostic criteria of CF over time and require monitoring, ideally by CF clinicians.

Literature review

There is clear evidence that babies demonstrate physiological changes from an early age in the absence of overt clinical symptoms or objective findings on examination. Investigative techniques including BAL, high resolution computed tomography (HRCT), infant lung function and lung clearance index (LCI) serve to confirm this.

Bronchoalveolar lavage

Kahn et al examined bronchoalveolar fluid (BALF) from 16 infants diagnosed with CF and identified airway inflammation (increased IL-8 levels and neutrophils) in infants as young as 4 weeks.[8] Inflammatory markers were evident in samples, irrespective of bacterial load. Armstrong et al reported that *Staphylococcus aureus* was present in BALF of almost 40% of CF infants (14/45), more than one third of whom were symptom free.[9] Although respiratory pathogens were found to be an important cause of inflammation, not all infected subjects had inflammatory cells or symptoms. This study also advised that infection was overestimated by throat cultures, suggesting that for many subjects, bacterial pathogens remain confined to the upper airways. Sly et al studied 57 newborn-screened infants in Australia.[15] All had a CT, BAL and bloods for inflammatory markers soon after diagnosis (median age 3.6 months). 80.7% had an abnormal CT with bronchial dilatation in 18.6%, bronchial wall thickening in 45% and gas trapping in 66.7%. The majority of infants had no respiratory symptoms at the time of the CT. 20% had infection: 4 with *Staphylococcus aureus* and 3 with *Pseudomonas aeruginosa*. 30% had detectable neutrophil elastase activity. Rosenfeld et al studied 40 infants over a two-year period and reported an increase in CF pathogens with age.[2] Infants had elevated markers of inflammation whether CF pathogens were recovered or not, although the concentrations of these markers increased with the density of CF pathogens in BALF. These infants were also reported to have obstructive lung disease (expiratory flows and air trapping). Nixon et al investigated the relationship between lower airway infection and inflammation, respiratory symptoms and lung function in infants and young children with cystic fibrosis diagnosed by newborn screening.[27] Thirty-six children (<3 years) underwent BAL and lung function testing. Lower airway infection was associated with a significant reduction in lung function. Although a daily moist cough within the week before testing was reported on 20/54 testing occasions, infection was only detected in 7 samples. Children with a daily cough had lower lung function than those without respiratory symptoms at the time of BAL. The authors concluded that both respiratory symptoms and airway infection have independent additive effects on lung function (unrelated to airway inflammation). The presence of a daily moist cough in young children with mild CF lung disease is independently associated with a reduction in lung function. In a retrospective review of a non-newborn screened population, Hillyard et al reported the presence of *Pseudomonas aeruginosa* in 20% (5/25) and *Staphylococcus*

aureus in 16% (4/25).[28] The median age of the study population was 12 months and lavage culture was reported to be positive in eight out of eighteen symptomatic children.

Computed Tomography of the Chest

Martinez et al showed that infants with CF have thickened airway walls, narrowed airway lumens and air trapping compared with controls on HRCT.[14] These measurements correlated with airway function. Mott et al and the AREST (Australian Respiratory Early Surveillance Program) CF group carried out a retrospective analysis of repeat CT scans on 143 children, ranging from 2 months to 6.5 years in a newborn screening programme to investigate if early structural lung disease persists and progresses over 1 year.[29] 19% of children never demonstrated bronchiectasis, but it was detected in 75% either on the initial or subsequent scan and persisted in 74% of these. Progression over time was evident in 63%. Air trapping was seen in 88% of scans. This persisted at the second scan in 81%. Progression over time was evident in 46%. Radiological progression of both bronchiectasis and air trapping was associated with severe genotype, worsening neutrophilic inflammation and pulmonary infection.

Ranganathan et al conducted a review of early CF lung disease and documented that bronchiectasis was present in asymptomatic infants with CF.[17] Free neutrophil elastase activity on BAL was present in 30% of infants with CF and was a predictor of bronchiectasis by the age of 3 years with air trapping identified as an additional risk factor. Bronchiectasis was found in 30-40% of 3-4 year olds and increased to 80% by the age of 5 despite normal lung function parameters.

Lung function

Lung function abnormalities in infants with CF have been reported as early as 1988.[30,31] Ranganathan et al (2004) conducted measurements of airway function in non-screened newly diagnosed infants made soon after diagnosis and at six months.[11] After adjusting for age, length, sex and exposure to maternal smoking, the authors reported a significant reduction in $FEV_{0.5}$ both soon after diagnosis and on repeat testing. This study implies that airway function is diminished in a non-screened population soon after diagnosis and the reduction persists during infancy.

Kozlowska et al reported findings of a longitudinal study of 48 CF children (non-screened, but managed at a specialist CF centre) and 33 healthy controls.[13] The diagnosis of CF itself accounted for a significant reduction in $FEV_{0.75}$ and FEF_{25-75} in preschool years. Wheeze on auscultation, recent cough and *Pseudomonas aeruginosa* infection (even if apparently effectively treated) were all independently associated with further reductions in lung function. This study demonstrated that CF, in the absence of complications, is associated with decreased lung function.

Lung clearance index (LCI) is a measure of ventilation inhomogeneity derived from a multi-breath washout (MBW) technique. Its clinical usefulness in early lung detection has surged over the last 10 years, particularly in children, where more sensitive objective measures are required.[32]

Lum et al studied 39 non-screened infants using MBW to measure LCI alongside raised lung volume rapid thoraco-abdominal compression (RVRTC) techniques.[33] Abnormalities were detected in 72% of infants (41% were detected by both techniques and a further 15% by each of the two tests performed).

Ah-Fong Hoo et al and the London CF Collaboration group assessed 71 newborn-screened infants with CF and contemporous healthy controls.[34] Elevated LCI was detected in 21% of CF infants and 25% demonstrated an abnormally low $FEV_{0.5}$. Use of both techniques identified abnormalities in 35% of the CF sample group. They concluded that despite protocol driven treatment from specialist centres, abnormal lung function, increased ventilation inhomogeneity, hyperinflation and diminished airway function was evident in some of the infants. This study noted abnormal lung function in the absence of respiratory symptoms.

Kieninger et al provided the first evidence that abnormal lung function exists as early as 8 weeks of age in >40% of infants with CF, measured by LCI and FRC, independent of clinical symptoms.[35] This resulted from a prospective cross-sectional observational study comparing 53 newborn CF patients with 57 healthy controls.

Davies G et al conducted an observational study investigating the degree and tracking of infant lung function abnormality during the first 2 years of life.[36] 62 CF newborn screened infants and 34 controls participated. No child had abnormal LCI or $FEV_{0.5}$ on all test occasions, precluding the ability to identify “high-risk” infants in early life. They concluded that in contrast to previous studies, changes in lung function are mild and transient during the first 2 years of life in newborn-screened infants with CF, when managed according to a standardised UK treatment protocol.

Adherence

There is little evidence regarding adherence to airway clearance in infants and young children with CF. Jakobsen et al demonstrated high adherence levels over a 6-week period using infant PEP in 100 screened babies.[37] The argument for establishing a daily routine to optimise adherence is not established. Non-adherence to treatment regimes in chronic disease has been reported to be as high as 50%.[21-23] Time-consuming interventions, which have no immediate palpable benefit, and those interventions which cause disruption to lifestyle are associated with poorer rates of adherence.[22-24] It has also been suggested that insistence on routine daily treatment may even reduce adherence during the adolescent years when the need for treatment may become greater.[38]

Physiotherapy

There is clear evidence to suggest early lung disease is present even in the absence of symptoms and it is widely accepted that early management of lung disease is essential. However, the early pathophysiological changes are often inflammatory in nature and not always associated with symptoms that respond to airway clearance. Conversely, if infection with likely sputum production is part of the early pathological picture, then early institution of airway clearance would appear sensible. Physiotherapy encompasses formal airway clearance, inhalation therapy, physical activity and structured exercise, and it is the role of the specialist CF physiotherapist to closely monitor and develop individualised appropriate programmes for each infant accordingly. There is very little in the current literature that addresses these specific issues in the infant cohort, but some small studies are relevant.

Button et al demonstrated that gastro oesophageal reflux (GOR) increased in physiotherapy regimens which used postural drainage incorporating a head down tilt when compared with regimens which used a modified postural drainage (omitting any head down tilt).[39,40] Long-term follow up of these infants also reported fewer respiratory complications in the group receiving modified postural drainage. Despite weaknesses in these studies (in particular with regard to subject numbers), the potentially detrimental effects of postural drainage raised have led many to recommend that the head-down-tipped position should no longer be used in infants during airway clearance regimens. A recent Cochrane review (2018) identified that the majority of reflux episodes reached the upper oesophagus and should make therapists carefully consider their treatment strategy.[41]

The immediate effects of four modes of treatment on lung function in 19 infants were assessed by Maayan et al during the first year of life.[42] The regimens were applied in a randomised fashion (inhaled salbutamol, inhaled N-acetylcysteine, chest physiotherapy or a combination of all 3). No significant changes in lung volumes were reported in individual groups, but there was a small improvement with the combined treatment group when compared with inhalation therapy or chest physiotherapy alone. Constantini et al compared the long-term efficacy of PEP mask versus postural drainage and percussion in infants with CF.[43] There was no difference in deterioration on chest radiograph or days per year of antibiotics over a one-year period. The authors concluded that PEP was safe to use in early childhood and equally effective as postural drainage and percussion, although patients and parents preferred PEP. Sharp et al carried out a retrospective audit to compare postural drainage and percussion with infant PEP and autogenic drainage (AD) in newborn screened infants.[44] They demonstrated a significant reduction in respiratory exacerbations requiring admission during the first year of life in the PEP group (mean 0.71) compared to PD and percussion (mean 1.66). Byrne et al offered a more individualised approach to physiotherapy management following the introduction of the newborn screening programme, whereby routine daily airway clearance was no longer advocated as standard.[45] Parents were taught ACTs, advised about respiratory symptoms and when to initiate treatment. 25 babies were included over a 3-year period. 18 families followed the new protocol, the remaining either had persistent respiratory symptoms or social issues necessitating the need for routine airway clearance from the outset. There were 11 hospital admissions, 10 for respiratory causes. All infants who changed from intermittent to routine ACTs was due to isolation of *Pseudomonas aeruginosa* (n=5). The remaining children continued into early childhood without the burden of daily treatment. A systematic review of AD and assisted AD was undertaken. However, due to lack of paediatric-specific randomised controlled trials, small sample sizes and unclear risk of bias, it was not possible to determine the efficacy and/or safety.[46]

In 2013 the Cystic Fibrosis Trust undertook a survey to identify the types of physiotherapy taught and practised in the UK infant population.[47] Results were collated from 17 paediatric specialist centres and 40 parents of CF infants. The results showed a shift away from a rigid regime for families with more flexibility and individual assessment.

In 2018, the ACPCF decided to review current practise nationally for infants aged 0-3 years with CF and CFSPID. 2 10-point questionnaires were developed using SurveyMonkey® software and included a mixture of multiple-choice and open questions. This was sent out via email to ACPCF members and direct emails to paediatric UK centre leads as identified on the ACPCF national database.[48,49]

In total, 39 responses were received for the CF questionnaire, 25 from specialist centres, 13 from network clinics and 1 unknown. The majority of infants had an initial physiotherapy review within one week of diagnosis (62%) and all infants within three weeks. Frequency of review varied from weekly to monthly in the early stages, extending to monthly during the first year. 26% of centres reported that they offered home visits to support this. All centres taught ACT's. The most frequent techniques taught were PEP mask (34%) and percussion (31%). Other techniques mentioned included autogenic drainage, vibrations, exercise, modified postural drainage, Bubble PEP (when old enough), gym ball bouncing, and blowing games. The majority of respondents chose more than one ACT. Various factors were reported to influence advice given on type, duration and frequency of airway clearance, the most prevalent being respiratory symptoms (37%).

Other factors included:

- parent/carer ability to carry out assessment and/or treatment;
- routine treatment to facilitate adherence;
- genetic mutation and/or sweat test result;
- comorbidities, eg post abdominal surgery, clotting, physiological principles;
- chest x-ray changes;
- microbiology;
- age;
- if advice was directed by the specialist centre;
- supportive evidence; and
- older CF sibling status.

If infants became inpatients, they received daily input. Some respondents specifically described advising once-a-day airway clearance, increasing to twice-a-day with symptoms/when unwell. Types of exercise recommended by centres included general developmental activity, gym ball exercises, tummy time, swimming, active play, baby group and gym classes, arm and leg exercises, floor play, activity encouraged as a family, baby massage, yoga and anything the child enjoys.

Parents/carers were advised to monitor for respiratory signs and symptoms. The phrase look, listen and feel was often referred to. Half of the centres reported providing parents with a specific assessment tool, of which almost half of these used the ACPCF assessment tool. The GOSH infant leaflet was also reported to be used. Most respondents reported that nebulised mucolytics would be considered, but are not used routinely.

23 responses were received and analysed for the CFSPID questionnaire. 17 identified themselves as working at paediatric specialist CF centres in the UK and Ireland. The remainder were from network centres associated with specialist centres.

The majority of CFSPID infants were seen within the CF service (83%). Other settings included respiratory and paediatric clinics. Approximately half of respondents reported that the physiotherapist reviewed all CFSPID infants, with the remaining 50% only seeing referred patients. Some reported that physiotherapy input depended on symptoms and others that there was no current formal pathway. Whether the infants were categorised into group A or B did not influence physiotherapy in the majority (65%). Physiotherapy advice given to parents of CFSPID infants included symptom recognition, ACTs, positioning and exercise. Some centres advised routine airway clearance while others recommended it only as indicated (persistent symptoms persistent and/or significant microbiology). As per the CF survey, the most commonly advised ACTs were PEP mask and percussion, followed by assisted autogenic drainage, vibrations, exercise, modified postural drainage, ACBT and oscillating devices.

The main factor influencing type, duration and frequency of airway clearance was symptoms (55%). Other factors given were age of child, severity of presenting disease, routine airway clearance as standard, microbiology, patient preference, sweat chloride level, symptom frequency, need for oral antibiotics, lung function, lung clearance index result, bronchoscopy findings, social situation, and experience that

often age leads to development of CF like symptoms. There was a wide variation of physiotherapy review for this population, from 2-4 weekly to annually. Many reported that attendance of this population in clinics and input of physiotherapy are person specific. No information resource was identified for physiotherapy input and CFSPID infants.

There were many open comments in this survey, many of which reflected the uncertainty of management. Some examples are: “unsure how to manage”; “some can be particularly symptomatic”; “often as infants get older they go on to develop CF like symptoms”; “important to visualise management”; “difficult to know if giving too much or too little input therefore good to collect data”; “important to monitor sweat chloride levels”; and “interested to get the view of patients and families”.

In summary, key recommendations from the Delphi consensus regarding assessment, treatment, activity and exercise for infants with CF are being followed.[7] In terms of the CFSPID population, there is a wide variation in physiotherapy input, reflecting the variability of clinical presentation and uncertainty regarding prognosis. Future work in this area should include long-term collation of patient data which will help to guide specialist physiotherapists in the development of specific guidelines and educational resources for this group of patients.

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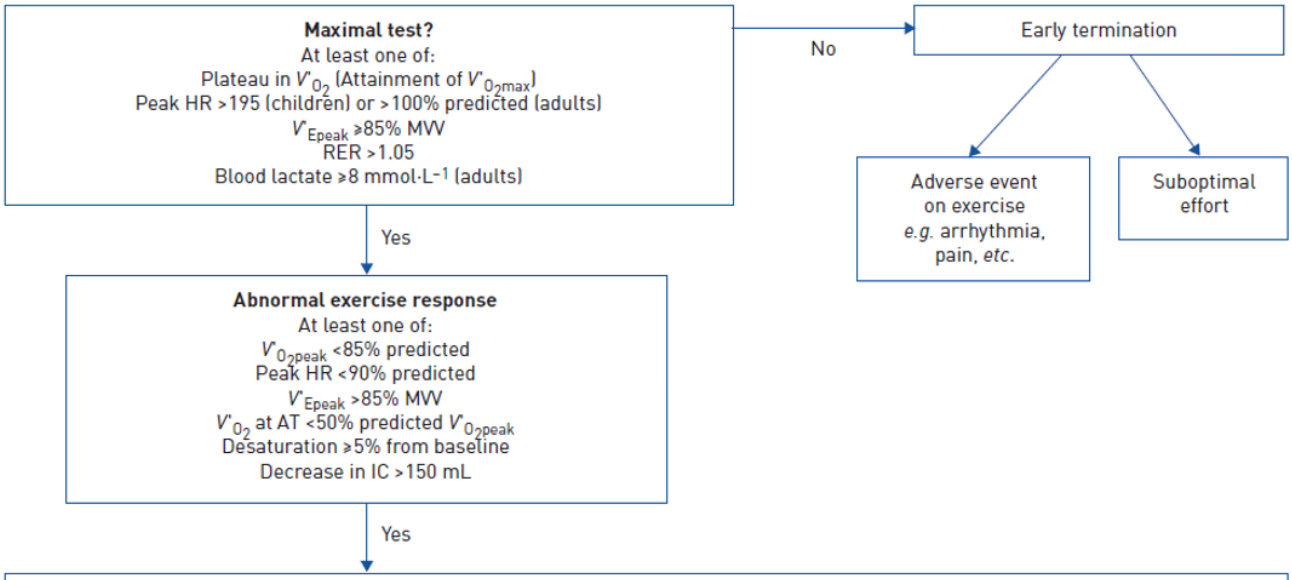
Appendix II

Appendix IIa

Schematic overview of how to determine whether a maximal effort has been given and the cause(s) of any exercise limitation.



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Appendix IIb

CPET Case Study Patient

Patient A (see Figure 1) (FEV_1 95% predicted), male (p.Phe508del/p.Ala457Pro, c.1369G>C) and aged 13 years attended for CPET at annual review. He attained a VO_{2peak} of 38.7 mL/kg/min (84% predicted), and a peak heart rate (HR_{peak}) of 184 beats/min. He had significant breathing reserve at peak exercise (V_{Epeak} 77L/min versus calculated MVV 108 L/min), meaning that he was not ventilatory limited during exercise. His anaerobic threshold (AT) occurred at 40% predicted VO_{2peak}.

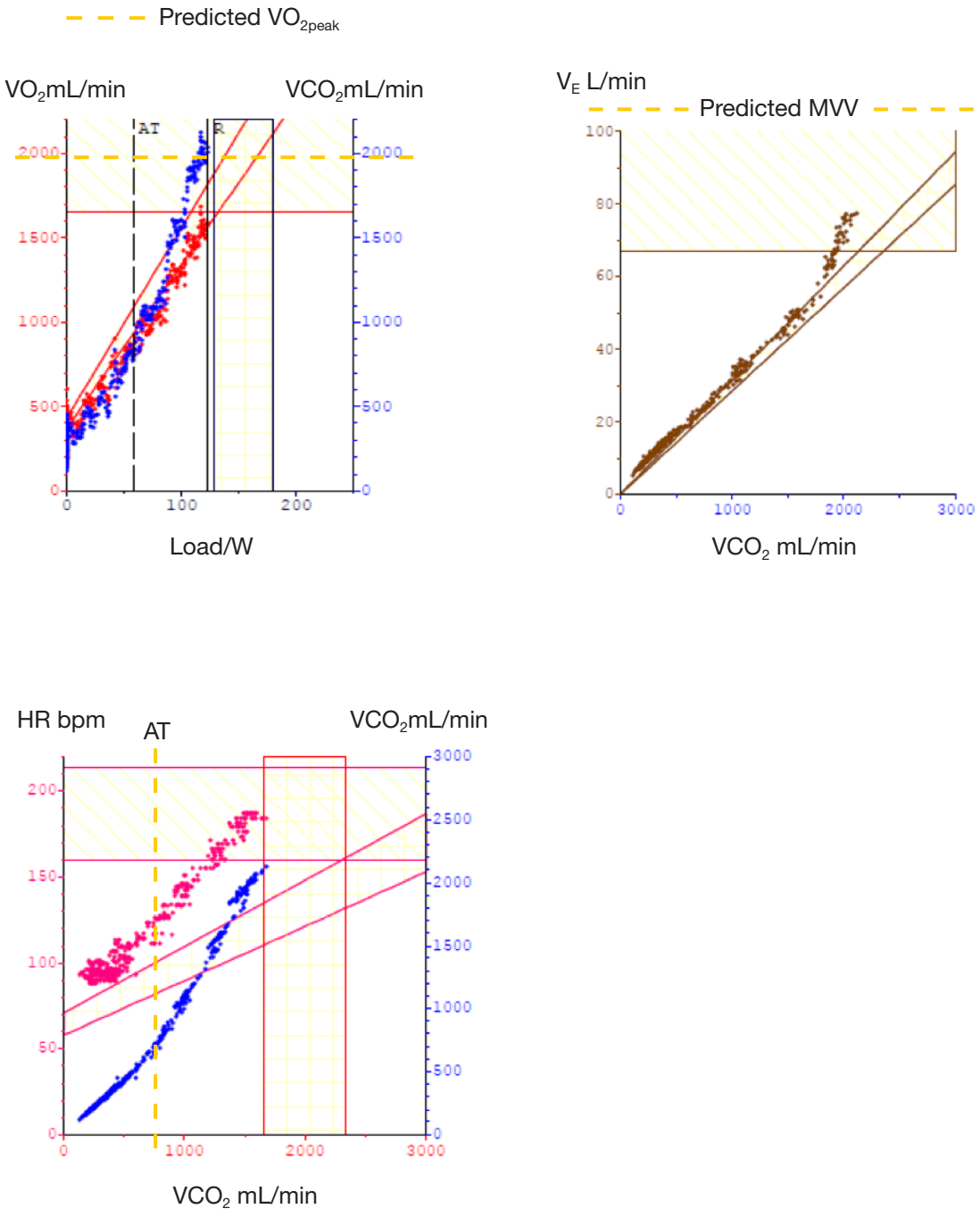
Taken collectively, the above CPET data suggested suboptimal exercise capacity, with deconditioning suggested by early onset of the AT. Selected data from panels 3, 4, and 5 of his 9-panel plot are displayed in Figure 2.

An action plan was made by his physiotherapy team who devised an individualised exercise programme. Improvements in both exercise capacity and physical conditioning were evident upon retesting 5 months later (see Figure 3). His VO_{2peak} had increased to 43.2 mL/kg/min (96% predicted), and AT had improved to 48% predicted VO_{2peak}. An identical HR_{peak} and similar breathing reserve were recorded.

Appendix IIc

Figure 1

Case example illustrating an exercise-limited and deconditioned CF patient (Selected data (Panels 3,4,5 shown) from CPET are displayed)



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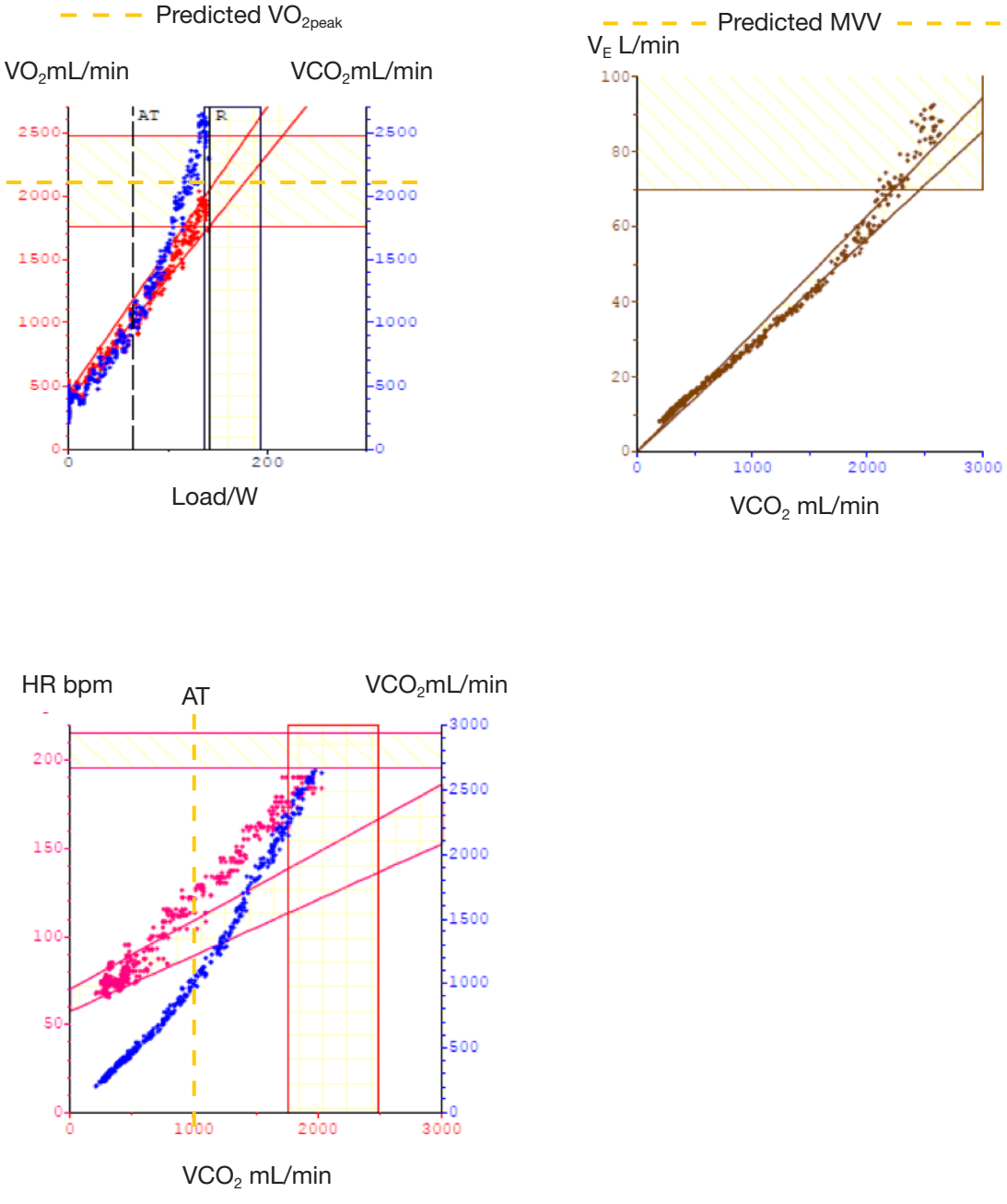
Appendix IId

Figure 2

Improvements in exercise capacity and AT in same patient following individualised exercise programme

(Selected data (Panels 3,4,5 shown) from CPET are displayed)



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Appendix IIe

Standard Operating Procedure for Maximal Cardiopulmonary Exercise Testing (CPET)

Following a short rest period, an unloaded phase should be undertaken. This phase is important for assessing baseline pulmonary gas exchange and ventilation associated with vertical leg movements. This phase also allows the patient further familiarisation with exercise on the treadmill cycle ergometer and to warm-up adequately. Since most cycle ergometers cannot provide a true minimum load of 0 W, a workload of 10 W should be used. A 3-minute duration is recommended, however in individuals with severe lung disease and/or severe deconditioning this phase may be shorter (but not less than 2 minutes) in order to perform the incremental exercise phase before the participant fatigues. If a treadmill is used, the lowest speed may be chosen for baseline measurements, eg 1.0-1.6 km/hour.[1]

After resting and unloaded phases, an incremental exercise phase to exhaustion should begin. Whilst the 2015 European statement on exercise testing in CF[2] recommends the Godfrey 'step' incremental protocol[3] (ie workload increases each minute on the minute), others have recommended the use of ramp incremental testing protocols.[4-6] Although it has not yet been directly investigated in people with CF, ramp and uniform minute-by-minute incremental protocols are both acceptable and provide similar outcomes, when total duration of the incremental phase is the same in healthy individuals. Importantly, whichever incremental protocol is used should be adapted to the individual's characteristics in order to allow adequate evaluation and follow-up. To assist with this and achieving a target incremental test duration of 8-12 minutes, a CF-specific equation to predict peak workload is now available[7] (Equation 1). Based on standard measures of anthropometry and FEV[1], this equation can be used to help calculate individualised workload increments for a cycle ergometry testing protocol:

Wpeak (W) = –142.865 + 2.998 × Age (years) – 19.206 × Sex (0 = male;1 = female) + 1.328 × Height (cm) + 23.362 × FEV1 (L)

Equation 1.

The most recent statement from the European Respiratory Society[1] also provides additional, alternative formulae and a CF example.

As outlined in the European Respiratory Society consensus document,[1] monitoring patients at the end of the incremental exercise phase (ie upon exhaustion) is important. They should be encouraged to continue unloaded pedalling or 2-3 minutes at a reduced speed of ~30 rpm when cycling (or very slow walking when on the treadmill). A prolonged recovery period may be necessary for some patients and observation during this time may identify any changes improvement in exercise recovery time after pulmonary rehabilitation and exercise programmes. During this period, cardiovascular monitoring (ECG, blood pressure, SpO_2 etc) should be performed. Since delayed post-exercise heart rate recovery is frequently observed in lung disease patients and associated with dynamic hyperinflation[8] and poor prognosis, HR recordings may offer additional useful information. Furthermore, assessment of perceived exertion, dyspnoea and leg fatigue should be performed using standardised scales suggested by Borg and others. In line with European Respiratory Society recommendations,[1] gas exchange measurements can be terminated, and the mask/mouthpiece removed in order to make the participant more comfortable (unless these measurements are required for specific evaluations during the recovery phase. In addition, inspiratory capacity manoeuvres may be performed during this phase of testing to assess the rate of recovery of dynamic hyperinflation, but this is mainly done for research purposes.[1]

Where maximal CPET has been used, it is important to confirm whether a maximal effort has been achieved in order to interpret the data accurately. The algorithm prided by the ERS Taskforce[1] is presented in Figure 1 to assist with this decision-making process. Additionally, when time allows and the participant is able, supramaximal verification has been shown to improve the reproducibility and accuracy[6,9] of maximal CPET outcome measures and confirm whether an individual has worked maximally. Such

verification testing has been shown to be safe and well tolerated in both children/adolescents with mild to moderate CF as well as adults and/or those with more severe CF pulmonary disease.[8]

If full CPET testing is unavailable it is recommended that the same ramp cycle and treadmill protocols be performed with all other measures available and using predictive metabolic equations to estimate oxygen consumption in lieu of direct gas analysis.[10] This should be undertaken with caution as predictive equations can only provide an estimate of 'true' exercise capacity.

References

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4 Radtke T, et al. ERS Statement on standardisation of cardiopulmonary exercise testing in chronic lung disease. Eur Respir Rev. 2019 Dec 18;28(154).

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Appendix IIf

Cardiopulmonary exercise test summary report

Hospital name:	Department:
Patient's surname:	Test date:
Patient's name:	Type of ergometer and metabolic cart:
DOB:	Reason for referral:
Consultant:	Clinical diagnosis:
Indication(s) for conducting the test:	

Technical

Protocol:
Describe exercise protocol employed, work increment as a function of time and total incremental exercise duration.

Technical comments:
Review criteria outlined in Appendix 1 to establish whether the test has led to the limit of tolerance. Report the source of equation used to express physiological variables as a fraction of predicted normal values.

Reason for termination of test:
Report the reason(s) indicated by the patient for terminating the test (breathlessness, leg discomfort or both). Indicate whether the patient complied well with the incremental effort or claimed discomfort with the exercise or breathing apparatus as a contributing factor to exercise limitation.

Exercise response

Aerobic capacity/anaerobic threshold*:
A VO_{2peak} of …. mL/min/kg (…% predicted normal) was achieved along with a peak workload of …. Watts (…% predicted normal) *or peak speed of … km/hour*. Anaerobic threshold (AT) occurred at …. mL/min/kg (…% predicted VO_{2max}. Corresponding values were …. METs at AT and…. METs at the limit of tolerance. Indicate whether VO_2/work rate slope (…. mL/min/Watt) was within the normal range.

Cardiovascular response:
Peak HR was …. beats/min (% predicted normal). Indicate any abnormalities detected by the ECG recordings and report systolic and diastolic BP at the limit of tolerance. Conclude if cardiovascular response was normal.

Ventilatory response:
Peak V_E was …. L/min (…% MVV)**. Report the change from baseline in inspiratory capacity (delta IC = …. mL). Report shortness of breath score ……. Conclude whether exercise limitation was of ventilatory origin.

Gas exchange:
Report ventilatory equivalents for VO_2 and VCO_2 at AT and at peak exercise. Report resting and peak SpO_2. Report the V_E/VCO_2 slope values. Conclude whether gas exchange response to exercise was normal.

Metabolic:
RER values were …. at rest, …. at AT and …. at the limit of tolerance.

Summary

Conclusion:
Comment on patient's effort and exercise capacity taking into consideration peak values for work rate, *speed*, VO_2 and AT. Comment on potential ventilatory, cardiovascular or peripheral muscle limitation or simply poor effort.

Compare the results with previous tests on the same patient and indicate when the test should be repeated.

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*Anaerobic threshold (AT) determined from breath-by-breath gas exchange measurements or blood lactate measurements.

** Report, if MVV was measured directly (sprint method) or estimated (provide equation).
Anaerobic threshold (AT); blood pressure (BP); heart rate (HR); inspiratory capacity (IC); metabolic equivalent (MET); maximum voluntary ventilation (MVV); respiratory exchange ratio (RER); peak oxygen saturation (SpO_2); carbon dioxide production (VCO_2); minute ventilation (V_E); oxygen uptake (VO_2).

Text in *italics* refers to treadmill exercise outcomes.

Please note that this summary report is augmented by data tables and graphs of exercise data summarised in table 4 of the main manuscript [Radtke T, et al. ERS Statement on standardisation of cardiopulmonary exercise testing in chronic lung disease. Eur Respir Rev. 2019 Dec 18;28(154)].

Appendix IIg

The Borg perceived exertion scale

15-point scale

- 6–20% effort
- 7–30% effort – Very, very light (Rest)
- 8–40% effort
- 9–50% effort – Very light – gentle walking
- 10–55% effort
- 11–60% effort – Fairly light
- 12–65% effort
- 13–70% effort – Somewhat hard – steady pace
- 14–75% effort
- 15–80% effort – Hard
- 16–85% effort
- 17–90% effort – Very hard
- 18–95% effort
- 19–100% effort – Very, very hard
- 20–Exhaustion

Borg G. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982; 14(5):377-81.

Borg G, et al. A category-ratio perceived exertion scale: relationship to blood and muscle lactates and heart rate. Med Sci Sports Exerc 1983; 15(6):523-528.

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Appendix III

Appendix IIIa

Sino-nasal outcome test (SNOT-22)

I.D:_____ **Sino-nasal outcome test (SNOT-22)** Date:_____

Below you will find a list of symptoms and social/emotional consequences of your rhinosinusitis. We would like to know more about these problems and would appreciate your answering the following questions to the best of your ability. There are no right or wrong answers, and only you can provide us with this information. Please rate your problems as they have been over the past two weeks. Thank you for your participation. Do not hesitate to ask for assistance if necessary.

1. Considering how severe the problem is when you experience it and how often it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale:	No problem	Very mild problem	Mild or slight problem	Moderate problem	Severe problem	Problem as bad as it can be		5 most important items
1. Need to blow nose	0	1	2	3	4	5		○
2. Nasal blockage	0	1	2	3	4	5		○
3. Sneezing	0	1	2	3	4	5		○
4. Runny nose	0	1	2	3	4	5		○
5. Cough	0	1	2	3	4	5		○
6. Post-nasal discharge	0	1	2	3	4	5		○
7. Thick nasal discharge	0	1	2	3	4	5		○
8. Ear fullness	0	1	2	3	4	5		○
9. Dizziness	0	1	2	3	4	5		○
10. Ear pain	0	1	2	3	4	5		○
11. Facial pain/pressure	0	1	2	3	4	5		○
12. Decreased sense of smell/taste	0	1	2	3	4	5		○
13. Difficulty falling asleep	0	1	2	3	4	5		○
14. Wake up at night	0	1	2	3	4	5		○
15. Lack of a good night's sleep	0	1	2	3	4	5		○
16. Wake up tired	0	1	2	3	4	5		○
17. Fatigue	0	1	2	3	4	5		○
18. Reduced productivity	0	1	2	3	4	5		○
19. Reduced concentration	0	1	2	3	4	5		○
20. Frustrated/restless/irritable	0	1	2	3	4	5		○
21. Sad	0	1	2	3	4	5		○
22. Embarrassed	0	1	2	3	4	5		○

2. Please mark the most important items affecting your health (maximum of 5 items) _____↑

Appendix IIIb

Nasal rinses

Sometimes, rinsing your nasal passages with a salt water solution can be helpful. This is known as nasal irrigation or nasal douching.

Rinsing your nasal passages helps wash away any excess mucus or irritants inside your nose, which can reduce inflammation and relieve your symptoms.

Nasal irrigation can be done using either a homemade salt water solution or a solution made with sachets of ingredients bought from a pharmacy. Small syringes or pots (which often look like small horns or teapots) are also available to help flush the solution around the inside of your nose.

To make the solution at home, mix a teaspoon of salt and a teaspoon of bicarbonate of soda into a pint of boiled water that's been left to cool to around body temperature (do not attempt to rinse your nose while the water is still hot).

You will probably only use a small amount of the solution. Throw away whatever is left.

To rinse your nose:

- standing over a sink, cup the palm of one hand and pour a small amount of the solution into it;
- sniff the water into one nostril at a time – an alternative is to use a syringe to insert the solution into the nose;
- repeat this until your nose feels comfortable (you may not need to use all of the solution).

While you do this, some solution may pass into your throat through the back of your nose. Although the solution is harmless if swallowed, try to spit out as much of it as possible.

You can carry out nasal irrigation several times a day. Make a fresh salt water solution each time.

Appendix IV Medications

ACPCF NMP
ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN CF
NON-MEDICAL PRESCRIBERS GROUP

Appendix IVa

Example of SOP for the performance of Drug Response Assessments (DRAs) and follow-up review of inhaled and nebulised medicines.

1. Scope

This SOP has been developed for use by qualified HCPC registered physiotherapists working within a CF centre who have been assessed as competent to perform drug response assessments (DRAs) (including medicine administration component) and review use of inhaled and nebulised medicine.

2. Aims and objectives

The aims of this SOP are as follows:

- to standardise the procedure for the performance of DRAs and follow-up of new inhaled/nebulised medicine and the information provided to patients/carers, to minimise the risk of patient-related adverse events;
- to give the responsibility of performing the entire DRA procedure, including medicine administration component, to one competent individual. This will avoid parts of the procedure being missed accidentally and minimise the risks to patient safety; and
- to streamline the process of performing DRAs, to improve clinical efficiency.

NB - within this and associated documents the word ‘patient’ refers to the person with CF, it also applies to the carer of a patient, if the patient does not have mental capacity/requires assistance and/or supervision with medicines’ administration.

3. Standards

Procedure for DRA under physiotherapist supervision

Preparation for DRA

- Ensure that medicine is therapeutically indicated as detailed in current Summary of Product Characteristics (SPC), available on the electronic Medicines Compendium (eMC) website.[1] In the case of nebulised 7% and 3% hypertonic saline, which are classed as medical devices, please refer to current Instructions for Use (IFU). If medicine is to be used outside of stated therapeutic indications or if dose recommended is not the standard adult dose, a CF consultant, or competent physiotherapist non-medical prescriber (NMP) must have approved use and documented this in the medical notes. Note that amikacin, amphotericin, ceftazadime, meropenem, tauroldine solution and vancomycin are used ‘off-label’ when nebulised, so there is no nebulisation-specific information in the SPC for these medicines. It is recommended local patient information leaflets are produced for these ‘off-label’ inhaled medications.
- Ensure that there are no known contraindications to medicine use as detailed in SPC, IFU or local patient information leaflets and that the patient is not known to have an allergy to it. If any contraindications or allergies to the medicine are identified, this must be discussed with a CF consultant prior to DRA and an appropriate plan must be made to minimise any risks to the patient if the DRA is considered to be the best course of action. This should be documented by the CF consultant in the medical notes.

- Ensure that the following have been considered with the patient in relation to their circumstances, in conjunction with a CF consultant, specialist respiratory registrar or competent physiotherapist NMP and a decision has been made to proceed with DRA; special warnings and precautions of use; interaction with other medicinal products and other forms of interaction; fertility, pregnancy and lactation; effects on ability to drive and use machines as detailed in SPC IFU or local patient information leaflets.
- The DRA medicine should be prescribed by a physician or competent physiotherapist NMP as a STAT dose. For details of correct/ advised medicine prescriptions see the appendices 'Nebulised/inhaled medications for people with cystic fibrosis overview'.
- Drug and food allergies should be recorded as locally advised by the prescriber but should be checked with the patient by the physiotherapist (and added to if required) prior to administration of DRA medicine.
- DRAs should be performed in rooms with easy access to medical assistance and oxygen therapy in case of an adverse event.
- Inform the patient of therapeutic indication of medicine as detailed in current Patient Information Leaflet (PIL), available on eMC website[1], IFU or local patient information leaflets available for 'off-label' use nebulisers.
- Inform patient of the most commonly reported potential adverse effects of medicine as detailed in PIL, IFU or local patient information leaflets. Depending on the medicine being assessed, there may be a number of additional less commonly reported side effects. Inform patient that this is the case.
- Gain patient's informed verbal consent to undergo DRA. If patient unable to give informed verbal consent due to lack of mental capacity, it may still be appropriate for them to undergo DRA, if it is considered to be in their best interests. In this situation, the patient's carer is required to take on the responsibility of undergoing training for administration of the medicine in the community.
- Obtain all equipment, paperwork (including prescription, which must be present at point of medicine administration) and medicine/ constituents that will be required during DRA.

Pre-trial objective assessment

- Peripheral oxygen saturations (SpO_2) should be measured.
- Spirometry should be performed by a competent practitioner, eg respiratory technician or physiotherapist. The American Thoracic Society/European Respiratory Society criteria for acceptable repeatability of spirometry readings[2] should be adhered to during the DRA and all subsequent medicine follow-ups.
- If the patient is unable to perform spirometry, auscultation pre and post DRA can be used to detect wheeze/bronchospasm alongside SpO_2.
- Auscultate in order to identify any retained secretions or wheeze.
- For DRAs of Bronchitol®, the Bronchitol® Initiation Dose Assessment (BIDA)[3] should be followed and the form completed. This determines when spirometry and SpO_2 should be measured in relation to the inhalation of increasing doses of Bronchitol®.

Pre-DRA bronchodilator

- The patient should administer their usual short-acting inhaled or nebulised bronchodilator, to reduce risk of bronchospasm. If not prescribed a short-acting bronchodilator, liaise with a CF consultant, specialist respiratory registrar or competent physiotherapist NMP regarding whether prescription of such medicine may be appropriate.
- Wait appropriate length of time for bronchodilator medicine to take effect (if applicable) ie 20 minutes following $Beta_2$ agonist bronchodilator, eg salbutamol, 45 minutes following antimuscarinic bronchodilator, eg ipratropium bromide.

Administration of DRA medicine by physiotherapist

- Normally the prescriber should not also administer the medication unless their local Trust policy allows it. If permitted then there needs to be a clear rational (for example to ensure that the pathway for patient care does not build in unnecessary extra steps/ processes), a thorough risk assessment and there should also be a process in place to limit errors (for example the prescription should be checked by a person who usually administers medicines (nurse/pharmacist/ physiotherapist) prior to administration).

- Remain with the patient throughout the entire DRA procedure to optimise patient safety.
- Make a positive identification of the patient by confirming demographic details and PID, to ensure that medicine is administered to the correct patient.
- Check the prescription as follows: patient's full name; date of birth; allergies, ward; consultant; drug approved name; correct dose; route; prescriber's signature; date of prescription; special instructions.
- Use personal protective equipment as appropriate and standard infection control precautions throughout the procedure, eg decontaminate hands appropriately and advise patient to do likewise before medicine/constituents handled/prepared.
- Check the medicine prior to administration as follows: dose being administered; expiry dates of medicine/constituents.
- During administration of DRA medicine, follow SPC, IFU or local patient information leaflets as appropriate with regards to:
  - preparation of DRA medicine, eg mixing of nebuliser solution;
  - correct operation of inhaler/nebuliser device in accordance with manufacturer's instructions; and
  - recommended procedure for inhalation of medicine.
- If preparation of medicine requires mixing of powder with a solvent, ie Colomycin®, Promixin®, Cayston® amikacin or Meropenem the physiotherapist should demonstrate the procedure. The patient or carer can then be observed performing this by the physiotherapist to assess their ability to do this accurately and safely if required.
- The physiotherapist should also assess the patient's ability to inhale the medicine using the correct procedure.
- Physiotherapist should sign the prescription to indicate the time at which the medicine is administered. If a physiotherapist NMP is performing the DRA but has prescribed the medicine it is not recommended they administer it. In this instance, a different CF physiotherapist, an NMC registered CF CNS or ward nurse (band 5 or above) would be responsible for the medicines administration component and the demonstration and assessment of medicine preparation (if applicable), as above.
- If an adverse effect occurs during the DRA, inhalation should be ceased and a physician informed, if appropriate (dependent on severity). If a severe adverse effect occurs, medical assistance should be summoned immediately and appropriate treatment provided.

Following DRA

- Ask patient to describe any adverse effect(s) experienced and rate the severity using a numerical recognition scale (NRS) from 0-10, where '10' is the worst adverse effect imaginable. The severity of any adverse effects may determine whether or not a trial period of medicine is undertaken. If a severe adverse effect occurs or if an adverse effect not stated in the SPC occurs, it should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) 'Yellow Card Scheme, in a timely manner.
- **For DRAs of Bronchitol®:**
  - As discussed previously, the Bronchitol® Initiation Dose Assessment (BIDA)[3] should be followed and the form completed. This determines when spirometry (performed by a competent practitioner) and SpO_2 should be measured in relation to the inhalation of increasing doses of Bronchitol®.
- **For DRAs of other medicines:**
  - Spirometry (performed by a competent practitioner) should be completed 5 minutes following end of inhalation (to assess for medicine-induced bronchospasm), SpO_2 measured and auscultation completed.
  - Assess for the presence of any constriction using following calculation:

$$\%\text{Constriction} = \left(\frac{\text{pre-DRA } FEV_1 - \text{post-DRA } FEV_1}{\text{Pre-DRA } FEV_1} \right) \times 100$$

Passed DRA

- If constriction is 10% or less this is a pass and the medicine is suitable for use.
- If constriction is 11-15% but the patient is asymptomatic this is a pass and the medicine is suitable for further use.

Failed DRA

- If constriction is 11-15% and the patient is symptomatic or constriction is >15% this is a fail and the medicine should not be continued.
- Ensure these findings are due to bronchospasm rather than loosened and retained sputum. If this is thought to be the case encourage airway clearance and consider repeat spirometry.
- Allow a further 10 minutes observed recovery time and repeat spirometry. If >15% constriction continues give a post DRA bronchodilator to reverse bronchospasm, allow a further 10 minutes observed recovery time and repeat spirometry.
- Once constriction has recovered to 10% or less and the patient is not symptomatic monitoring can be stopped and the patient is safe to leave.
- If constriction remains >10% persistently seek urgent medical review and continue to monitor the patient closely.

If DRA failed

- Consider repeat DRA at a later date (ie, repeat DRA when the patient is well if it is identified that the patient was unwell and this is the possible cause of failed DRA).
- Consider for alternate medicine DRA.
- If you are unsure how to proceed escalate to a CF consultant/discuss with the CF specialist team.

Information provided for patients continuing with trial period of medicine

Physiotherapist to provide information detailed in PIL, IFU or local patient information leaflets for patient on the following:

1. Preparation of medicine, eg mixing of nebuliser solution.
2. Correct operation of inhaler/nebuliser device in accordance with manufacturer's instructions.
3. Recommended procedure for inhalation of medicine.
4. Daily dose schedule and recommended interval between doses, as stated in PIL, IFU or local patient information leaflets. If there is no documented recommended interval between doses, for twice daily medicine, the locally agreed recommendation is ideally 10-12 hours (but a minimum of 8 hours) between doses.
5. Optimum timing of medicine in relation to other prescribed inhaled/nebulised medicine and airway clearance. In general, this would be as follows:
   a. **short-acting inhaled/nebulised bronchodilator**
   b. **inhaled/nebulised mucolytic/osmotic agent** prior to airway clearance technique (ACT). In the case of dornase alfa however, current evidence[4] indicates that benefit is not affected by its timing with regards to time of day used or ACT, ie inhalation following ACT is no more or less effective than the traditional recommendation of inhaling it 30 minutes prior to ACT. Therefore, in the absence of strong evidence to suggest that one timing regimen is superior to another, the timing of dornase alfa inhalation can be largely based on practical or individual preference with respect to the above. However, if nebulised prior to ACT we recommend at least a 30-minute interval between the end of inhalation and the commencement of ACT based on evidence that dornase alfa makes CF sputum pourable within this time frame.[5,6]
   c. **inhaled/nebulised antibiotic** following ACT. These should also be taken within active period of preceding short-acting bronchodilator, eg no longer than 4 hours following salbutamol or ipratropium bromide. Consideration should be given to potential interaction between inhaled antibiotics and dornase alfa as this may lead to dornase alfa inactivity.
   d. **inhaled/nebulised steroid** following ACT.
6. Before use, all medicine and its constituents, eg water for injections ampoules, should be checked to ensure that correct dose is being administered and expiry date has not been exceeded.

7. If a dose of medicine is missed/forgotten, what action to take, if any.

8. If too much medicine is taken or if it is swallowed accidentally, the patient should seek advice from their medical team as soon as possible during normal working hours or GP/local accident and emergency department out of hours.

9. If any adverse effect(s) occur during trial period, the patient should cease medicine use and medical advice should be sought as above. If the patient ceases the medicine for any other reason, medical advice should also be sought, as this may lead to worsening chest symptoms.

10. If, during the trial period, a new situation regarding precautions of taking the medicine arises, eg patient becomes pregnant or they have been commenced on a new medicine that should not be taken in conjunction with trial medicine, they should inform the CF team. In this situation, a CF consultant, specialist respiratory registrar or competent physiotherapist NMP should assess risk/benefit of the individual continuing with the trial medicine.

11. Manufacturer's instructions for the care of (including cleaning and sterilisation, if appropriate) the inhaler/nebuliser device and related consumables should be followed.

12. If required for nebulisation (see local guidance), filter pads used within PARI Filter/Valve Sets should be discarded and replaced following each dose.

13. Appropriate storage of medicine/constituents.

14. Safe disposal of empty packaging and administration equipment, eg capsule cards, glass ampoules, inhaler devices, components of nebuliser chambers in the community (see Table 1 below for locally agreed guidance at the West Midlands Adult CF Centre). Advice should include time after which administration devices should be discarded, eg TOBI® Podhaler® devices should be discarded after 7 days.

Table 1

Component/constituent for disposal	Safe disposal in community
Residual unwanted medicine, eg residual volume in eFlow®rapid handset	Sharps box
Residual unwanted diluents, eg water for injections/0.9% sodium chloride solution in open ampoule	Pour down sink
Empty plastic ampoules	Domestic waste
Empty glass ampoules	Sharps box
Used syringes	Domestic waste
Inhaler devices (Bronchitol®, Colobreathe®, TOBI Podhaler®)	Domestic waste
Empty capsules and capsule cards (inhaled medicines)	Domestic waste
Any unused medicine or its constituents (opened or unopened) that are unwanted, eg due to intolerance/exceeding expiry date	Return to community or hospital pharmacy
eFlow®rapid and PARI TurboBOY®: plastic components of nebuliser chambers, eFlow®rapid aerosol heads, PARI TurboBOY® connection tubing	Return to hospital for clinical waste disposal

eFlow®rapid and PARI TurboBOY®: live parts of nebuliser devices, eg air compressor/control unit, power adaptors, grey eFlow®rapid nebuliser connection cord	Return to PARI Medical Ltd or to hospital for electrical waste disposal
I-neb®: mouthpiece, discs, medicine chamber and lid, drug guide and washing basket	Domestic waste
I-neb®: I-neb body (control unit), power cord and battery charger	Patient to return to Philips Respironics

15. Any medicine-specific instructions/ precautions stated in PIL, IFU or local patient information leaflets not already covered above, eg:

a. if medicine should only be inhaled using the administration device(s) and related consumables recommended by the medicine manufacturers and if stipulated, no other medicine should be inhaled via a device/consumable designed for a specific medicine, eg Cayston® should only be administered via an eFlow®rapid using an Altera® handset and no other nebulised drug should be administered using this handset;

b. if the medicine should not be mixed with any other medicinal product in a nebuliser chamber, eg dornase alfa;

c. whether the appearance of the medicine may vary, eg Bramitob® is normally a slightly yellow colour but some variations in colour might be observed, despite being stored as recommended;

d. the appropriate discarding of any opened but unused medicine/ constituent, eg

- only 1ml of 2.5ml dornase alfa ampoule is required for one dose within the I-neb® device and the remaining 1.5ml should be discarded. Opened ampoules of any medicine should never be stored for re-use
- there will always be a residual volume of medicine in a regular eFlow®rapid handset, at the end of inhalation which should be discarded

e. In the event of haemoptysis, cease dornase alfa and seek appropriate medical assistance/advice. Re-start 48 hours following last episode, unless otherwise instructed;

f. As far as is feasible, nebulised antibiotics should be inhaled in a well-ventilated room, away from other people. This may not be possible however if a patient's carer is required to supervise the patient during nebulisation;

g. If a mixed, refrigerated, second dose of meropenem has changed significantly in colour from when it was first mixed, it should NOT be used. Second doses MUST be used within 12 hours of original mixing.

Completion of DRA

- Ensure that patient has returned to pre-DRA level of wellness, if they experienced any adverse effects during DRA, before they leave hospital (if an outpatient) or before being left unsupervised (if an inpatient).
- If patient in agreement with trialling medicine following a passed DRA, arrangements should be made to supply sufficient medicine for duration of trial period. For most medicine there is 1 month trial period (6 weeks for Bronchitol®). However, antibiotics being used for attempted pathogen eradication may be prescribed for up to 3 months.

Documentation of DRA details

- The following information should be recorded on the **'CF physiotherapy drug response assessment (DRA) proforma'** which should be inserted into patient's medical records, according to the date of the DRA: all objective measurements, eg spirometry results, SpO_2, auscultation; the ability of patient/carer to prepare nebuliser solutions which require mixing (if applicable); the ability of patient to use inhaler/nebuliser device correctly;

the ability of patient to follow recommended procedure for inhalation; subjective data, eg patient-reported adverse effects; education provided relating to new medicine.

- Completed BIDA forms used for DRAs of Bronchitol® should be attached to (and filed with) completed **'CF physiotherapy drug response assessment (DRA) proforma'**
- Document in patent's main clinical record that DRA of medicine has been performed (and for details of this, refer to **'CF physiotherapy drug response assessment (DRA) proforma'**) and the outcome, eg for 1 month follow-up of medicine, patient not to continue with medicine.
- File any paper recording sheets in patient's medical records as per local policy.

Medicine follow-up

1 month/6 week follow-up
The use of all new inhaled/nebulised medicine should be reviewed following a trial period of 1 month (with the exception of Bronchitol®, in which a 6 week follow-up is undertaken). This review will be completed by qualified HCPC registered physiotherapists working within the CF centre who are competent to perform DRAs of medicine.

- Ask patient to describe any adverse effect(s) experienced and rate the severity using a numerical recognition scale from 0-10, where '10' is the worst adverse effect imaginable. The severity of any adverse effects may determine whether or not medicine is continued on a long-term basis.
- Spirometry should be performed by a competent practitioner and SpO_2 measured.
- Discuss with patient and CF consultant, specialist respiratory registrar or competent physiotherapist NMP, as appropriate, regarding potential continuation of medicine based on the above.
- Record all objective data, eg spirometry results, SpO_2 and subjective data relevant to 1 month/6 week follow-up on the **'CF physiotherapy inhaler/nebuliser follow-up record'**.
- Assess patient's understanding of new medicine and whether they continue to use/store it etc. appropriately. Record any education/advice provided at 1 month/6 week follow-up on the **'CF physiotherapy inhaler/ nebuliser follow-up record'**.
- Insert **'CF physiotherapy inhaler/nebuliser follow-up record'** into patient's medical records, alongside **'CF physiotherapy drug response assessment (DRA) proforma'**.

If patient to continue with medicine following 1 month/6 week follow-up

a. Advise patient if medicine to be taken continuously on a daily basis or on an on/off alternating month basis. If it is to be taken on an alternating month basis, ensure patient is aware of what medicine, if any, should be taken in the new medicine 'off' month (this should be agreed with a CF consultant, specialist respiratory registrar or competent physiotherapist NMP).

b. Contact pharmacist regarding completion of 1 month/6 week pharmacy medicine follow-up, as appropriate. They will provide patient with information on obtaining future supplies of medicine, if required.

6 month follow-up
The use of all new inhaled/nebulised medicine should be reviewed following a period of 6 months. This review will be completed by qualified HCPC registered physiotherapists working within the CF centre.

This should be performed as described in '1 month/6 week follow-up' with 6 month data/information.

If patient to continue with medicine long-term following 6 month follow-up

a. Contact pharmacist regarding completion of 6 month pharmacy medicine follow-up.

4. Responsibilities and roles

It is the responsibility of each physiotherapist who has been assessed as competent to perform DRAs and reviews of inhaled/nebulised medicine to ensure that they are familiar with:

- the contents of this SOP and adhere to it when performing DRAs; and
- the most up-to-date SPC, IFU and local patient information leaflets relating to specific medicines.

It is also the responsibility of each CF CNS and ward nurse, should they be required to perform the administration/training component of the DRA (to avoid a physio NMP prescribing the medicine and then administering it), to be familiar with the above.

5. Training requirements

Qualified HCPC registered physiotherapists who are undergoing competency training for performing DRAs of inhaled and nebulised medicine should:

- have worked within the CF centre, consistently for a minimum of 1 year;
- be Band 6 or above;
- familiarise themselves with the contents of this SOP;
- familiarise themselves with the contents of most up-to-date SPC, IFU and local patient information leaflets relating to specific medicines;
- undergo appropriate electronic prescribing training (for administration rights);
- have completed the appropriate local medicines management training modules (please refer to local policy);
- receive education from CF specialist pharmacist; and
- undergo assessment of knowledge/ understanding of all medicines that will be administered by DRA competent physiotherapist or specialist nurse.

In order to establish competence, the physiotherapist will undergo assessment by a qualified nurse assessor in which they must:

- demonstrate the ability to prepare all medicines which require mixing used at the center, ie nebulised Colomycin®, Promixin®, Cayston®, meropenem and amikacin; and
- complete a final competency assessment, in which they are observed performing an entire DRA of 2 inhaled (i.e. TOBI Podhaler®, Colobreathe® or Bronchitol®) and 2 nebulised medicines and are assessed against required standards.

Please see **'Example of medicine administration competency SOP' and 'Example of competency assessment document'**

References

1 https://www.medicines.org.uk/emc/

2 ATS/ERS (2005) ATS/ERS Series: Standardisation of lung function testing. European Respiratory Journal. Volume 26, pages 319-338.

3 Pharmaxis (August 2014) Bronchitol Initiation Dose Assessment.

4 Dentice R, Elkins M. Timing of dornase alfa inhalation for cystic fibrosis. Cochrane Database of Systematic Reviews 2011, Issue 5. Art. No.: CD007923. DOI: 10.1002/14651858. CD007923.pub2.

5 Shak S, Capon DJ, Hellmiss R, Marsters SA. Recombinant human DNase I reduces the viscosity of cystic fibrosis sputum. Proceedings of the National Academy of Sciences USA 1990;87(23):9188-92 as cited in Reference 3 above.

6 Conway SP, Littlewood JM (1997) rhDNase in cystic fibrosis. British Journal of Hospital Medicine. Vol 57, no. 8, pages 371-372.

Related appendices

- Nebulised/inhaled medications for people with cystic fibrosis overview
- CF physiotherapy drug response assessment (DRA) proforma
- CF physiotherapy inhaler/nebuliser follow-up record
- Example of medicine administration competency SOP
- Example of competency assessment document

With thanks to S. Cameron,

Edited for ACPCF NMP Group by
C. Brown Jan 2020.
West Midlands Regional Adult Cystic Fibrosis (CF) Centre, University Hospitals Birmingham (UHB) NHS Foundation Trust.

Appendix IVb

ACPCF NMP
ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN CF
NON-MEDICAL PRESCRIBERS GROUP

Example of SOP for the performance of Drug Response Assessments (DRAs) in the time of COVID-19

Information related to COVID-19 is in blue

1. Scope

We are aware that during the COVID-19 pandemic across the UK DRAs in our cohort were frequently delayed and/or performed in very different circumstances. Our aim was to come together as the ACPCF non-medical prescribing group to create a consensus document for best DRA practice moving forward in the time of COVID-19. We will continue to evaluate this document and any updates, if required promptly, will be circulated via the ACPCF and Regional representatives.

This SOP has been developed for use by qualified HCPC registered physiotherapists working within a CF centre who have been assessed as competent to perform drug response assessments (DRAs) (including medicine administration component) and review use of inhaled and nebulised medicine.

2. Aims and objectives

The aims of this SOP are as follows:

- to standardise the procedure for the performance of DRAs and follow-up of new inhaled/nebulised medicine and the information provided to patients/carers, to minimise the risk of patient-related adverse events;
- to give the responsibility of performing the entire DRA procedure, including medicine administration component, to one competent individual. This will avoid parts of the procedure being missed accidentally and minimise the risks to patient safety; and
- to streamline the process of performing DRAs, to improve clinical efficiency.

NB - within this and associated documents the word 'patient' refers to the person with CF, it also applies to the carer of a patient, if the patient does not have mental capacity/requires assistance and/or supervision with medicines' administration.

3. Standards

Procedure for DRA under physiotherapist supervision

Preparation for DRA

- Ensure that medicine is therapeutically indicated as detailed in current Summary of Product Characteristics (SPC), available on the electronic Medicines Compendium (eMC) website.[1] In the case of nebulised 7% and 3% hypertonic saline, which are classed as medical devices, please refer to current Instructions for Use (IFU). If medicine is to be used outside of stated therapeutic indications or if dose recommended is not the standard adult dose, a CF consultant, or competent physiotherapist non-medical prescriber (NMP) must have approved use and documented this in the medical notes. Note that amikacin, amphotericin, ceftazadime, meropenem, tauroldine solution and vancomycin are used 'off-label' when nebulised, so there is no nebulisation-specific information in the SPC for these medicines. It is recommended local patient information leaflets are produced for these 'off-label' inhaled medications.
- Ensure that there are no known contraindications to medicine use as detailed in SPC, IFU or local patient information leaflets and that the patient is not known to have an allergy to it. If any contraindications or allergies to the medicine are identified, this must be discussed with a CF consultant prior to DRA and an appropriate plan must be made to

minimise any risks to the patient if the DRA is considered to be the best course of action. This should be documented by the CF consultant in the medical notes.

- Ensure that the following have been considered with the patient in relation to their circumstances, in conjunction with a CF consultant, specialist respiratory registrar or competent physiotherapist NMP and a decision has been made to proceed with DRA; special warnings and precautions of use; interaction with other medicinal products and other forms of interaction; fertility, pregnancy and lactation; effects on ability to drive and use machines as detailed in SPC IFU or local patient information leaflets.
- The DRA medicine should be prescribed by a physician or competent physiotherapist NMP as a STAT dose. For details of correct/ advised medicine prescriptions see the appendices 'Nebulised/inhaled medications for people with cystic fibrosis overview'.
- Drug and food allergies should be recorded as locally advised by the prescriber but should be checked with the patient by the physiotherapist (and added to if required) prior to administration of DRA medicine.
- DRAs should be performed in rooms with easy access to medical assistance and oxygen therapy in case of an adverse event.
- Inform the patient of therapeutic indication of medicine as detailed in current Patient Information Leaflet (PIL), available on eMC website[1], IFU or local patient information leaflets available for 'off-label' use nebulisers.

Location of DRA

- DRAs should be routinely performed in hospital in a single-patient room with easy access to medical assistance and oxygen therapy in case of an adverse event.
- It is recommended that an in-hospital DRA is performed for any inhaled or nebulised drug that the patient is naïve to OR if a patient has not taken the drug for >12 months or there has been a significant change in the patient's condition since they last took a dose.
- 'Virtual' or home DRAs could be considered in the following circumstances, only if the CF specialist team are all in agreement (including CF specialist physiotherapist, consultant and pharmacist);
  - >12 months since last test dose of trial drug;
  - no adverse events associated with using the drug previously;
  - no significant change in clinical condition since last taken.
- NB there may be situations outside of this stated where the MDT considers a 'virtual' or home DRA the safest option. Please note that all 'virtual' or home DRAs are considered 'at risk' and a thorough multidisciplinary risk assessment should be undertaken prior to deciding on this course of action. Risk assessment should consider the following:
  - lung function of patient;
  - DRA history;
  - if they failed/passed DRAs in the past;
  - if/when they failed, why they failed; and
  - if they are considered 'atopic'.

  This process and the team members involved should be documented in the notes.
- Prior to deciding on a 'virtual' or home DRA, consider alternatives to home that would allow access to appropriate medical staff and equipment. For example, a safe place within the hospital grounds, or a safe place in the community such as a clinic or GP surgery.

Prior to in-hospital DRAs

- Follow local guidance to assess patient's COVID-19 status prior to DRA (this may include calling the patient the day before the DRA to complete a COVID-19 symptom assessment, and some trusts will require a negative COVID-19 swab prior to out-patient attendance). If assessment results suggest COVID-19, discuss with CF MDT and consider, as required, delaying DRA, or alternative assessment and treatments.
- Inform the patient of your local trust outpatient appointment infection control policy (ie to attend alone or how many parent/guardians can attend, use of alcohol gel on entry to hospital and

again on entry to the clinical area, wearing a mask/face covering while walking through the hospital etc.)

- Advise patient to bring in their own home spirometer.
- On arrival to the clinical area the patient should be shown immediately to their single-patient room. Ideally a window will be kept open and the door will be closed throughout the DRA process.

Pre DRA, face-to-face with patient (prior to aerosol generating procedure (AGP) component)

- As this step of the DRA is prior to the AGP component it could be completed in 'Level 1 PPE' rather than 'Level 2 PPE' if preferred (for 'Level 1 PPE' follow local and national guidelines for non-AGP face-to-face patient contact).

- Inform patient of the most commonly reported potential adverse effects of medicine as detailed in PIL, IFU or local patient information leaflets. Depending on the medicine being assessed, there may be a number of additional less commonly reported side effects. Inform patient that this is the case.
- Gain patient's informed verbal consent to undergo DRA. If patient unable to give informed verbal consent due to lack of mental capacity, it may still be appropriate for them to undergo DRA, if it is considered to be in their best interests. In this situation, the patient's carer is required to take on the responsibility of undergoing training for administration of the medicine in the community.
- Obtain all equipment, paperwork (including prescription, which must be present at point of medicine administration) and medicine/constituents that will be required during DRA.

Pre-trial objective assessment

- We advise spirometry should be considered an AGP. Additionally, many of the drugs taken in a DRA stimulate a strong, often productive cough in our cohort. We therefore recommend the physiotherapist should wear 'Level 2 PPE' for the DRA (for 'Level 2' PPE follow local and national guidelines for PPE during AGPs)*
- A sign should be attached to the outside of the room to inform anyone entering to enter only if in 'Level 2 PPE'*

  ***unless patient is unable to perform spirometry and DRA is for a drug which is not expected to stimulate a productive cough, in these circumstances we advise 'Level 1 PPE' for non-AGP face-to-face contact may be sufficient but should be assessed according to the national and local guidelines.**

- It is recommended that the physiotherapist is not directly in front of the patient while completing spirometry and where possible maintains a 2-metre distance from the patient both during spirometry and for the duration of the DRA.

- Peripheral oxygen saturations (SpO_2) should be measured.
- Spirometry should be performed by a competent practitioner, eg respiratory technician or physiotherapist. The American Thoracic Society/European Respiratory Society criteria for acceptable repeatability of spirometry readings[2] should be adhered to during the DRA and all subsequent medicine follow-ups.
- If the patient is unable to perform spirometry, auscultation pre and post DRA can be used to detect wheeze/bronchospasm alongside SpO_2.
- Auscultate in order to identify any retained secretions or wheeze.
- For DRAs of Bronchitol®, the Bronchitol® Initiation Dose Assessment (BIDA)[3] should be followed and the form completed. This determines when spirometry and SpO_2 should be measured in relation to the inhalation of increasing doses of Bronchitol®.

Pre-DRA bronchodilator

- The patient should administer their usual short-acting inhaled or nebulised bronchodilator, to reduce risk of bronchospasm. If not prescribed a short-acting bronchodilator, liaise with a CF consultant, specialist respiratory registrar or competent physiotherapist NMP regarding whether prescription of such medicine may be appropriate.
- Wait appropriate length of time for bronchodilator medicine to take effect (if

applicable) ie 20 minutes following $Beta_2$ agonist bronchodilator, eg salbutamol, 45 minutes following antimuscarinic bronchodilator, eg ipratropium bromide.

Administration of DRA medicine by physiotherapist

- Normally the prescriber should not also administer the medication unless their local Trust policy allows it. If permitted then there needs to be a clear rational (for example to ensure that the pathway for patient care does not build in unnecessary extra steps/processes), a thorough risk assessment and there should also be a process in place to limit errors (for example the prescription should be checked by a person who usually administers medicines (nurse/pharmacist/physiotherapist) prior to administration).
- Remain with the patient throughout the entire DRA procedure to optimise patient safety.
- Make a positive identification of the patient by confirming demographic details and PID, to ensure that medicine is administered to the correct patient.
- Check the prescription as follows:
  - patient's full name
  - date of birth
  - allergies
  - ward
  - consultant
  - drug approved name
  - correct dose
  - route
  - prescriber's signature
  - date of prescription
  - special instructions.

- Use appropriate infection control precautions throughout the procedure in line with local and national guidelines, eg remove gloves, decontaminate hands and replace gloves as required and advise patient to decontaminate hands before medicine/constituents handled/prepared.

- Check the medicine prior to administration as follows: dose being administered; expiry dates of medicine/constituents.
- During administration of DRA medicine, follow SPC, IFU or local patient information leaflets as appropriate with regards to:
  - preparation of DRA medicine, eg mixing of nebuliser solution;
  - correct operation of inhaler/nebuliser device in accordance with manufacturer's instructions; and
  - recommended procedure for inhalation of medicine.
- If preparation of medicine requires mixing of powder with a solvent, ie Colomycin®, Promixin®, Cayston® amikacin or Meropenem the physiotherapist should demonstrate the procedure. The patient or carer can then be observed performing this by the physiotherapist to assess their ability to do this accurately and safely if required.
- The physiotherapist should also assess the patient's ability to inhale the medicine using the correct procedure.
- Physiotherapist should sign the prescription to indicate the time at which the medicine is administered. If a physiotherapist NMP is performing the DRA but has prescribed the medicine it is not recommended they administer it. In this instance, a different CF physiotherapist, an NMC registered CF CNS or ward nurse (band 5 or above) would be responsible for the medicines administration component and the demonstration and assessment of medicine preparation (if applicable), as above

(in 'Level 2 PPE' if pre-DRA spirometry has been performed).

- If an adverse effect occurs during the DRA, inhalation should be ceased and a physician informed, if appropriate (dependent on severity). If a severe adverse effect occurs, medical assistance should be summoned immediately and appropriate treatment provided.

Following DRA

- Ask patient to describe any adverse effect(s) experienced and rate the severity using a numerical recognition scale (NRS) from 0-10, where '10' is the worst adverse effect imaginable. The severity of any adverse effects may determine whether or not a trial period of medicine is undertaken. If a severe adverse effect occurs or if an adverse effect not stated in the SPC occurs, it should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) 'Yellow Card Scheme, in a timely manner.

- **For DRAs of Bronchitol®:**
  - As discussed previously, the Bronchitol® Initiation Dose Assessment (BIDA)[3] should be followed and the form completed. This determines when spirometry (performed by a competent practitioner) and SpO_2 should be measured in relation to the inhalation of increasing doses of Bronchitol®
- **For DRAs of other medicines:**
  - Spirometry (performed by a competent practitioner) should be completed 5 minutes following end of inhalation (to assess for medicine-induced bronchospasm), SpO_2 measured and auscultation completed.
  - Assess for the presence of any constriction using following calculation:

$$\%\text{Constriction} = \left(\frac{\text{pre-DRA } FEV_1 - \text{post-DRA } FEV_1}{\text{Pre-DRA } FEV_1} \right) \times 100$$

Passed DRA

- If constriction is 10% or less this is a pass and the medicine is suitable for use.
- If constriction is 11-15% but the patient is asymptomatic this is a pass and the medicine is suitable for further use.

Failed DRA

- If constriction is 11-15% and the patient is symptomatic or constriction is >15% this is a fail and the medicine should not be continued.
- Ensure these findings are due to bronchospasm rather than loosened and retained sputum. If this is thought to be the case encourage airway clearance and consider repeat spirometry.
- Allow a further 10 minutes observed recovery time and repeat spirometry. If >15% constriction continues give a post DRA bronchodilator to reverse bronchospasm, allow a further 10 minutes observed recovery time and repeat spirometry.
- Once constriction has recovered to 10% or less and the patient is not symptomatic monitoring can be stopped and the patient is safe to leave.
- If constriction remains >10% persistently seek urgent medical review and continue to monitor the patient closely.

If DRA failed

- Consider repeat DRA at a later date (ie, repeat DRA when the patient is well if it is identified that the patient was unwell and this is the possible cause of failed DRA).
- Consider for alternate medicine DRA.
- If you are unsure how to proceed escalate to a CF consultant/discuss with the CF specialist team.

Information provided for patients continuing with trial period of medicine

Physiotherapist to provide information detailed in PIL, IFU or local patient information leaflets for patient on the following:

1. Preparation of medicine, eg mixing of nebuliser solution.
2. Correct operation of inhaler/nebuliser device in accordance with manufacturer's instructions.
3. Recommended procedure for inhalation of medicine.
4. Daily dose schedule and recommended interval between doses, as stated in PIL, IFU or local patient information leaflets. If there is no documented recommended interval between doses, for twice daily medicine, the locally agreed recommendation is ideally 10-12 hours (but a minimum of 8 hours) between doses.
5. Optimum timing of medicine in relation to other prescribed inhaled/nebulised medicine and airway clearance. In general, this would be as follows:
    a. **short-acting inhaled/nebulised bronchodilator**
    b. **inhaled/nebulised mucolytic/osmotic agent** prior to airway clearance technique (ACT). In the case of dornase alfa however, current evidence[4] indicates that benefit is not affected by its timing with regards to time of day used or ACT, ie inhalation following ACT is no more or less effective than the traditional recommendation of inhaling it 30 minutes prior to ACT. Therefore, in the absence of strong evidence to suggest that one timing regimen is superior to another, the timing of dornase alfa inhalation can be largely based on practical or individual preference with respect to the above. However, if nebulised prior to ACT we recommend at least a 30-minute interval between the end of inhalation and the commencement of ACT based on evidence that dornase alfa makes CF sputum pourable within this time frame.[5,6]
    c. **inhaled/nebulised antibiotic** following ACT. These should also be taken within active period of preceding short-acting bronchodilator, eg no longer than 4 hours following salbutamol or ipratropium bromide. Consideration should be given to potential interaction between inhaled antibiotics and dornase alfa as this may lead to dornase alfa inactivity.
    d. **inhaled/nebulised steroid** following ACT.
6. Before use, all medicine and its constituents, eg water for injections ampoules, should be checked to ensure that correct dose is being administered and expiry date has not been exceeded.
7. If a dose of medicine is missed/forgotten, what action to take, if any.
8. If too much medicine is taken or if it is swallowed accidentally, the patient should seek advice from their medical team as soon as possible during normal working hours or GP/local accident and emergency department out of hours.
9. If any adverse effect(s) occur during trial period, the patient should cease medicine use and medical advice should be sought as above. If the patient ceases the medicine for any other reason, medical advice should also be sought, as this may lead to worsening chest symptoms.
10. If, during the trial period, a new situation regarding precautions of taking the medicine arises, eg patient becomes pregnant or they have been commenced on a new medicine that should not be taken in conjunction with trial medicine, they should inform the CF team. In this situation, a CF consultant, specialist respiratory registrar or competent physiotherapist NMP should assess risk/benefit of the individual continuing with the trial medicine.

11. Manufacturer's instructions for the care of (including cleaning and sterilisation, if appropriate) the inhaler/nebuliser device and related consumables should be followed.

12. If required for nebulisation (see local guidance), filter pads used within PARI Filter/ Valve Sets should be discarded and replaced following each dose.

13. Appropriate storage of medicine/constituents.

14. Safe disposal of empty packaging and administration equipment, eg capsule cards, glass ampoules, inhaler devices, components of nebuliser chambers in the community (see Table 1 below for locally agreed guidance at the West Midlands Adult CF Centre). Advice should include time after which administration devices should be discarded, eg TOBI® Podhaler® devices should be discarded after 7 days.

Table 1

Component/constituent for disposal	Safe disposal in community
Residual unwanted medicine, eg residual volume in eFlow®rapid handset	Sharps box
Residual unwanted diluents, eg water for injections/0.9% sodium chloride solution in open ampoule	Pour down sink
Empty plastic ampoules	Domestic waste
Empty glass ampoules	Sharps box
Used syringes	Domestic waste
Inhaler devices (Bronchitol®, Colobreathe®, TOBI Podhaler®)	Domestic waste
Empty capsules and capsule cards (inhaled medicines)	Domestic waste
Any unused medicine or its constituents (opened or unopened) that are unwanted, eg due to intolerance/exceeding expiry date	Return to community or hospital pharmacy
eFlow®rapid and PARI TurboBOY®: plastic components of nebuliser chambers, eFlow®rapid aerosol heads, PARI TurboBOY® connection tubing	Return to hospital for clinical waste disposal
eFlow®rapid and PARI TurboBOY®: live parts of nebuliser devices, eg air compressor/control unit, power adaptors, grey eFlow®rapid nebuliser connection cord	Return to PARI Medical Ltd or to hospital for electrical waste disposal
I-neb®: mouthpiece, discs, medicine chamber and lid, drug guide and washing basket	Domestic waste
I-neb®: I-neb body (control unit), power cord and battery charger	Patient to return to Philips Respironics

15. Any medicine-specific instructions/ precautions stated in PIL, IFU or local patient information leaflets not already covered above, eg:

a. if medicine should only be inhaled using the administration device(s) and related consumables recommended by the medicine manufacturers and if stipulated, no other medicine should be inhaled via a device/consumable designed for a specific medicine, eg Cayston® should only be administered via an eFlow®rapid using an Altera® handset and no other nebulised drug should be administered using this handset;

b. if the medicine should not be mixed with any other medicinal product in a nebuliser chamber, eg dornase alfa;

c. whether the appearance of the medicine may vary, eg Bramitob® is normally a slightly yellow colour but some variations in colour might be observed, despite being stored as recommended;

d. the appropriate discarding of any opened but unused medicine/ constituent, eg

- only 1ml of 2.5ml dornase alfa ampoule is required for one dose within the I-neb® device and the remaining 1.5ml should be discarded. Opened ampoules of any medicine should never be stored for re-use
- there will always be a residual volume of medicine in a regular eFlow®rapid handset, at the end of inhalation which should be discarded

e. In the event of haemoptysis, cease dornase alfa and seek appropriate medical assistance/advice. Re-start 48 hours following last episode, unless otherwise instructed;

f. As far as is feasible, nebulised antibiotics should be inhaled in a well-ventilated room, away from other people. This may not be possible however if a patient's carer is required to supervise the patient during nebulisation;

g. If a mixed, refrigerated, second dose of meropenem has changed significantly in colour from when it was first mixed, it should NOT be used. Second doses MUST be used within 12 hours of original mixing.

Completion of DRA

- Ensure that patient has returned to pre-DRA level of wellness, if they experienced any adverse effects during DRA, before they leave hospital (if an outpatient) or before being left unsupervised (if an inpatient).
- If patient in agreement with trialling medicine following a passed DRA, arrangements should be made to supply sufficient medicine for duration of trial period. For most medicine there is 1 month trial period (6 weeks for Bronchitol®). However, antibiotics being used for attempted pathogen eradication may be prescribed for up to 3 months.

Post-DRA room cleaning

- Following the DRA, appropriate cleaning of the room should take place according to local infection prevention and control guidance. This must include the room being left with the window open, door closed, signage to inform people not to enter the room for 20-60 minutes following completion of the DRA (to reflect the room ventilation/number of air exchanges) and appropriate surface cleaning.

Documentation of DRA details

- The following information should be recorded on the **'CF physiotherapy drug response assessment (DRA) proforma'** which should be inserted into patient's medical records, according to the date of the DRA: all objective measurements, eg spirometry results, SpO_2, auscultation; the ability of patient/carer to prepare nebuliser solutions which require mixing (if applicable); the ability of patient to use inhaler/nebuliser device correctly; the ability of patient to follow recommended procedure for inhalation; subjective data, eg patient-reported adverse effects; education provided relating to new medicine.

- Completed BIDA forms used for DRAs of Bronchitol® should be attached to (and filed with) completed **'CF physiotherapy drug response assessment (DRA) proforma'**
- Document in patent's main clinical record that DRA of medicine has been performed (and for details of this, refer to **'CF physiotherapy drug response assessment (DRA) proforma'**) and the outcome, eg for 1 month follow-up of medicine, patient not to continue with medicine.
- File any paper recording sheets in patient's medical records as per local policy.

Medicine follow-up

1 month/6 week follow-up
The use of all new inhaled/nebulised medicine should be reviewed following a trial period of 1 month (with the exception of Bronchitol®, in which a 6 week follow-up is undertaken). This review will be completed by qualified HCPC registered physiotherapists working within the CF centre who are competent to perform DRAs of medicine.

- Ask patient to describe any adverse effect(s) experienced and rate the severity using a numerical recognition scale from 0-10, where '10' is the worst adverse effect imaginable. The severity of any adverse effects may determine whether or not medicine is continued on a long-term basis.
- Spirometry should be performed by a competent practitioner and SpO_2 measured.
- Discuss with patient and CF consultant, specialist respiratory registrar or competent physiotherapist NMP, as appropriate, regarding potential continuation of medicine based on the above.
- Record all objective data, eg spirometry results, SpO_2 and subjective data relevant to 1 month/6 week follow-up on the **'CF physiotherapy inhaler/nebuliser follow-up record'**.
- Assess patient's understanding of new medicine and whether they continue to use/store it etc. appropriately. Record any education/advice provided at 1 month/6 week follow-up on the **'CF physiotherapy inhaler/ nebuliser follow-up record'**.
- Insert **'CF physiotherapy inhaler/nebuliser follow-up record'** into patient's medical records, alongside **'CF physiotherapy drug response assessment (DRA) proforma'**.

If patient to continue with medicine following 1 month/6 week follow-up

a. Advise patient if medicine to be taken continuously on a daily basis or on an on/off alternating month basis. If it is to be taken on an alternating month basis, ensure patient is aware of what medicine, if any, should be taken in the new medicine 'off' month (this should be agreed with a CF consultant, specialist respiratory registrar or competent physiotherapist NMP).

b. Contact pharmacist regarding completion of 1 month/6 week pharmacy medicine follow-up, as appropriate. They will provide patient with information on obtaining future supplies of medicine, if required.

6 month follow-up
The use of all new inhaled/nebulised medicine should be reviewed following a period of 6 months. This review will be completed by qualified HCPC registered physiotherapists working within the CF centre.

This should be performed as described in '1 month/6 week follow-up' with 6 month data/information.

If patient to continue with medicine long-term following 6 month follow-up

a. Contact pharmacist regarding completion of 6 month pharmacy medicine follow-up.

4. Responsibilities and roles

It is the responsibility of each physiotherapist who has been assessed as competent to perform DRAs and reviews of inhaled/nebulised medicine to ensure that they are familiar with:

- the contents of this SOP and adhere to it when performing DRAs; and
- the most up-to-date SPC, IFU and local patient information leaflets relating to specific medicines.

It is also the responsibility of each CF CNS and ward nurse, should they be required to perform the administration/training component of the DRA (to avoid a physio NMP prescribing the medicine and then administering it), to be familiar with the above.

5. Training requirements

Qualified HCPC registered physiotherapists who are undergoing competency training for performing DRAs of inhaled and nebulised medicine should:

- have worked within the CF centre, consistently for a minimum of 1 year;
- be Band 6 or above;
- familiarise themselves with the contents of this SOP;
- familiarise themselves with the contents of most up-to-date SPC, IFU and local patient information leaflets relating to specific medicines;
- undergo appropriate electronic prescribing training (for administration rights);
- have completed the appropriate local medicines management training modules (please refer to local policy);
- receive education from CF specialist pharmacist; and
- undergo assessment of knowledge/ understanding of all medicines that will be administered by DRA competent physiotherapist or specialist nurse.

In order to establish competence, the physiotherapist will undergo assessment by a qualified nurse assessor in which they must:

- demonstrate the ability to prepare all medicines which require mixing used at the center, ie nebulised Colomycin®, Promixin®, Cayston®, meropenem and amikacin; and
- complete a final competency assessment, in which they are observed performing an entire DRA of 2 inhaled (i.e. TOBI Podhaler®, Colobreathe® or Bronchitol®) and 2 nebulised medicines and are assessed against required standards.

Please see **'Example of medicine administration competency SOP' and 'Example of competency assessment document'**

References

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2 ATS/ERS (2005) ATS/ERS Series: Standardisation of lung function testing. European Respiratory Journal. Volume 26, pages 319-338.

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4 Dentice R, Elkins M. Timing of dornase alfa inhalation for cystic fibrosis. Cochrane Database of Systematic Reviews 2011, Issue 5. Art. No.: CD007923. DOI: 10.1002/14651858. CD007923.pub2.

5 Shak S, Capon DJ, Hellmiss R, Marsters SA. Recombinant human DNase I reduces the viscosity of cystic fibrosis sputum. Proceedings of the National Academy of Sciences USA 1990;87(23):9188-92 as cited in Reference 3 above.

6 Conway SP, Littlewood JM (1997) rhDNase in cystic fibrosis. British Journal of Hospital Medicine. Vol 57, no. 8, pages 371-372.

Related appendices

- Nebulised/inhaled medications for people with cystic fibrosis overview
- CF physiotherapy drug response assessment (DRA) proforma
- CF physiotherapy inhaler/nebuliser follow-up record
- Example of medicine administration competency SOP
- Example of competency assessment document

With thanks to S. Cameron*,

Edited for ACPCF NMP Group by C. Brown* 28th July 2020 on behalf of and with thanks to the ACPCF non-medical prescribing group

*West Midlands Regional Adult Cystic Fibrosis (CF) Centre, University Hospitals Birmingham (UHB) NHS Foundation Trust.

Appendix IVc

Drug Response Assessment (DRA) flowchart

Action:

Instruction/guidance:

Preparation

Ensure prescription and trial form completed and medication checked
Collect equipment: Nebuliser kit, compressor, spirometer, oxygen saturation monitor, stethoscope

Pre-trial assessment:
Spirometry
Oxygen saturations
Auscultation

Take 3 reproducible forced spirometry readings required (ATS guidelines within 5% of each other)
If unable to perform reproducible lung function then auscultation can be used to detect wheeze pre and post dose

Administer pre-test bronchodilator (if required)

Administer inhaled drug

Re-assess:
(5mins pos-dose inhalation)
Lung function
Oxygen saturations
Auscultation

Take up to 3 reproducible spirometery readings
Calculate if bronchoconstriction - % drop in FEV_1 after dose given:

FEV_1 actual value (pre – post)/pre x 100
Re-auscultate to compare to baseline

Analysis for possible bronchospasm
(measured by $Sp0_2$ and spirometry)

<10% constriction? — **Pass**

10-15% constriction and **asymptomatic**? — **Pass**

10-15% constriction and **symptomatic**? — **Fail**

>15% constriction? — **Fail**

No:
Test dose successful

Yes:
Test dose failed

Ensure these findings are due to bronchospasm rather than loosened and retained sputum (encourage airway clearance, consider repeat spirometry and auscultation)

Report back to referrer and proceed with course of inhaled medication

Recover

If >15% constriction after 10 min post-drug, give post-test bronchodilator to reverse bronchospasm

Plan

Consider test dose to be repeated on a separate visit (discuss with referrer)
Pre-treat with a bronchodilator or consider alternate medication

Adapted from RBH NHS Trust with kind permission

Appendix IVd

ACPCF NMP
ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN CF
NON-MEDICAL PRESCRIBERS GROUP

CF physiotherapy inhaler/nebuliser follow-up record

File in patient's main medical notes, according to date of first drug review

Patient name & PID / label:	**Inhaler/nebuliser (state constituents if applicable):**	
	Date of DRA:	
	Date of 1/12 or 6/52 follow-up:	
	Date of 6/12 follow-up:	

Observations

Assessment	FEV_1	FEV_1% predicted	SpO_2
Pre-DRA	l	%	%
1/12 or 6/52 follow-up	l	%	%
6/12 follow-up	l	%	%

Tolerance of medicine

Follow-up	Adverse reaction(s) reported & severity (NRS scale 1-10, where 10 most severe)	Continuing with medicine?
1/12 or 6/52		
6/12		

For patients continuing with medicine

(✓If patient/carer has correct understanding OR insert your initials if re-advised)

In accordance with PIL/IFU and CF physiotherapy DRA SOP assess patient's/carer's understanding of the following:	**1/12 or 6/52 review**	**6/12 review**
Medicine preparation (include time by which prepared drug must be used)		
Operation of administration device		
Procedure for inhalation		
Daily dose schedule (including recommended time between doses)		
Order/timing in relation to other inhaled/nebulised medicine & ACT (including time by which medicine should be taken following short-acting bronchodilator)		
Checking expiry date of medicine/constituents for each dose		
Action if missed dose		
Action if too much medicine taken/swallowed accidentally		
If adverse effects occur, should cease use & seek appropriate medical assistance/advice		
If new precautions of use arises in future, cease use & seek medical advice		
If medicine should only be taken using specific device/consumables		
If no other medicine should be taken using device/consumables for new medicine		
On manufacturer's instructions for care of (including cleaning and sterilisation, if appropriate) administration device and consumables		
If required for nebulisation, filter pads are discarded & replaced for each dose		
Appropriate storage of medicine/constituents		
Safe disposal of unused drug & constituents/administration equipment		
On any other drug specific instructions/precautions in PIL, IFU or local patient information leaflet if not covered above		

Follow-up **(physio to initial box)**

In accordance with CF Physiotherapy DRA SOP:	**1/12 or 6/52**	**6/12**
Contact pharmacist (re.) obtaining further medicine supplies, if required		
Advise patient regarding date of medicine review. Date agreed:		

If antibiotic, advise on ongoing regimen (✓) Please note any changes here:

Continuous use short-term for attempted eradication. State duration:	Continuous use long-term	Alternating months. State alternating antibiotic(s):
☐	☐	☐

Follow-up	Additional comments
1/12 or 6/52	
6/12	

Follow-up	Physiotherapist name (print)	Signature	Date	ID number	Designation
1/12 or 6/52					
6/12					

With thanks to S. Cameron, Edited for ACPCF NMP Group by C. Brown Jan 2020. West Midlands Regional Adult Cystic Fibrosis (CF) Centre, University Hospitals Birmingham (UHB) NHS Foundation Trust.

Appendix IVe

ACPCF NMP
ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN CF
NON-MEDICAL PRESCRIBERS GROUP

Example of a Medicine Administration Competency SOP

1. Summary	For qualified physiotherapists registered with the Health & Care Professions Council (HCPC) working within a cystic fibrosis (CF) centre to demonstrate competence in the completion of DRAs and the administration of inhaled and nebulised medicine (including medicines administration component) through skill, knowledge and application. Competency achievement is required before the physiotherapist can perform DRAs alone.
2. Scope	Administration of DRAs of inhaled/nebulised medicine.
3. Applicable to	Qualified HCPC registered physiotherapists, bands 6 and above who will be administering DRAs of inhaled and nebulised medicine within the CF centre.
4. Related policy and legislation	All relevant local policies, procedures and guidelines (under the following headings) should be accessible on the Trust intranet site. The most up-to-date version must always be used. ▪ Estates and Facilities ▪ Health and Safety ▪ Information Communications Technology ▪ Infection Control ▪ Information Governance ▪ Medical Devices ▪ Medicines Management ▪ Nursing ▪ Safety and Governance **Health & Care Professions Council (HCPC)** ▪ Standards of conduct, performance and ethics. ▪ Standards of proficiency - Physiotherapists. **Chartered Society of Physiotherapy (CSP)** ▪ Code of Members' Professional Values and Behaviour. The physiotherapist should always refer to the most up-to-date policy available.
5. Eligible to assess	Qualified Assessor who is competent to administer medicine.
6. Standard to be achieved	The physiotherapist must be able to perform the skill safely and effectively without support and demonstrate appropriate background knowledge of both the procedure (detailed in the CF physiotherapy DRA SOP) and the medicine to be administered. The physiotherapist should, at all times, adhere to relevant local policies, procedures and guidelines and also regulatory body standards and codes of conduct (see section 4. above).

7. Training required	Supervised practice in clinical setting with a competent practitioner.
8. Training and resources available	Local training as appropriate, for example: ▪ Trust Preceptorship Module ▪ Medicine Step up Module (includes Electronic Prescribing) ▪ Clinical Induction for newly qualified registered nurses ▪ VITAL Medication Module ▪ ISKILLS training resources ▪ Trust Safety Manual ▪ Lesson of the Month ▪ Nursing Alerts ▪ Electronic Non-Administration Codes ▪ Online BNF ▪ Medicine Management Sharepoint site ▪ UCLH (University College London Hospital) IV drug guide ▪ Medication SUI (serious untoward incident)
9. Author	This document has been developed by Sarah Cameron (CF Physiotherapist) and Edited by C Brown for the ACPCF NMP group Jan 2020. Document created by modification of the HEFT Amended MM34 Medicine Administration Competency (4) (2014), produced by the following: Practice and Professional Development Team 2006. Reviewed by Practice and Professional Development Team 2008. Revised by HEFT Education Faculty and Sally Lomas Clinical Educator for Surgery 2012. Reviewed by Maria Mackenzie Corporate Nurse and Caroline Maries Tillott Patient Safety Advisor 2014.

With thanks to S. Cameron,

Edited for ACPCF NMP Group by C. Brown Jan 2020.
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Appendix IVf

ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN CF
NON-MEDICAL PRESCRIBERS GROUP

Example of Competency Assessment Document

Assessment of competence in performing DRAs and administration of inhaled/nebulised medicine

This document has been developed to record the assessment of competence of qualified HCPC registered physiotherapists working within a CF centre performing DRAs of inhaled and nebulised medicine. The HEFT Medicine Administration Competency (2014) has formed the basis of this document.

Physiotherapists undergoing competency assessment must first have completed the training requirements stated in the 'SOP for the performance of drug response assessments (DRAs) and follow-up review of inhaled and nebulised medicines'.

1. Supervised practice

Supervised practice of inhaled/nebulised medicine (state name below)	Date	Assessor name	Assessor signature
Inhaled drug 1:			
Inhaled drug 2:			
Nebulised drug 1:			
Nebulised drug 2:			

2. Assessment of competence in nebuliser solution preparation

Assessment of competence in mixing nebuliser solutions	Date	Pass/fail	Assessor name	Assessor signature	Trust ID no
Nebulised colistimethate sodium:					
Colomycin®					
Promixin®					
Cayston®					
Amikacin					
Meropenem					

3. Final competence assessment

To establish competence, the physiotherapist must demonstrate that the following components of the DRA (as detailed fully in 'SOP for the performance of Drug Response Assessments (DRAs) and follow-up review of inhaled and nebulised medicines' and in accordance with the Trust's Medicines Policy) are considered/completed to a satisfactory standard.	**Assessment of competence** (pass/fail against each component)	
	1st attempt	2nd attempt
Preparation - prior to DRA **1.** Medicine is therapeutically indicated **2.** Contraindications/allergies and precautions to use considered and decision made to proceed with DRA **3.** Inform patient of therapeutic indication **4.** Inform patient of potential side effects **5.** Gain patient's (or carer's, if applicable) informed verbal consent to undergo DRA **6.** Spirometry and SpO_2 measured (if DRA of Bronchitol® BIDA should be followed) **7.** Obtain all medicine/constituents, equipment and paperwork including prescription (EP or paper chart) to minimise risk of interruption **8.** Ensure patient administers own bronchodilator, as appropriate **9.** Ensure in area where easy access to medical assistance, oxygen supply		

Patient identification and administration **1.** Remain with patient throughout DRA **2.** Make a positive identification of patient **3.** Check the prescription (should be present at point of administration). Check drug and food allergies on prescription and add to if required, in discussion with patient/carer **4.** Use personal protective equipment as appropriate and standard infection control precautions throughout the procedure (advise patient to do the same as appropriate) **5.** Check medicine/constituents are correct prior to administration and expiry dates not exceeded. **6.** Follow SPC, IFU or local patient information leaflet with regards to: **a.** preparation of DRA **b.** correct operation of inhaler/nebuliser device **c.** recommended procedure for inhalation of medicine **7.** If medicine preparation requires mixing of powder/solvent, demonstrate procedure for the patient/carer. Patient/carer can then be observed performing this to assess ability **8.** Assess patient's ability to inhale medicine using correct procedure **9.** Sign prescription to indicate time medicine administered **10.** If adverse effect occurs, inhalation should be ceased and a physician informed if appropriate or medical assistance summoned immediately		
Following DRA **1.** Ask patient to describe any adverse effect(s). Severe adverse effects should be reported to the MRHA Yellow Card Scheme and Pharmacy **2.** Spirometry should be completed 5 minutes following end of inhalation and SpO_2 measured (if DRA of Bronchitol® BIDA should be followed) **3.** Calculate % constriction to determine (along with consideration of any adverse effects) whether appropriate to pursue trial period of medicine **4.** Deal appropriately and safety with >10% constriction, escalating if required		

Information provided for patients/carers continuing with trial period of medicine As detailed in PIL, IFU and local patient information leaflets and DRA SOP: **1.** Preparation of medicine **2.** Correct operation of inhaler/nebuliser device in accordance with manufacturer's instructions **3.** Recommended procedure for inhalation of medicine **4.** Daily dose schedule and recommended interval between doses **5.** Optimum timing of medicine in relation to other prescribed inhaled/nebulised medicine and ACT **6.** Action to take if a dose of medicine is missed/forgotten **7.** Action to take if too much medicine taken or swallowed accidentally **8.** Action to take if experiences adverse effects **9.** Action to take if stops using medicine **10.** Action to take if new situation re. precautions of taking medicine arises **11.** Manufacturer's instructions for the care of (including cleaning and sterilisation, if appropriate) the inhaler/nebuliser device and related consumables **12.** If required for nebulisation, filter pads used within PARI Filter/Valve Sets should be discarded and replaced following each dose **13.** Appropriate storage of medicine/constituents **14.** Safe disposal of empty packaging and administration equipment **15.** Any medicine specific instructions/precautions not already covered		
Completion of DRA **1.** Patient returned to pre-DRA level of wellness, if experienced adverse effects during DRA, before leaving hospital (out-patient) or before being left unsupervised (inpatient) **2.** If patient to continue with trial period of medicine make arrangements for supply		
Documentation of DRA details **1.** Complete the 'CF Physiotherapy drug response assessment (DRA) proforma' (if Bronchitol® DRA, BIDA should also be completed) and insert in main clinical record **2.** Document in main clinical record that DRA of medicine has been performed (and for details of this, refer to 'CF Physiotherapy drug response assessment (DRA) proforma') and the outcome, eg for one month follow-up of medicine or patient not to continue with medicine **3.** File paper records in patient's medical records		

Assessment of competence in performing full DRA procedure	Date	Pass/fail	Assessor name	Assessor signature	Trust ID no
Inhaler or nebuliser name (1st attempt):					
Inhaler or nebuliser name (2nd attempt if failed 1st):					

Competence statement

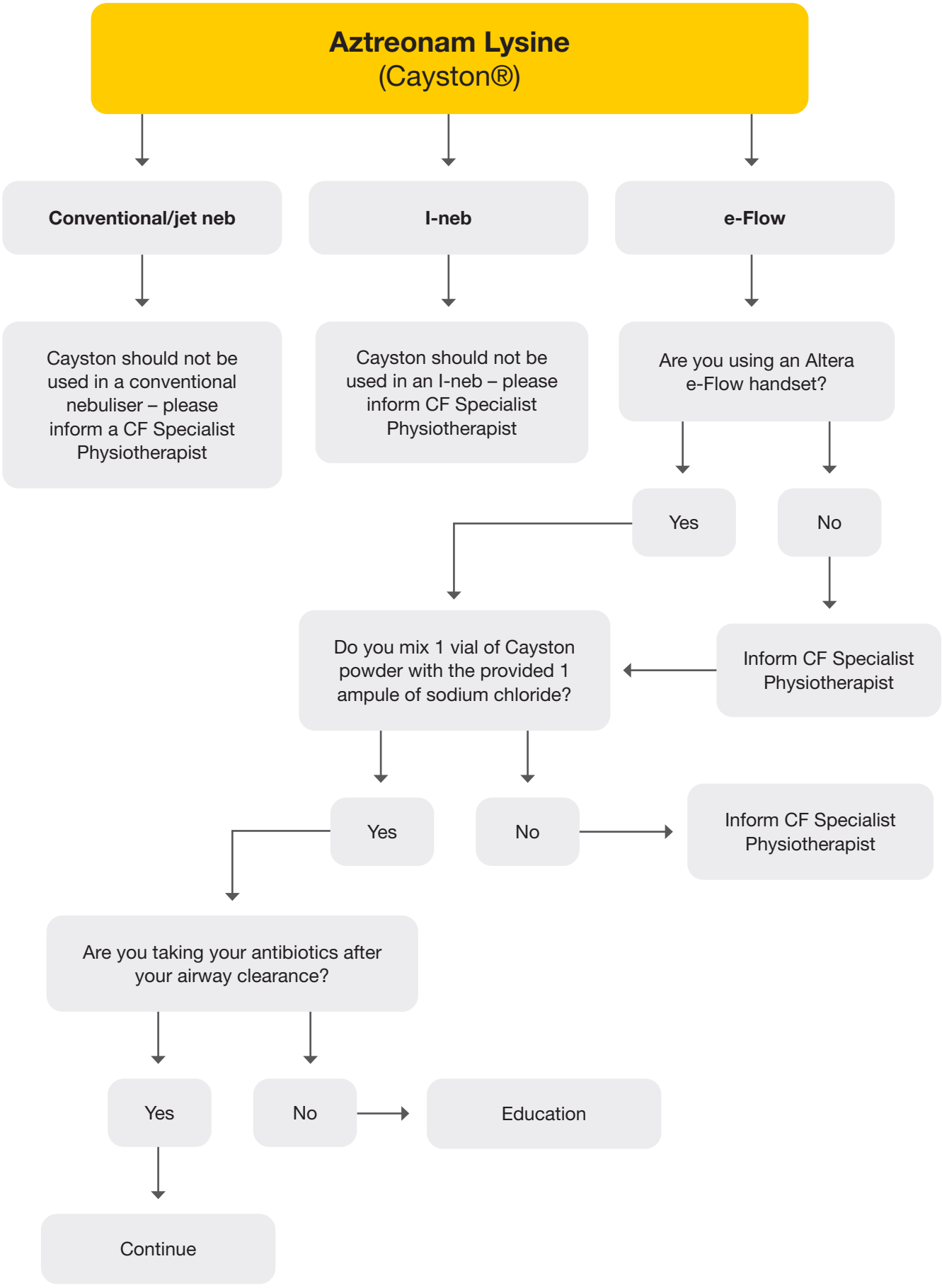
This is to state that ……has passed the medicine administration competency for performing DRAs of inhaled and nebulised drugs used within the West Midlands Regional Adult CF Centre on ……(date)

With thanks to S. Cameron,

Edited for ACPCF NMP Group by C. Brown Jan 2020.
West Midlands Regional Adult Cystic Fibrosis (CF) Centre,
University Hospitals Birmingham (UHB) NHS Foundation Trust.

Appendix IVg

Examples of flowcharts



Tobramycin (Bramitob®)

Conventional/jet neb

Do you have a PARI LC Plus for tobramycin?

- Yes
- No → Provide patient with one

Do you have a filter?

- Yes
- No → Provide patient with one

Driving gas

- Air → Continue
- O_2 → Inform a CF Specialist Physiotherapist

I-neb

Bramitob should not be given via an I-neb

e-Flow

Are you using this handset separate to DNase?

- Yes
- No → Inform a CF Specialist Physiotherapist

Are you using a filter?

- Yes → Continue
- No → Inform a CF Specialist Physiotherapist

Are you taking your antibiotics after your airway clearance?

- Yes → Continue
- No → Education

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Tobramycin (TOBI® or Tymbrineb®)

ASSOCIATION OF CHARTERED PHYSIOTHERAPISTS IN CF NON-MEDICAL PRESCRIBERS GROUP

Conventional/jet neb

Do you have a PARI LC Plus for tobramycin?

- Yes
- No → Provide patient with one

Do you have a filter?

- Yes
- No → Provide the patient with one

Driving gas

- Air → Continue
- O_2 → Inform a CF Specialist Physiotherapist

I-neb

Have you got a lilac chamber?

- Yes
- No → If you also take Promixin then you can ring the company to obtain one: 0800 1300857. Or ask your CF team

Are you using other medication in this chamber?

- No
- Yes → Inform a CF Specialist Physiotherapist

Do you carry out 2 fills of the chamber for each treatment dose?

- Yes
- No → Education/inform Physiotherapist

Continue

Download and print off data

- Yes
- No

e-Flow

Are you using this handset separate to DNase?

- Yes
- No → Inform a CF Specialist Physiotherapist

Are you using a filter?

- Yes → Continue
- No → Inform a CF Specialist Physiotherapist

Are you taking your antibiotics after your airway clearance?

- Yes → Continue
- No → Education

Colistimethate Sodium

Are you using Colomycin®?

Yes

Conventional/jet neb

Have you got a Pari LC Plus for antibiotics?

Yes

Continue

Do you mix 4mls volume of diluent with 2MU colomycin?

Yes

Driving gas

Air or compressor

Continue

No

Discuss with CF Specialist Physiotherapist

O_2

Discuss with CF Specialist Physiotherapist

No

Provide patient with one

e-Flow

Do you mix 4mls volume of diluent with 2MU Colomycin?

Yes

Continue

No

Discuss with CF Specialist Physiotherapist

No

Are you using Promixin®?

I-neb

Do you mix 1ml volume of diluent with 1MU Promixin?

Yes

Do you take your Promixin in the grey chamber?

Yes

Download I-neb data

No

Contact the company to get a chamber 0800 1300857

No

Discuss with CF Specialist Physiotherapist

Are you taking your antibiotics after your airway clearance?

Yes

Continue

No

Education

OXFORD ADULT CYSTIC FIBROSIS CENTRE

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Dornase Alfa (DNase)

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Conventional/jet nebuliser

Using a separate side stream with a mouthpiece?

- Yes → What driving gas is being used?
  - Air or compressor → Continue
  - O_2 → Inform a CF Specialist Physiotherapist
- No → Provide the patient with one → What driving gas is being used?

I-neb

Have you got a green chamber?

- Yes → Are you using other medication in this chamber?
  - Yes → Please note only DNase should be run through green chamber. Inform a physiotherapist
  - No → Continue → Download data
    - Yes
    - No
- No → If you also take Promixin then you can ring the company to obtain one: 0800 1300857. Or ask your CF team → Are you using other medication in this chamber?

e-Flow

Using a separate handset?

- Yes → Continue
- No → Inform a CF Specialist Physiotherapist

Are you taking DNase at least 30 mins prior to airway clearance?

- Yes → Continue
- No → Have you discussed an alternative timing with the Specialist Physiotherapist
  - Yes → Continue
  - No → Inform a CF Specialist Physiotherapist

Hypertonic saline
7%/3%

Conventional/jet neb

Using a side stream with a mouthpiece?

- Yes → Driving gas
  - Air or compressor → Continue
  - O_2 → Inform a CF Specialist Physiotherapist
- No → Provide the patient with one → Driving gas

I-neb

Have you got a lilac chamber?

- Yes → Are you using other medication in this chamber?
  - Yes → Continue → Download data
    - Yes
    - No
  - No → Education/ inform Physiotherapist
- No → If you also take Promixin then you can ring the company to obtain one: 0800 1300857. Or ask your CF team → Are you using other medication in this chamber?

e-Flow

Are you using a separate handset to DNase?

- Yes → Continue
- No → Discuss with CF Specialist Physiotherapist

Are you taking your hypertonic saline before your airway clearance?

- Yes → Continue
- No → Education

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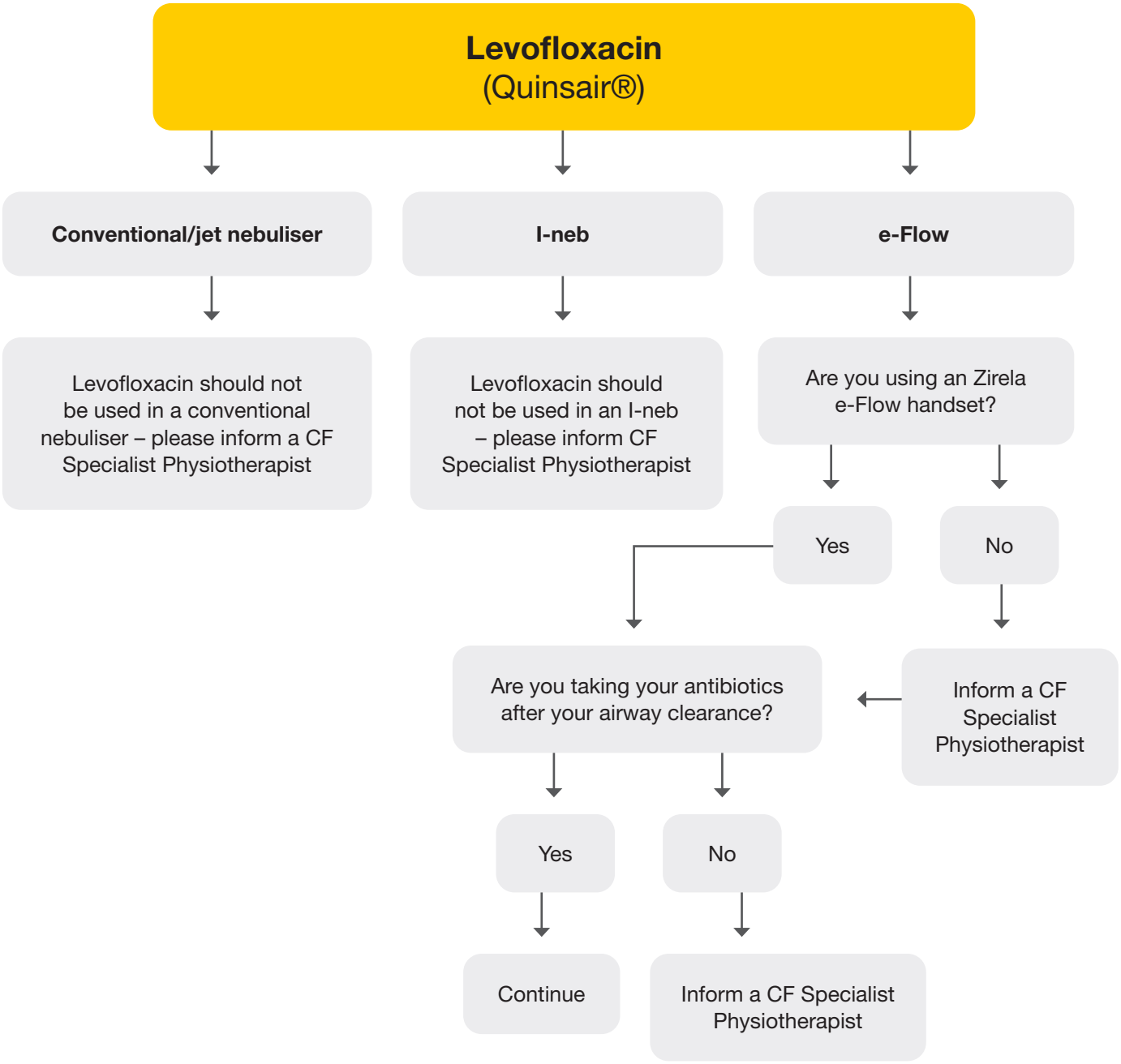

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Appendix IVh

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Nebulised/inhaled medications for people with cystic fibrosis overview

This is a quick reference guide to the nebulised and inhaled medications used in cystic fibrosis. It is intended to only be used by clinicians who have received appropriate training and who are familiar with the summary of product characteristics (SPC) of each licenced medicine and the indications, prescription and delivery details of the commonly used 'off-label' medicines used for inhalation in cystic fibrosis.

Note that all people commencing a new nebulised/inhaled medication, or when the medication hasn't been used for the last 12 months, should have a supervised drug response assessment (DRA) as per documented DRA procedure. Please refer to the clinical commissioning policy and NICE guidance regarding the criteria for use of the licensed medications.

For any medications not included in this overview please refer to the British National Formulary (BNF) for prescribing information. Useful administration advice for inhalers not included in this overview advice can be found at: www.rightbreathe.com

Useful definitions

'Licenced' medications

"A marketing authorisation or product licence defines a medicine's terms of use: its summary of product characteristics (SPC) outlines, among other things; the indication(s), recommended dose(s), contraindications, and special warnings and precautions for use on which the licence is based, and it is in line with such use that the benefits of the medicine have been judged to outweigh the potential risks. Furthermore, a licensed medicine: has been assessed for efficacy, safety, and quality; has been manufactured to appropriate quality standards; and when placed on the market is accompanied by appropriate product information and labelling."[1]

'Off-label' use of medications

There are clinical situations when the use of medicines outside the terms of the licence (ie 'off-label') may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. This has become common practice in inhaled medications in CF where licensed options are limited. In the table below we use the term 'off-label' where use is outside of the medicine's licence.[1]

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Amikacin Use as a nebuliser is **'off-label'**.	*Mycobacterium abscessus*	**Paediatric:** <12 years: 250mg twice daily. >12years: 500mg twice daily. **Adult:** 500mg twice daily. In paediatrics and adults ideally 12 hours between doses.	Conventional compressor & PARI LC® Plus or Sprint with filter attachment. Some centres advise that patients can use eFlow®rapid with a **regular eFlow®rapid handset** with filter attachment to reduce treatment time, though there is no robust data to support this.	**250mg:** 1ml Amikacin for injection (250mg/ml) with 3ml sodium chloride 0.9%. **500mg:** 2ml Amikacin for injection (250mg/ml) with 2ml sodium chloride 0.9%.	Glass ampoules, preferably issue syringes and needles.
Amphotericin (Ambisome) Use as a nebuliser is **'off-label'**.	*Aspergillus*	**Paediatric:** <10 years: 5mg twice daily. >10 years: 10mg twice daily. **Adult:** 25mg twice daily Ideally 12 hours between doses.	Conventional compressor & PARI LC® Plus or Sprint with filter attachment.	**5mg:** 50mg vial Amphotericin with 10ml water for injection. Use 1ml of this solution and dilute further with 2ml of water for injection (minimum volume of 3ml for nebulisation). **10mg:** 50mg vial Amphotericin with 10ml water for injection. Use 2ml of solution and dilute with a further 1ml of water for injection (minimum volume of 3ml for nebulisation). **25mg:** 50mg vial Amphotericin with 12ml sterile water. 6ml to be nebulised. Remaining mixed solution can be kept in fridge for second daily dose (discarded if not used within 24 hours).	Liposomal amphotericin (Ambisome) should be prescribed NOT the non-lipid amphotericin (Fungizone). Rubber bung on vial not removable therefore will need syringes (10ml) and needles.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Aztreonam (Cayston®)	*Pseudomonas aeruginosa* Is also used **'off-label'** for Burkholderia cepacia >6 years Consider **'off-label'** use in <6 years if clinically indicated	75mg three times daily. Minimum 4 hours between doses.	eFlow®rapid using **Altera® handset** with filter attachment (Altera® handset included in monthly Cayston® pack).	1 vial aztreonam powder (75mg) with 1 ampoule sodium chloride 0.17% (included in Cayston® pack).	**Keep in fridge but can be kept out of a fridge but below 25°C for 28 days.** Usual starting regimen is 28 days on/28 days off. Alternating with another inhaled antibiotic or continuous treatment may be indicated if deterioration in month off treatment.
Ceftazidime Use as a nebuliser is **'off-label'**.	*Burkholderia cepacia*	1g twice daily. Ideally 12 hours between doses.	Conventional compressor & PARI LC® Plus or Sprint with filter attachment.	Reconstitute 1g with 3ml water for injection.	Tastes awful which can impact tolerance.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Colistimethate Sodium (Promixin®) Via an I-neb.	*Pseudomonas aeruginosa*	**Paediatric:** <8 years: 0.5mu twice daily. >8 years: 1mu twice daily. **Adult:** 1mu twice daily. Ideally 12 hours between doses. **Note these priming doses of Promixin® used with the I-neb give a received dose equivalent to those listed below for Colomycin. This is due to increased efficiency of the I-neb over the eflow.**	I-neb, grey chamber. Data also exists for increased dosing using a lilac chamber.	**0.5mu:** 1mu Promixin® reconstituted with 2ml water for injection. 1ml to be nebulised. Remaining 1ml kept in fridge for second daily dose (discard after 24 hours). **1mu:** 1mu Promixin® reconstituted with 1ml water for injection.	Promixin® must be used in order to obtain disks needed for I-neb use. Syringes needed (1 or 2ml syringes). In case of bronchoconstriction, or where already using nebulised salbutamol, Promixin® may be reconstituted with salbutamol 2.5mg (2ml for paeds <2 years and 1ml for paeds >2 years/ adults). **Must be used immediately, do not store in fridge for later use.** If reconstituting with water/sodium chloride, acceptable to reconstitute 2 doses and store second dose in fridge **to be used within 24 hours** or discard.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Colistimethate Sodium (Colomycin)	*Pseudomonas aeruginosa*	**Paediatric:** <8 years: 1mu twice daily. >8 years: 2mu twice daily. **Adult:** 2mu twice daily. Ideally 12 hours between doses.	eFlow®rapid with a **regular eFlow®rapid handset** OR a conventional compressor & PARI LC® Plus or Sprint with filter attachment.	**1mu:** 1mu Colomycin reconstituted with 4ml water for injection or sodium chloride 0.9%. **2mu:** 2mu Colomycin reconstituted with 4ml water for injection or sodium chloride 0.9%.	Syringes needed (5ml) In case of bronchoconstriction, or where already using nebulised salbutamol, Colomycin may be reconstituted with 2 vials of salbutamol 2.5mg **Must be used immediately, do not store in fridge for later use.** If reconstituting with water for injection or sodium chloride 0.9%, acceptable to reconstitute 2 doses of Colomycin and store second dose in fridge **to be used within 24 hours** or discard.
Colistimethate Sodium (Colobreathe®)	*Pseudomonas aeruginosa* >6 years	1.66mu twice daily. Ideally 12 hours between doses.	Turbospin® powder inhaler (inhaler in pack).	No reconstitution required. One capsule to be inhaled twice daily.	Cough may be an issue and can be related to technique.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Dornase Alfa (DNase/ Pulmozyme®)	*Mucolytic* >6 years Consider **'off-label'** use in <6 years if clinically indicated.	2.5mg once daily. The SPC states 'some patients over the age of 21 years may benefit from twice daily dosage'. Consider twice daily in patients with se¬vere disease or during exacerbations.	Conventional compressor & PARI LC® Plus or Sprint OR eFlow®rapid with a **regular eFlow®rapid handset**. **'Off-label'** use with the I-neb is supported by data.	No reconstitution required. **eFlow®rapid or conventional compressor:** 2.5mg in 2.5ml (1 vial). **I-neb:** 1 fill of green chamber (discard remainder).	**Keep in fridge .** **Do not complete airway clearance for 30 mins post nebulisation.** Consider potential interaction with nebulised antibiotics when recommending a treatment regimen.
Hypertonic Sodium chloride 7% (Nebusal®, Resp-ease®) Note 6% & 3% (Mucoclear®) also available **Classed as medical devices, please refer to current instructions for use (IFU)**	Osmotic agent. Recommended if DNase not tolerated OR as an additional therapy if clinical deterioration or difficulty clearing chest despite DNase.	7% in 4 ml (1 vial) twice daily. Can increase to four times daily if needed.	Conventional compressor & PARI LC® Plus or Sprint , I-neb OR eFlow®rapid with a **regular eFlow®rapid handset**.	No reconstitution required. **I-neb:** 2 fills of lilac chamber (discard remainder). **eFlow®rapid or conventional compressor:** 4ml (1 vial).	Often used as required rather than regular twice a day. Can be used with conventional compressor & PARI LC® Plus or Sprint alongside PARI PEPTM S, Aerobika® or Acapella®. This may reduce deposition but may improve adherence and clearance.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Levofloxacin (Quinsair®)	*Pseudomonas aeruginosa* >18 years Consider **'off-label'** use in <18 years if clinically indicated.	240mg twice daily. Ideally 12 hours, minimum 8 hours between doses.	eFlow®rapid using **Zirela® handset** with filter attachment (Zirela® handset included in monthly Quinsair® pack).	No reconstitution required. 2.4ml (240mg) vial via the eFlow®rapid using **Zirela® handset** with filter attachment.	Keep in the foil package to protect the neb from light. Usual starting regimen is 28 days on/28 days off. Alternating with another inhaled antibiotic as required. Bitter taste of levofloxacin can impact tolerance. Anecdotally sucking dark chocolate/ strong tasting sweets after dose can improve tolerance. Note unusual high systemic absorption compared with other nebulised antibiotics (approx. 50%). Caution should be exercised with concurrent use of other fluroquinolones such as Ciprofloxacin.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Mannitol (Bronchitol®)	Recommended if DNase not tolerated OR if clinical deterioration despite DNase. >18 years Consider **'off-label'** use in <18 years if clinically indicated.	400mg twice daily. The doses should be taken morning and night with the evening dose taken 2-3 hours before bedtime.	Osmohaler inhaler device in pack.	No reconstitution required. Ten capsules to be inhaled twice daily. Note multiple inhalations may be needed to clear inhaler.	Cough is expected, if coughing too much consider if technique could be improved. Note that anecdotally some people who feel tight chested with a full dosing regimen have found a reduced dose (**'off-label'**) beneficial for airway clearance, eg some completing 10 capsules once daily, some reducing the number of capsules per dose.
Meropenem Use as a nebuliser is **'off-label'**.	*Pseudomonas aeruginosa and Burkholderia cepacia* if unable to tolerate or continuing to deteriorate on licenced alternatives. *Mycobacterium abscessus.* Used where sensitivities indicate OR as an alternating neb with Amikacin if continuing to deteriorate.	**Paediatric:** 6-12 years: 125mg twice daily. >12 years: 250mg twice daily. **Adult:** 250mg twice daily. In both paediatrics and adults ideally 12 hours between doses.	Conventional compressor & PARI LC® Plus or Sprint with filter attachment. Some centres advise that patients can use eFlow®rapid with a **regular eFlow®rapid handset** with filter attachment to reduce treatment time, though there is no robust data to support this.	**125mg:** 500mg Meropenem to be reconstituted with 8ml water for injection. 2.5ml of this solution is then mixed with 0.5mls water for injection. This 3mls is the nebulised. **250mg:** 500mg Meropenem to be reconstituted with 8ml water for injection. 4ml (250mg) to be nebulised. Remaining mixed solution can be kept in fridge for second daily dose (discarded if not used within 12 hours or if discolouration observed).	Rubber bung on vial not removable therefore will need syringes (10ml) and needles.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Tauroldine Solution 2% Use as a nebuliser is **'off-label'**.	*Burkholderia cepacia* Post-transplant	4ml of 2% solution twice daily. Ideally 12 hours between doses.	Conventional compressor & PARI LC® Plus or Sprint with filter attachment.	Pre-made, draw up as needed. Keep in fridge once used for first time. Discard as per pharmacy instructions.	Rubber bung on vial not removable therefore will need syringes (5ml) and needles.
Tobramycin (Bramitob)	*Pseudomonas aeruginosa* *Burkholderia cepacia* >6 years Consider **'off-label'** use in <6 years if clinically indicated.	300mg (4mls) twice daily. Ideally 12 hours, minimum 6 hours between doses.	Licenced through conventional compressor & PARI LC® Plus or Sprint with filter attachment. Some centres advise that patients can use **'off-label'** with Ineb or eFlow®rapid with a **regular eFlow®rapid handset** with filter attachment to reduce treatment time, though there is no robust data to support this.	**Conventional compressor or eFlow®rapid:** 300mg in 4ml (1 vial). **I-neb:** 2 fills of lilac chamber.	**Keep in fridge** (allow to come to room temperature before nebulising). Only licensed in children over 6 but is used >6 months. Usual starting regimen is 28 days on/28 days off (unless eradication 3 months continuously), however alternating with another inhaled antibiotic may be indicated if deterioration in month off treatment.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Tobramycin (TOBI® or Tymbrineb)	*Pseudomonas aeruginosa* *Burkholderia cepacia* >6 years Consider **'off-label'** use in <6 years if clinically indicated.	TOBI® or Tymbrineb are chemically identical. 300mg (5mls) twice daily. Ideally 12 hours, minimum 6 hours between doses.	Licenced through conventional compressor & PARI LC® Plus or Sprint with filter attachment. **'Off-label'** use with an I-neb or eFlow®rapid with a **regular eFlow®rapid handset** with filter attachment is supported by data.	**Conventional compressor or eFlow®rapid:** 300mg in 5ml (1 vial). **I-neb:** 2 fills of lilac chamber.	**Keep in fridge** (allow to come to room temperature before nebulising). Only licensed in children over 6 but is used off licence in >6 months. Usual starting regimen is 28 days on/28 days off (unless eradication 3 months continuously), however alternating with another inhaled antibiotic may be indicated if deterioration in month off treatment.
Tobramycin (TOBI Podhaler® inhalation powder)	*Pseudomonas aeruginosa* *Burkholderia cepacia* >6 years	4x28mg capsules (112mg) twice daily. Ideally 12 hours, minimum 6 hours between doses .	Podhaler inhaler device in pack.	Four capsules (4x28mg, 112mg total) to be inhaled twice daily.	Cough may be an issue and can be related to technique.

Medication	Usual indication	Prescription	Delivery system	Reconstituting	Notes
Tobramycin (Vantobra®)	*Pseudomonas aeruginosa* *Burkholderia cepacia* >6 years Consider **'off-label'** use in <6 years if clinically indicated.	170mg twice daily. Ideally 12 hours, minimum 6 hours between doses.	eFlow®rapid using **Tolero® handset** with filter attachment (Tolero® handset included in monthly Vantobra® pack).	No reconstitution required. 1.7ml (170mg) vial via the eFlow®rapid using **Tolero® handset** with filter attachment.	**Keep in fridge** (allow to come to room temperature before nebulising). Usual starting regimen is 28 days on/28 days off (unless eradication 3 months continuously, however alternating with another inhaled antibiotic may be indicated if deterioration in month off treatment.
Vancomycin Use as a nebuliser is **'off-label'**.	*MRSA*	**Paediatric:** 5mg/kg twice daily. **Adult:** 250mg twice daily. Ideally 12 hours between doses. Usually a five day duration of treatment for eradication. **Always state 500mg vials to be issued from pharmacy not 1g vials.**	Conventional compressor & PARI LC® Plus or Sprint with filter attachment.	**Use 500mg vial.** Reconstitute 500mg Vancomycin with 8ml water for injection. **Paediatric dose (5mg/kg):** Draw up required dose and make up to a total of 4ml with water for injection. **250mg:** 4ml of reconstituted solution to be nebulised and remaining 4ml to be kept in fridge for second daily dose, discard if not used within 24 hours.	Rubber bung on vial not removable therefore will need syringes (10ml) and needles.

References

[1] Medicines and Healthcare products Regulatory Agency (2014) Off-label or unlicensed use of medicines: prescribers' responsibilities. Available at: www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities [Accessed 19/02/2020]

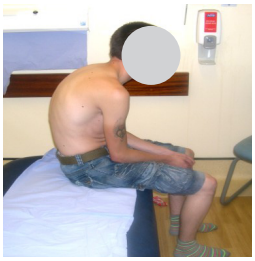
Appendix V

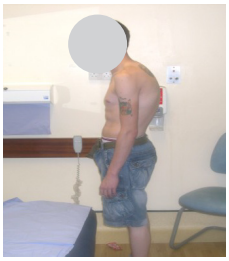
MANCHESTER ADULT CYSTIC FIBROSIS CENTRE

ACPCF
Association Of Chartered Physiotherapists In Cystic Fibrosis

Manchester Musculoskeletal Screening Tool

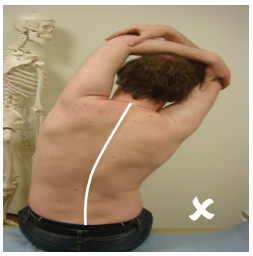
1. Do you have any episodes of pain? **Y / N**
   (If yes, complete MPQ)
2. Do you have any episodes of leaking urine, or an urgent or frequent need to pass water? **Y / N**
   (If yes, complete ICIQ)
3. Do you have any concerns about your posture? **Y / N**
4. What is the cause of pain? Musculoskeletal **Y / N**
   Other: (e.g. surgery, gout, unknown)……
5. Is there a fixed thoracic kyphosis?

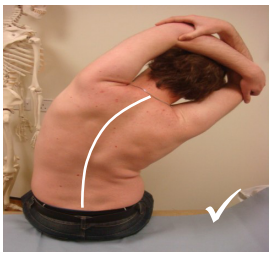




In sitting:

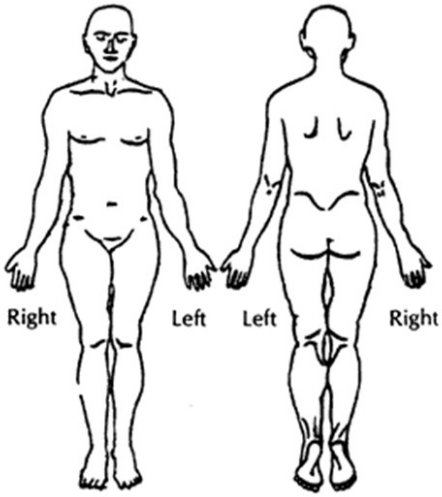
6. Is patient able to lift both arms straight above head level with ears?
7. With arms across chest is patient able to rotate upper body to 45°?
8. With arms above head is patient able to lean to 30°?





Date:
Name:
DOB:
Height:
Gender: M / F
Microbiological group:
FEV1 today:
Diabetes: Y / N
Experiencing exacerbation: Y / N

Mark site of pain on body chart



Score (admin use only)

Q	Y	N
1		
2		
3		
4		
5		
6		
7		
8		
MPQ	Max 50	
VAS	Max 100	
ICIQ	Max 21	
Outcome	A-G	

Outcome

Refer to Screening Pathway Matrix for outcome:

- **A.** If all ticks are in shaded boxes then no action required (see ‘Recommendation’ on page 4)
- **B.** Posture and exercise leaflet
- **C.** Pelvic floor leaflet
- **D.** Musculoskeletal physiotherapy assessment
- **E.** Refer to continence specialist
- **F.** Patient declined intervention, screen in 1 year
- **G.** Refer for specialist assessment

Therapist name/signature:

Manchester Musculoskeletal Screening Tool: MPQ

Short Form McGill Pain Questionnaire

A. Please describe your pain during the last 7 days (✓ one box on each line.)

	None	Mild	Moderate	Severe
1. Throbbing	0 ☐	1 ☐	2 ☐	3 ☐
2. Shooting	0 ☐	1 ☐	2 ☐	3 ☐
3. Stabbing	0 ☐	1 ☐	2 ☐	3 ☐
4. Sharp	0 ☐	1 ☐	2 ☐	3 ☐
5. Cramping	0 ☐	1 ☐	2 ☐	3 ☐
6. Gnawing	0 ☐	1 ☐	2 ☐	3 ☐
7. Hot/burning	0 ☐	1 ☐	2 ☐	3 ☐
8. Aching	0 ☐	1 ☐	2 ☐	3 ☐
9. Like a weight	0 ☐	1 ☐	2 ☐	3 ☐
10. Tender	0 ☐	1 ☐	2 ☐	3 ☐
11. Splitting	0 ☐	1 ☐	2 ☐	3 ☐
12. Tiring/exhausting	0 ☐	1 ☐	2 ☐	3 ☐
13. Sickening	0 ☐	1 ☐	2 ☐	3 ☐
14. Fearful	0 ☐	1 ☐	2 ☐	3 ☐
15. Punishing/cruel	0 ☐	1 ☐	2 ☐	3 ☐

B. Rate your pain during the past 7 days

The following line represents pain of increasing intensity from “no pain” to “worst possible pain”.
Place a vertical line (|) across the line in the position that best describes your pain during the **past 7 days**.

No pain — **Worst possible pain**

C. Present pain intensity

0 ☐ No pain
1 ☐ Mild
2 ☐ Discomforting
3 ☐ Distressing
4 ☐ Horrible
5 ☐ Excruciating

Investigator’s use only:

**** Visual Analogue Scale (VAS) score:*** ☐☐☐ mm

**** MPQ Score:***
S = *sum of 1-11* ***A*** = *sum of 12-15* ***E*** = *C*

Max:33 Max:12 Max:5

Total MPQ score = *S+A+E*

Max:50

MANCHESTER ADULT CYSTIC FIBROSIS CENTRE

Manchester Musculoskeletal Screening Tool: ICIQ

Initial number

ICIQ-UI Short Form

CONFIDENTIAL

Today's date (d d m m y y)

Many people leak urine some of the time. We are trying to find out how many people leak urine, and how much this bothers them. We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the PAST FOUR WEEKS.

1 Please write in your date of birth:

d d m m y y

2 Are you *(tick one):*

Female ☐ Male ☐

3 How often do you leak urine? *(Tick one box)*

never ☐	0
about once a week or less often ☐	1
two or three times a week ☐	2
about once a day ☐	3
several times a day ☐	4
all the time ☐	5

4 We would like to know how much urine you think leaks.

How much urine do you usually leak (whether you wear protection or not)? *(Tick one box)*

none ☐	0
a small amount ☐	2
a moderate amount ☐	4
a large amount ☐	6

5 Overall, how much does leaking urine interfere with your everyday life?

Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 10
not at all — a great deal

ICIQ score: sum scores 3+4+5 ☐☐

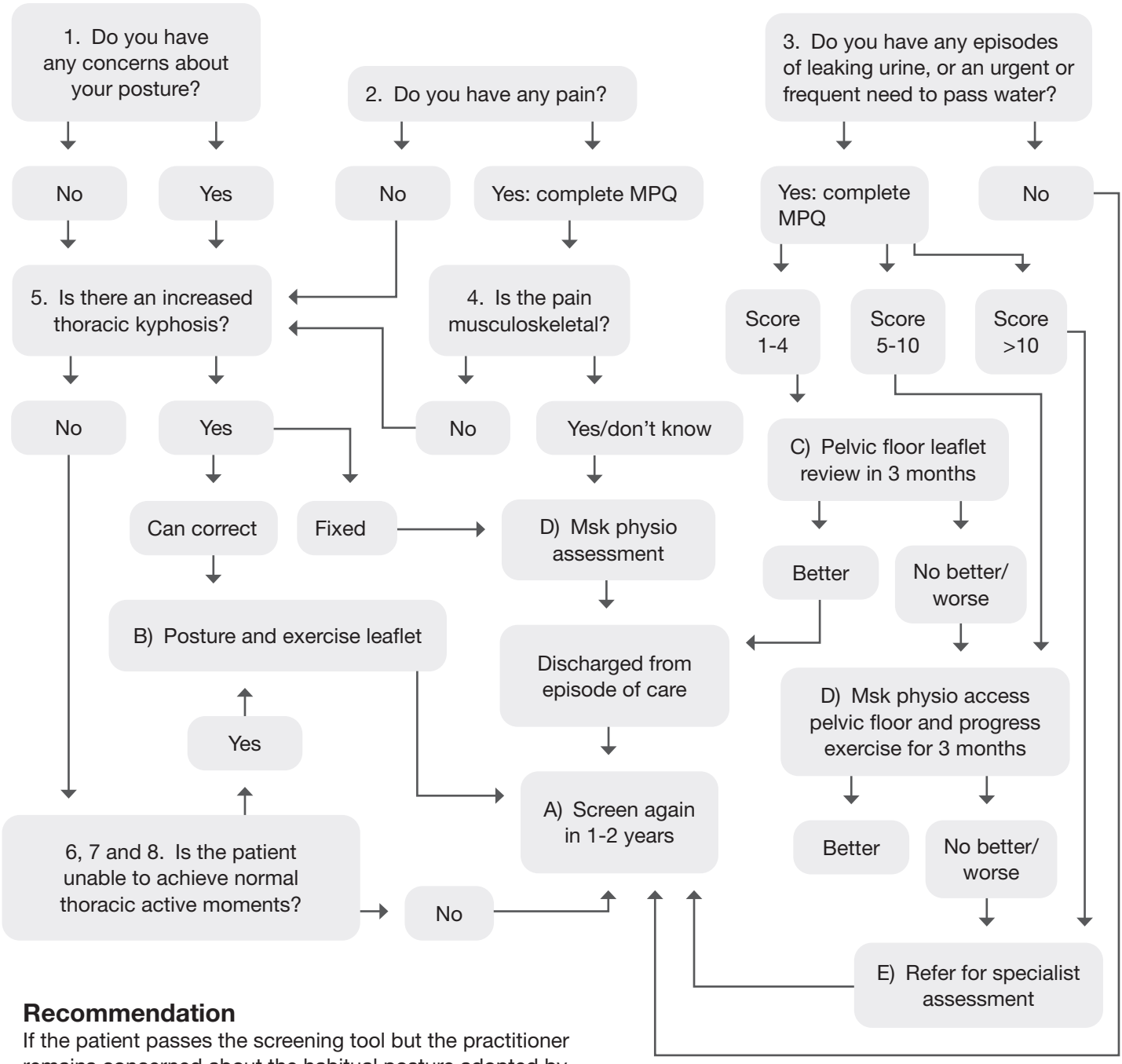
6 When does urine leak? *(Please tick all that apply to you)*

- never – urine does not leak ☐
- leaks before you can get to the toilet ☐
- leaks when you cough or sneeze ☐
- leaks when you are asleep ☐
- leaks when you are physically active/exercising ☐
- leaks when you have finished urinating and are dressed ☐
- leaks for no obvious reason ☐
- leaks all the time ☐

MANCHESTER ADULT CYSTIC FIBROSIS CENTRE

Thank you very much for answering these questions.

Screening Pathway Matrix



Recommendation

If the patient passes the screening tool but the practitioner remains concerned about the habitual posture adopted by the patient, advice or a specialist assessment should be offered. This will inform the patient about optimal postures which may prevent problems in the future.

Disclaimer

Appendix VI

Summary of evidence-based best practice guidelines relating to nebuliser hygiene in CF

- New nebuliser parts should be washed and disinfected before first use **(Recommendation 2)**.
- During a hospital admission and at home, wash the nebuliser parts after each use **(Recommendation 3)**.
- Nebulisers should be washed and re-disinfected immediately prior to use after greater than 24 hours of inactivity **(Recommendation 4)**.

At home recommendations	Inpatient recommendations
Wash hands thoroughly with soap and water and use hand disinfector gel before starting the cleaning process **(Recommendation 1)**	Wash hands thoroughly with soap and water and use hand disinfector gel before starting the cleaning process. Gloves should be worn by healthcare professionals with hand hygiene performed after removal of gloves **(Recommendation 1)**
Disconnect nebuliser from the compressor unit and dissemble into their constituent components **(Recommendation 11)**	Disconnect nebuliser from the compressor unit and dissemble into their constituent components **(Recommendation 11)**
Washing Wash nebuliser components in a solution of warm tap water **(Recommendation 12)** and dishwashing liquid in accordance with the detergent manufacturer's guidance **(Recommendation 14)**. **Location** Do not wash nebuliser parts directly in kitchen or bathroom sinks **(Recommendation 8)** or the dishwasher **(Recommendation 9)**. This should be done in a dedicated plastic, glass or metal bowl in the patients' kitchen **(Recommendation 10)**. **Rinsing** Sterile water must be used during a final rinse, when immediate disinfection is not possible **(Recommendation 13)**. **Disposal of waste water** Disposal of waste water should be via the toilet, ensuring the toilet lid is closed prior to flushing **(Recommendation 17)**.	**Washing** Wash nebuliser components in a solution of warm tap water **(Recommendation 12)** and dishwashing liquid in accordance with the detergent manufacturer's guidance **(Recommendation 14)**. **Location** This should be done in a disposable bowl, metal bowl or basin **(not directly in a sink- Recommendation 5)** in the patients' room. **(Recommendation 6)** **Rinsing** Sterile water must be used during a final rinse, when immediate disinfection is not possible **(Recommendation 13)**. **Disposal of waste water** Metal bowl and waste water should be sent to the ward sluice **(Recommendation 15)**. Waste water should be disposed of here and the metal bowl should be sterilised by autoclaving **(Recommendation 16)**.

Disinfection Washed and rinsed nebulisers should be disinfected after each use **(Recommendation 7)** using an electric baby bottle steam disinfector, **(Recommendation 18)**.	**Disinfection** Washed and rinsed nebulisers should be disinfected immediately after each use **(Recommendation 7)** using an electric baby bottle steam disinfector **(Recommendation 18)**. OR Reusable nebulisers may be autoclaved, where the nebuliser manufacturer states that the device can be safely autoclaved **(Recommendation 19)**.
Storage Leave the disinfected nebuliser parts undisturbed in the disinfector until the next use (within 24 hours). Should the parts be disturbed (i.e. lid lifted off for any reason) then the disinfection process should be repeated and the parts left undisturbed until the next use (within 24 hours) **(Recommendation 20)**.	**Storage** Leave the disinfected nebuliser parts undisturbed in the disinfector until the next use (within 24 hours). Should the parts be disturbed (i.e. lid lifted off for any reason) then the disinfection process should be repeated and the parts left undisturbed until the next use (within 24 hours) **(Recommendation 20)**.
After disinfection Wash hands thoroughly with soap and water and use hand disinfector gel after the cleaning and disinfection process prior to reassembling the nebuliser device **(Recommendation 1)**.	**After disinfection** Wash hands thoroughly with soap and water and use hand disinfector gel after the cleaning and disinfection process prior to reassembling the nebuliser device **(Recommendation 1)**.

Appendix VII

Nebuliser manufacturers cleaning instructions

Manufac-turer	Web link/ reference	Name of device	Type	Recommendations							Other	Replace
				Wash	Rinse after washing	Frequency of washing	Disinfect	Rinse after disinfection	Dry	Frequency of disinfecting		
Philips Respironics	Sidestream Plus Reusable high efficiency nebulizer Instructions for Use Ref 1092001 Published 2013 Koninklijke Philips Electronics N.V. [online] Available at: https://youtu.be/qFPFwbRr-OM [Accessed 15/08/19]	SideStream Plus	Breath en-hanced jet	Wash all items in hot soapy water.	Rinse in clean water.	After each use.	Boil in water with 2-3 drops of dish washing liquid for 10 minutes.	Rinse in clean water for 2 minutes.	Air dry	1/week	May be washed once a week contained in a basket on top rack of dishwasher. To reduce risk of infection, clean and disinfect by boiling in hot water between treatments.	Every 12 months
Philips Respironics	SideStream reusable kit Phillips Respironics Published 2018 Koninklijke Philips N.V.	SideStream reusable kit	jet	Wash all items (except tubing) in hot, soapy water.	Rinse all parts in clean water for 2 minutes.	After each use.	Boil (except mask and tubing) in water with 2-3 drops of dish washing liquid for 10 minutes.	Rinse all parts in clean water for 2 minutes.	Air dry	1/week	Wipe mask with dry clean cloth and air dry.	After 12 months use
Philips Respironics	SideStream disposable kit Ref 448,448A Philips respironics Published 2013 Koninklijke Philips Electronics N.V.	SideStream disposable kit	jet	Wash in warm, soapy water.	Rinse in clean, cold water.	After each use.	N/A	N/A	N/A	N/A	Do not immerse tubing in water. Wipe mask with clean dry cloth an air dry.	After 30 days use

Manufac-turer	Web link/ reference	Name of device	Type	Recommendations							Other	Replace
				Wash	Rinse after washing	Frequency of washing	Disinfect	Rinse after disinfection	Dry	Frequency of disinfecting		
Philips Respironics	I-Neb AAD system User guide Philips Respironics Published 2015 Koninklijke Philips N.V.	I-neb	AAD + PMT	Place mouth-piece, medi-cation chamber, medica-tion lid and drug guide in (supplied) washing basket. Submerge the basket in warm soapy water (3 drops of liquid detergent) and move basket back and forth.	Rinse parts (still in basket) in soft, distilled or filtered water. If the water is hard, rinse with water that has been boiled and allowed to cool.	After each use.	Submerge the parts in the washing basket, in a pan of soft, distilled or filtered water with 3 drops of liquid detergent. Bring to the boil and boil for 10 minutes.	Rinse with soft, distilled or filtered water.	Shake off excess water and allow to air dry.	Once per week	Use an antiseptic wipe to wipe away any moisture around the horn and sensor port cover. Not suitable for dishwasher or microwave. Do not use bleach or any other cleaning agents.	After 6 months
Philips Respironics	Cleaning your Aerogen Go Philips Respironics 1118514 Rev 00	Aerogen Aeroneb Go	VMT	Wash the nebulizer unit (med-ication cup &cap, nebulizer body, base and mouth-piece) in solution of warm water and dish washing soap. Do not soak.	Rinse under running, hot, tap water.	Rinse after each use, wash daily.	Rinse under running, hot, tap water. Bring a pan of distilled water to the boil and leave parts immersed in boiling water for maximum 20 minutes.	N/A	Shake off excess water and allow parts to fully air dry.	Optional weekly		1 year warranty

Manufacturer	Web link/ reference	Name of device	Type	Recommendations							Other	Replace
				Wash	Rinse after washing	Frequency of washing	Disinfect	Rinse after disinfection	Dry	Frequency of disinfecting		
PARI	PARI LC Family Instructions for Use (Cleaning and disinfection at home) Published 2016 PARI Pharma GmbH. [online] Available at: https://www.pari.com/fileadmin/user_upload/PARI.com_UK/Doc/IF-U/022D0098-O-de-en-IFU-LC-Family-Nebuliser.pdf [Accessed 15/08/19]	Pari LC Pari LC Plus Pari LC Plus Junior Pari Baby Pari LC Star	Breath enhanced jet	Place all disassembled components in warm tap water with a little dishwashing liquid for at least 5 minutes.	Rinse all parts thoroughly in running water.	After each use.	**A.** Place all parts in boiling water for 5 minutes. Using a clean pot and fresh water with reduced calcium content. **B.** Standard thermal disinector for baby bottles with a run time of at least 6 minutes **C**. Microwave Disinfector - place the product components in the disinfector with enough space between them to allow the steam to reach all surfaces reliably. 850-950W 4 minutes cooling time minutes 600-850W 6 minutes cooling time 2 minutes **D.** Chemical cleaning with disinfection carried out in a single cycle using 2% solution of Bomix®plus and soak for 5 minutes	For chemical disinfection rinse all parts thoroughly in running water.	Place on a dry, clean and absorbent surface and let them dry completely. When dry, wrap in a clean, lint-free cloth.	After cleaning	Remove all parts from pot or disinfector a s soon as disinfection has finished. Dry the parts.	After 1 year

Manufacturer	Web link/ reference	Name of device	Type	Recommendations							Other	Replace
				Wash	Rinse after washing	Frequency of washing	Disinfect	Rinse after disinfection	Dry	Frequency of disinfecting		
PARI	PARI LC SPRINT Family Instructions for Use Published 2015 PARI Pharma GmbH. [online] Available at: https://www.pari.com/fileadmin/user_upload/PARI.com-INT/Documents/IFU/023D1001-Instructions-for-use-PARI-LC-SPRINT-Nebuliser.pdf [Accessed 15/08/19]	PARI LC SPRINT PARI LC SPRINT Sinus PARI LC SPRINT Baby PARI LC SPRINT Junior PARI LC SPRINT Star	Breath enhanced jet	Place all disassembled components in warm tap water with a little dish washing for 5 minutes.	Rinse all parts thoroughly in running water.	After each use.	**A.** Boil in water for 5 minutes - use a clean pot and fresh water with reduced calcium content. **B.** Standard disinfector for baby bottles - run time of at least 6 minutes. **C.** Microwave disinfector - place the product components in the disinfector with enough space between them to allow the steam to reach all surfaces reliably. 850-950W 4 minutes 600-850W 6 minutes plus 2 mins cooling time **D.** Chemical disinfection 2% solution of Bomix® plus and soak for 5 minutes.	N/A if method A, B or C used. For method D, rinse after disinfection in running water.	Place on dry, clean, absorbent surface and let dry completely.	After cleaning	Wrap in clean, lint-free cloth and keep in dry, dust-free environment. NOTICE The LC interrupter is not designed to withstand exposure to microwaves, and must therefore not be disinfected in a microwave oven.	After 1 year

Manufacturer	Web link/ reference	Name of device	Type	Recommendations							Other	Replace
				Wash	Rinse after washing	Frequency of washing	Disinfect	Rinse after disinfection	Dry	Frequency of disinfecting		
PARI	Instructions for use eFlow® rapid nebuliser system Published 2018 PARI Pharma GmbH. [online] Available at: https://www.pari.com/fileadmin/user_upload/PARI.com-INT/Documents/IFU/178D1007-Instructions-for-use-eFlow-rapid.pdf [Accessed 15/08/19]	eFlow® Rapid Tolero® Zirela® Altera®	VMT	Place in warm tap water with a little dish washing for 5 minutes.	Rinse under running tap water.	Immediately after each use.	A. Thermal disinfector with operating time of 6 minutes B. boil in distilled water for at least 5 minutes C. Chemical disinfection with quaternary ammonium compounds - suggested Bomix® plus (Bode) for 5 minutes	Not specified.	Place on dry, clean surface and allow to dry completely.	At least once/day	Store in a clean, dust-free place eg nebuliser bag Microwave disinfector not suitable.	Nebuliser handset 1 year Aerosol head 3-6 months

Manufacturer	Web link/ reference	Name of device	Type	Recommendations							Other	Replace
				Wash	Rinse after washing	Frequency of washing	Disinfect	Rinse after disinfection	Dry	Frequency of disinfecting		
Omron Healthcare Inc.	Omron Instruction Manual Microair® vibrating mesh technology Model NE-U22V Published OMRON Healthcare Inc. 2007. [online] Available at: https://omronhealthcare.com/products/microair-nebulizer-neu22v/ [Acccessed 15/08/19]	Microair® Model NE-U22V	VMT	Nebulise a small amount of distilled water for 1-2 minutes.	Rinse with distilled water.	After each use.	Make disinfecting solution of **A**. 1 part white vinegar, 3 parts distilled water or **B.** Mild detergent soap (dishwashing soap in distilled water) Nebulise a small amount of the solution for 1-2 minutes. Soak parts in the disinfecting solution for 10-15 minutes	Rinse with distilled water.	**A.** gently wipe with a soft clean cloth **B.** allow to air dry in a clean environment	Daily - after the last treatment of the day.	Store in storage case or in clean environment. Do not use household bleach. Do not rinse in strong running water. Not suitable for microwave oven.	
Hudson RCI		Hudson T Up-Draft	jet	emailed								
Vital Signs Inc		Marquest Acorn II	jet	emailed								
Phillips Respironics		Inspiron	jet	emailed	discontinued							
Philips Respironics		Halolite	AAD		discontinued							
Philips Respironics		Prodose	AAD		discontinued							

Appendix VIII

ACT devices cleaning sheet

Device: Acapella® choice vibratory PEP device

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
Smiths Medical International, Ltd. 1500 Eureka Park, Lower Pemberton, Ashford, Kent TN25 4BF	Clean on a regular basis, or right after each use, especially if used inconjunction with a nebulizer.	Soak disassembled device and mouthpiece in warm, soapy water as required to remove visible contaminants.	Liquid dish detergent (Dawn or equivalent), 2tbsp/1 gallon water.	Rinse thoroughly with sterile water.	Boil in water up to twice daily for 5 minutes. In addition, Smiths Medical suggests the use of distilled or sterile water to lessen the potential of clacifying metallic components.	Will functionally withstand autoclaving at temperatures not to exceed 136°C for a maximum of 30 cycles.	Dishwasher safe. Place the parts on the top shelf.	Soak 5 minutes, twice daily. Compatible with 70% isopropyl alcohol. Rinse with sterile water (made by boiling water for 5 minutes).	Cidex® or equivalent	Air dry. Drain the device by placing it in a normal resting position.	Bleach is not recommended - may deteriorate the nickel plated mechanism. Do not microwave.

Device: PEP/RMT™

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
Wellspect Healthcare, DENTSPLY IH Limited, Building 3, The Heights, Weybridge, Surrey, KT13 0NY	Not specified.	Wash the disassembled parts in warm water or automatic washing machines designed for medical equipment will normally include program cycles for heat disinfection.	Use a detergent suitable for the products' materials.	Rinse in clean water.	Use clean water, boil parts for at least 10 minutes.	Use standard autoclaving equipment adjusted for max 121°C, or 134°C, whichever is applicable for the product.	Automatic washing machines designed for medical equipment will normally include program cycles for heat disinfection.	To avoid premature material deterioration only use compatible chemical and disinfectant brands. Follow the manufacturer's instructions for the detergent or chemical disinfectant as to dilution and exposure time. Substances containing phenol should be avoided. After exposing the parts to the chemical disinfectant, rinse thoroughly in clean water to remove all residues.		Leave parts to dry and/or cool completely before reassembling the part.	After cleaning, disinfecting and/or sterilizing carefully inspect all parts for damage or excessive wear and replace if necessary. In case of material deterioration, e.g. cracking, the parts should be replaced. Some methods may cause discolouration of silicone parts without having an impact on their function. The face masks have an expected lifetime of 1–3 years, depending on usage.

Device: LUNG FLUTE®

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
Medical Acoustics, LLC 640 Ellicott St. Buffalo, NY 14203 USA (888) 820-0970 www.lungflute.com	The reed inside your LUNG FLUTE® should be replaced about every two weeks depending on the frequency of use. Clean the LUNG FLUTE® when you replace the reed. If a film build up is noted inside the LUNG FLUTE® or if it does not dry between sessions, wash it more frequently.	Wash with mild dish soap and hot water.	Mild dish soap.				Follow your organization's internal procedure for disinfecting anaesthesia breathing circuits, eg wet pasteurization at 70°C for 30 minutes with detergent cleaning. This is accomplished with washer disinfectors.			Allow the pieces to air dry or dry them manually before reassembling.	

Device: BUBBLE PEP: Hydrapep

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
Resolve Healthcare www.hydrapep.com.au	Change water between sessions and wash daily.	Wash daily - is dishwasher safe.	Not specified.								

Device: AEROBIKA™

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
Trudell Medical International		Wash in warm soapy water. Allow to soak for 15 minutes. Agitate gently.	Not specified.	Rinse in warm distilled water and shake out any excess.	Electronic steam steriliser is recommended. May also be boiled or a microwave steam bag used.		Can be cleaned on the top rack of a dishwasher.	Bleach or a respiratory disinfectant may be used. Isopropyl alcohol. Hydrogen peroxide.		Allow to airdry thoroughly.	

Device: RC-CORNET®

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
R. Cegla GmbH & Co. KG Horresser Berg 1 56410 Montabaur	At least twice weekly.	Disconnect the mouthpiece with the valve hose from the curved tube and insert the drying spatula into the hose. Important: Throughout the cleaning process, the drying spatula must keep the valve hose open to prevent it from sticking together. All parts may be cleaned in a vaporizer, by means of steam or in boiling water at temperatures between 121°C and 134°C.	Not specified.		Further cleaning possibilities: RC-Clean cleaning bag Disassemble the RC-Cornet® . Place all parts in the cleaning bag.					During the drying process, the drying spatula is designed to hold the valve tube open to prevent the tube from sticking.	

Device: Flutter

Manufacturer	Washing				Disinfection					Dry	Other
	Frequency	Wash	Detergent	Rinse	Boil	Autoclave	Dishwasher	Chemical			
								Alcohol	Glutaraldehydes		
Clement Clarke Cartel Business Estate Edinburgh Way, Harlow CM20 2TT Tel: 01279 414969 Email:resp@clement-clarke.com	After each session.	Rinse after each use. Every two days disassemble your FLUTTER and wash in a solution of mild soap or detergent. Rinse.	Mild soap or detergent.	Rinse all components with tap water.		Autoclave at 137°C	DO NOT clean in diswasher. This will cause damage to the components.	Lancerzyme® Chlorine dioxide generator (egTristel), Sodium hypochlorite (NaOCL) eg Milton, Sodium dichloroisocyanurate (NaDCC)eg presept or actichlor			Do not use chlorine, bleach or other chlorine-containing products.

The Cystic Fibrosis Trust is the only UK-wide charity dedicated to fighting for a life unlimited by cystic fibrosis (CF) for everyone affected by the condition. Our mission is to create a world where everyone living with CF will be able to look forward to a long, healthy life.

At the Trust we are:

- Investing in cutting-edge research
- Driving up standards of clinical care
- Providing support and advice to people with CF and their families
- Campaigning hard for the issues that really matter

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Fighting for a Life Unlimited