

Australia 2023

Standards of Care For Cystic Fibrosis

Tonia A Douglas and Siobhain Mulrennan
Steering Committee Chair and co-Chair



These Standards have been endorsed by the Thoracic Society of Australia and New Zealand

Douglas TA, Mulrennan S, Fitzgerald DA, Prentice B, Frayman K, Messer M, Bearcroft A, Boyd C, Middleton P, Wark P.
Standards of Care for Cystic Fibrosis, Australia 2023. Cystic Fibrosis Australia, North Ryde, Sydney.

Cystic Fibrosis Australia (CFA) is the national body representing all Australians living with cystic fibrosis and the proud custodian of these Standards of Care. CFA strives for the best outcomes for the cystic fibrosis community through advocacy, increasing access to therapies, supporting research, and improving quality of care and clinical outcomes. These revised Standards of Care will support improved clinical care and highest quality outcomes so that people living with cystic fibrosis can have longer, healthier lives. With sincere thanks to the steering committee and all the contributors, this document will pave the way for better outcomes for everyone living with cystic fibrosis.

Contents

Contents	3
Introduction.....	6
Preface.....	7
Purpose and Scope	7
Consultation Process	9
Steering Committee.....	9
The Interdisciplinary Expert Reference Group.....	10
Endorsement	10
Review Process.....	11
Disclosure Statement.....	11
Abbreviations and Acronyms.....	12
Methods.....	14
Search Strategies	14
Inpatient Care	15
Background.....	17
Experience in Australia	18
Facilities.....	19
Staff	19
Services	20
Admission to Hospital and Emergency Access	21
Intravenous Access.....	23
Medicines and Drug Treatment	23
Physiotherapy - Assessment and Treatment.....	24
Nutrition and Dietetic Therapy - Assessment and Treatment.....	25
Discharge Planning.....	26
References.....	27
Home Therapy	28
Background.....	30

Evidence	30
Adult Studies	31
Paediatric studies	32
Experience and practice in Australia	32
Recommendations.....	33
References.....	37
Outpatient Care	39
Background.....	41
Experience in Australia	42
Recommendations for Outpatient Care Personnel, services, and facilities	43
Frequency of outpatient reviews.....	45
Routine Clinic Visit	45
Annual Review	47
Infection Control.....	54
First Outpatient Visit.....	55
Following new CF diagnosis.....	55
Transfer from another CF centre	56
Rapid review clinic.....	57
Telehealth clinic.....	57
Atypical CF.....	58
.....	58
Other specialist outpatient services	59
Endocrinology	59
Gastroenterology and hepatology	59
Genetic services	60
Communication	60
Patient Contact Arrangement	60
Reports.....	60
Team communication	61
Exacerbation plan.....	61

Health promotion	61
Education	61
Immunisation	62
Dental health.....	62
Avoidance of environmental tobacco smoke and hepatotoxins	63
Research and Clinical Trials	63
Shared care arrangements	63
The role of the general practitioner	64
References	65
Diagnosis of Cystic Fibrosis	69
Making the diagnosis of cystic fibrosis in neonates.....	71
CF Newborn Screening (NBS)	71
Clinical considerations around NBS.....	73
Uncertainties around NBS diagnosis.	75
Prenatal diagnosis of cystic fibrosis.....	76
Initial education for the family / young person with CF	78
.....	79
Follow-up	79
Diagnosis of cystic fibrosis in the adolescent and adult years	79
Diagnostic Workup in an adolescent or adult with features of CF	80
Management of the adolescent or adult with proven CF at the time of diagnosis.....	82
Management of the adolescent or adult with suspected CF or CF related disorder/CFSPID	82
References	83
Appendix 1	85
Potential conflicts of interest	85

Introduction

The landscape of Cystic Fibrosis care in Australia and internationally has changed considerably since the first iteration of the Cystic Fibrosis Standards of Care was published in 2008. The COVID-19 pandemic led to the adoption of Telehealth into routine clinical care across Australia with widespread endorsement by people with CF and their caregivers. Nontuberculous mycobacterial infections have provided new challenges in the management of lung disease and infection control. The era of CFTR modulator therapies has well and truly arrived, and the benefits are being realised from early childhood to adulthood with reductions in hospital admissions, improved lung health and nutritional trajectories, and expectations of greatly improved quality of life and life expectancy.

Adult patients now account for over half the population of people with CF in Australia, and there is increasing emphasis on ageing healthily and providing care that accommodates the needs of active and productive members of society. Longevity in CF brings increasing disease complexity for many and greater demands on CF services to provide resources and expertise in the management of age-related complications and diseases. Paediatric CF care in Australia will inevitably evolve as children gain access to CFTR modulator and novel therapies at younger ages and we anticipate delayed progression or even prevention of lung disease in children. We do not yet fully understand the impact of these therapies on CF disease trajectory and models of care delivery.

The Standards of Care document remains central to defining what is expected of cystic fibrosis multidisciplinary teams in the provision of care for people living with cystic fibrosis in Australia. In addition, the Standards of Care document serves as an advocacy platform for people with CF, outlining what is expected as the essentials for consistently improving outcomes.

As the care of people with cystic fibrosis continues to develop and improve, and at a rapid pace in this current era, so the Standards of Care document has evolved into an on-line resource that will be updated regularly and respond to the changing landscape of CF care and the changing needs of people with CF.

Chapters will be added, and existing chapters reviewed as part of a “living document” for the care of people with cystic fibrosis in Australia. All the previous content has been updated to provide the latest evidence to guide recommendations. Additional emphasis has been placed on the psychological aspects of living with cystic fibrosis for people and their families living with CF, the role of Cystic Fibrosis Transmembrane Regulator (CFTR) modulators and consideration of the differing needs and standards for care across the lifespan.

**Dominic Fitzgerald and Tonia Douglas,
on behalf of the Steering Committee**

Preface

Purpose and Scope

The purpose of the revised Standards of Care document is to define what is expected of health care providers and health-systems delivering care to people with CF in Australia. The scope of this revised document has been extended to reflect the differing needs of people with CF across the lifespan, and specific standards for care at key developmental and life stages. In this document social and cultural markers and transitions in CF care have been used to distinguish each life stage.

The areas of CF care covered by the revised Standards will include:

- Facilities, staffing, and services required at CF centres and CF clinics
- Inpatient care
- Home therapy
- Outpatient care
- Outreach Services
- Newly diagnosed people with CF
- Role of cystic fibrosis organisations
- CF care across the lifespan:
 - *Infancy and childhood*
 - *Transition and young adult care*
 - *Pregnancy and family planning*
 - *Ageing with CF*
 - *End of life care and transplantation*

Each chapter provides standards of care for people with CF and includes a brief literature review with recommendations for clinical care based on the available evidence. It is not intended to be a clinical guideline and should be read in conjunction with best-practice guidelines listed in the chapters and including the following:

Nutrition guidelines for cystic fibrosis in Australia and New Zealand (NZ), 2017

Australasian clinical practice guidelines for social work in cystic fibrosis, 2017

Physiotherapy for cystic fibrosis in Australia and New Zealand: A clinical practice guideline, 2016

The authors believe that creation of these standards is an essential process in ensuring equitable and high-quality CF care is accessible to all patients across Australia.

This document provides standards by which CF centres across Australia can benchmark their facilities and services and forms the basis for peer review and quality improvement initiatives. It also highlights

resource limitations and other barriers that may prevent centres from implementing standards and best practice care. To this effect, the standards have an important role in advocacy for, and the commissioning of, CF resources. It is the goal of our patients, their families, and the CF professional community that all CF centres in Australia endeavour to meet these standards and provide the best care possible.

Consultation Process

Consistent with the original document development, the revision of the standards of care was proposed by the cystic fibrosis centre directors committee, supported by consumer representation and Cystic Fibrosis Australia.

A steering committee of representatives from the CF centre directors committee, original authors of the 2008 document, and consumer representatives and advocates, coordinated the development of the revised standards of care. Regular teleconferences were held throughout 2020-23 to outline the scope and purpose of the revised document, and to create writing groups for the chapters. Standards were established and updated through review of existing scientific literature, published guidelines, and consensus statements.

Drafts of the updated chapters were authored and underwent peer review by members of the expert reference group including nurses, specialist physicians, psychosocial health professionals, consumer representatives, and allied health professionals. Where evidence for best practice was weak or unavailable, recommendations for care were established through consensus from experts and contributors.

This document development process will be applied as new chapters are revised and updated within this “live document”.

Steering Committee

Dr Tonia Douglas – (Chair) - Queensland Children’s Hospital, Brisbane - physician

Professor Siobhain Mulrennan – (Co-Chair) - Charles Gairdner Hospital, Perth - physician

Professor Dominic Fitzgerald – Children’s Hospital at Westmead, Sydney - physician

Professor Peter Wark – John Hunter Hospital, NSW - physician

Dr Bernadette Prentice – Sydney Children’s Hospital, Sydney - physician

Dr Katherine Frayman – Royal Children’s Hospital, Melbourne, Victoria - physician

Professor Peter Middleton – University of Sydney, New South Wales - physician

Jo Armstrong – CEO Cystic Fibrosis Australia - consumer advocate

Mr Mitch Messer – consumer representative, community involvement coordinator, Telethon Kids Institute, Perth - consumer representative

Ms Caz Boyd – consumer representative

Ms Amanda Bearcroft – registered nurse and consumer representative

Nicki Mileham – Cystic Fibrosis Australia - consumer advocate.

The Interdisciplinary Expert Reference Group

The committee acknowledges the expertise of the many specialist health care professionals (nursing, medical and allied health) and the invaluable contribution of consumer representatives who provided authorship, chapter reviews, feedback, and suggestions for chapter development throughout the drafting of these revised standards. The steering committee is very grateful to each of them for their valuable time and commitment.

Dr Stella Li – clinical psychologist, Children’s Hospital, Westmead, Sydney, New South Wales

Sue Morey – nurse practitioner CF, Sir Charles Gairdner Hospital, Perth, Western Australia

Professor Phil Robinson – physician, Royal Children’s Hospital, Melbourne

Penny Mitchell – clinical nurse consultant CF, Queensland Children’s Hospital, Brisbane, Queensland

Dr Jagdev Singh – physician, Children’s Hospital Westmead, Sydney, New South Wales

Professor Hiran Selvadurai - physician, Children’s Hospital Westmead, Sydney, New South Wales

Tamara Lazzarin – CF physiotherapist, Queensland Children’s Hospital, Brisbane, Queensland

Jordan Henderson – CF dietitian, Sir Charles Gairdner Hospital, Perth, Western Australia

Annie O’Donohue – senior CF dietitian, Queensland Children’s Hospital, Brisbane, Queensland

Tamara Thornton – senior CF physiotherapist, Sir Charles Gairdner Hospital, Perth, Western Australia


Sharon Hunt – clinical nurse consultant CF, The Children’s Hospital Westmead, Sydney, New South Wales

Dr Scott White – obstetrics and gynaecology specialist, maternal and fetal medicine, King Edward Memorial Hospital, Perth, Western Australia

Professor Andrew Biggin – endocrinologist, Children’s Hospital Westmead, Sydney, New South Wales

Kyle Collis – consumer representative

Megan France – physician, The Prince Charles Hospital, Brisbane, Queensland.



The revised chapters have been endorsed by the Thoracic Society of Australia and New Zealand (TSANZ).

Review Process

It is intended that this “live document” will be available as an online resource and will be reviewed, added to, and updated regularly to create a resource that is contemporary and responsive to the rapidly changing landscape of CF care. Updates of the standards will incorporate new evidence from the scientific literature and the consensus of experts and stakeholders in CF care and will reflect the growing number of contributors to authorship and review.

Disclosure Statement

The development of the 2023 Standards of Care was supported by Cystic Fibrosis Australia and by voluntary and in-kind contributions from the team at Deloitte. Potential conflicts of interest by membership of the Steering Committee are listed in Appendix 1.

Abbreviations and Acronyms

ACFDR	Australian Cystic Fibrosis Data Registry
ATAGI	Australian Technical Advisory Group on Immunisation
BPAP	Bi-level positive airway pressure
BMI	Body mass index
CF	Cystic fibrosis
CFA	Cystic Fibrosis Australia
CFRD	Cystic fibrosis-related diabetes
CFSPID	Cystic fibrosis Screen Positive Inconclusive Diagnosis
CFTR	Cystic fibrosis transmembrane conductance regulator protein
CT scan	Computerised tomography scan
CRC	Colo-rectal cancer
CXR	Chest radiograph or Chest X-ray
CVC	Central venous catheter
DEXA scan	Dual energy x-ray absorptiometry scan
DIOS	Distal intestinal obstruction syndrome
ENT	Ear nose and throat
FEV ₁	Forced expiratory volume in one second
FBC	Full blood count
GP	General practitioner

ICU	Intensive care unit
IRT	Immunoreactive trypsinogen
IV	Intravenous
IVAD	Intravenous access device
LFT	Liver function tests
MBW	Multiple breath washout
MDT	Multidisciplinary team
MRI	Magnetic resonance imaging
MRSA	Methicillin resistant <i>Staphylococcus aureus</i>
NBS	CF newborn screening
NIV	Non-invasive ventilation
NTM	Nontuberculous mycobacteria
OGTT	Oral glucose tolerance test
OPD	Outpatient department
PBS	Pharmaceutical Benefits Scheme
PICC	Peripherally inserted central catheter
PERT	Pancreatic enzyme replacement therapy
PPE	Personal protective equipment
RACP	Royal Australasian College of Physicians
RCT	Randomised controlled trial
RMO	Resident medical officer
TSANZ	Thoracic Society of Australia and New Zealand
US	Ultrasound
VRE	Vancomycin-resistant <i>Enterococcus</i>

Methods

Search Strategies


Literature searches for this document were conducted using MEDLINE, PubMed, CINAHL, PsycINFO and the Cochrane Library using the terms relevant for each of the sections. Searches were limited to articles in English and newly published literature from 31/12/2008 (from the 2008 Standards of care document) up to 31/12/2022 was included. Literature published prior to 2008 was considered if no new evidence was available. Manual search of reference lists was undertaken, and appropriate proceedings of conferences were reviewed by the lead authors of each of the sections. Given the limited

evidence available for many areas of cystic fibrosis practice, both randomised control trials and research conducted with less robust design were included. Abstracts were reviewed with descriptions of the care of patients with CF relevant to each specific section. Reference lists for each of the selected published papers were also reviewed for reports not identified in the search. Published clinical guidelines and associated reference lists were also reviewed, their relevance assessed and included where appropriate.

Inpatient Care

Siobhain Mulrennan, Sue Morey,
Megan France



- 
- Standard 1** CF centres should have the expertise to meet the inpatient needs of people with CF.
- Standard 2** CF centres should have the facilities, staff, and services to manage all complications of CF, and the ability to arrange timely access to specialist care in the same hospital or other health care facilities as needed.
- Standard 3** CF centres should have ward accommodation and facilities that meet the needs of people with CF.
- Standard 4** People with CF should not share rooms with CF or non-CF patients and should be managed in single rooms with appropriate infection control guidance.
- Standard 5** All CF centres should have plans and systems for rapid or emergency assessment and admission of patients with CF.
- Standard 6** When patients with CF are admitted to hospital and not under the direct care of the CF team there should be prompt communication with the CF centre staff to optimise care.
- Standard 7** CF centres should have protocols for management of all common co-morbidities and complications of CF.

Background

Adults and children with CF frequently require admission to hospital. While CFTR modulator therapies are reducing hospitalisation rates across Australia, admission is still a key event in the lives of people with CF. The most common reason for admission is pulmonary exacerbation. Other, less frequent indications include complications of respiratory disease (e.g., pneumothorax, haemoptysis), suboptimal nutrition, gastrointestinal disease (e.g. Distal Intestinal Obstruction Syndrome (DIOS), complications of CF related liver disease, unstable diabetes mellitus, renal impairment and renal disease, psycho-social problems, and peri-operative and peri-procedure care.

Admissions to hospital may result from non-CF problems such as trauma or elective surgery. Thus, people with CF may be cared for by hospital staff less familiar with CF management and the specific needs of patients with CF, which has the potential to lead to errors in management and patient dissatisfaction.

It is important for hospital staff to recognise the characteristics and needs of patients with CF. It is important to be aware that people with CF:

- May have frequent admissions to hospital.
- Often find admission to hospital stressful despite frequent admissions, particularly children undergoing procedures.

- Are often younger than other adult patients in an adult inpatient setting.
- Have a longer average length of stay, typically 10 – 14 days.
- May remain ambulant and independent for much of their admission.
- May request leave for study, work, or recreation which should be considered and negotiated to maintain quality of life.
- Have specific dietary needs.
- Require specific infection control practices.
- Have admissions that are usually planned but may be urgent.
- Feel most comfortable with staff who are familiar with CF management and when patient knowledge and ideas around treatment are acknowledged and valued.
- People with CF, particularly adults, are often highly knowledgeable about their own condition and their care needs and are likely to be suitable to self-manage with clinician oversight, aspects of their own care in an inpatient setting, for example Pancreatic Enzyme Replacement Therapy (PERT) administration and dose selection, blood sugar monitoring, gastrostomy feeding and aspects of airway clearance.

Experience in Australia

Over one thousand people with CF are hospitalised on one or more occasions in Australia each year¹.

As noted in the [Australian CF Data Registry](#) adults >18 years living with CF now form the majority of patients across Australia. Adult patients have traditionally had longer inpatient stays than children and adolescents. In 2019 the median number of accumulated days receiving intravenous (IV) therapy in hospital was 14 days for both children and adults¹. Care of adults with CF is becoming increasingly complex due to improved survival for those with severe disease, increased

accumulation of co-morbidities both related and unrelated to CF, increased social responsibilities that accompany longer life and complications of care over many years. The care of adolescents and young adults requires special consideration in view of their unique health care and developmental needs, with provision of inpatient care preferably within a young adult/adolescent friendly environment.

Recommendations

The facilities, staff and services needed to care for people with CF in hospital are those required for a CF centre as defined previously². People with CF may be admitted to a different ward or hospital to their usual CF centre or CF ward and attending staff have a responsibility to communicate with the CF multidisciplinary team to ensure each patient receives optimal CF care. The following represent consensus views of the steering and expert reference groups (expert opinion) and are consistent with the National Institute for Health and Care Excellence guidelines on the diagnosis and management of cystic fibrosis (www.nice.org.uk/guidance/ng78)³

Facilities

- Hospital facilities needed to manage complications of CF should be readily available and easily accessed.
- Ward accommodation
- Admission to a ward familiar with caring for people with CF or chronic respiratory disease is highly recommended, ideally a respiratory medicine ward.
- Single rooms and bathrooms are required for patients for optimal infection control ^{2,4,5}
- Space is required within the inpatient room for associated medical equipment, e.g. BIPAP circuits, gastrostomy feeds, IV antibiotics and physiotherapy equipment.
- Additional space for caregivers of children, partners, and family members of adults with CF should be considered.
- Sufficient space and equipment within the inpatient room to study, play and / or work is required.
- Space and equipment for exercise within the patient's single room.
- Space and equipment for food preparation / storage within the patient's single room
- Hospital food services able to provide appropriate food that is age- and culturally appropriate and which meets CF-specific dietary needs. Individual patient menu/meal choices and timely bedside meal delivery for patients in isolation are required standards of nutritional care for people with CF.
- Designated hospital play and leisure areas for children and adolescents who are able to leave their rooms according to infection control policies.

Staff

- The CF multidisciplinary team and relevant specialists should be readily available.
- Where possible and appropriate people with CF should be admitted under the care of a CF physician and CF team. If this is not medically appropriate (e.g., acute surgical problem or regional hospital) the CF team must be notified by the attending staff who have a responsibility to communicate and maintain close contact with the CF centre team throughout the admission.
- Health professionals caring for people with CF should have the necessary training and skills in the provision of CF care.

Services

- Acute and emergency access services for people with CF are required. Emergency departments should have policies for people with CF to receive urgent care including admission to hospital. The CF physician should be notified as soon as Emergency department staff members have assessed the patient's condition to discuss diagnosis and management.
- The CF centre should have policies and protocols for admission, investigations, treatment, and monitoring of progress and these policies shared with regional hospital CF providers. This should include protocols for the detection and management of respiratory status deterioration, CF related complications, pain management and infection control.
- All hospital medical and nursing staff should know how to access CF care protocols and how to seek advice from the CF team after hours. Access to a CF consultant for advice after hours should be available.
- The specialist CF centre should have the ability to manage all CF related problems, particularly emergencies such as haemoptysis, pneumothorax, respiratory failure, bowel obstruction and bleeding oesophageal varices. Protocols for the management of these complications should be readily available to both the CF centre and regional providers as needed.
- Planning and provision of appropriate venous access should be undertaken prior to admission or soon after admission (see below).
- Protocols for use of all medicines required by people with CF, particularly intravenous antibiotics, should be available ⁶
- Physiotherapy assessment treatment and an individualised exercise program should be undertaken in accordance with published national [physiotherapy guidelines](#) ¹¹
- Dietetic therapy assessment and provision of appropriate diet and enteral feeding should be provided within 24-48 hours of admission, reviewed regularly during admission and prior to discharge¹²
- Specialist CF pharmacists should be available to educate and advise people with CF and their caregivers about medicines during inpatient admissions and on discharge from hospital and provide advice and support to other healthcare professionals and regional pharmacists about CF medicines and prescribing.
- Detailed psychosocial assessment and counselling, including the effect of hospitalisation on emotional well-being, work, education, and home life should be provided in accordance with the [clinical practice guidelines](#) for social work in CF.
- The CF specialist nurse should provide support and education for the ward-based nursing staff within working hours and oversee inpatient progress.
- Inpatient care should follow robust local infection control policy in line with current international recommendations ⁽²⁻⁵⁾. Hospitals should have specific infection control policies for

patients with *Mycobacterium abscessus*, *Burkholderia cepacia* complex infection, MRSA or VRE infection⁵⁻¹⁰. These policies should provide clear guidelines around staff precautions, patient equipment, the movement of patients within shared areas of the hospital (e.g. pharmacy, medical Imaging, pulmonary function laboratory, gymnasium, hospital school).

- Inpatient admission may be regarded by the CF team as an opportunity to continue education of patients and families. Co-development of individualised health maintenance and emergency action plans with patients and caregivers is recommended.
- Use time in hospital for optimisation of management of current problems and an opportunity to screen for complications such as

CF-related diabetes mellitus, and those that require laboratory investigations and specialist consultations.

- Policies and services to support home intravenous antibiotic therapy are highly desirable.
- School, vocational, and tertiary education should be supported for inpatients.
- The cystic fibrosis multidisciplinary team should have access to specialist expertise relevant to cystic fibrosis in the following areas: microbiology, pulmonary function testing, diabetes and endocrinology, gastroenterology, hepatology, renal, rheumatology, psychiatry, interventional radiology, surgical specialties including ENT, obstetrics and gynaecology, pain management and palliative care.

Admission to Hospital and Emergency Access

- Clear policies should be in place to ensure key hospital staff (including switchboard operators and CF/respiratory ward staff) are aware of the out-of-hours contact arrangements for people with CF.
- The patient's diagnosis of CF should be readily identifiable in the medical records.
- The CF centre should inform people with CF and their carers how to access help during out of hours.

- The admitting medical staff should notify the CF medical team and CF ward of the presenting medical problem and of the hospital admission.
- Check sputum microbiology results for presence of multi-resistant organisms.
- including *Staphylococcus aureus* (MRSA), *Vancomycin-resistant enterococcus* (VRE), *Mycobacterium abscessus* or *Burkholderia cepacia* complex. If these organisms are present, follow CF infection prevention and control guidelines for management in hospital.

- Initial assessment should include identification of all CF and non-CF related medical and psychosocial problems.
- Check history of adverse drug reactions with the patient/family and their medical record.
- Initial investigations should be appropriate for the presenting problem and for assessment of status of respiratory disease.

For the latter, patients should have:

- Lung function testing when able to be performed (e.g. FEV₁ and FVC).
 - Oxyhaemoglobin saturation (SpO₂) monitoring, where clinically indicated
 - Arterial or capillary blood gases measured if high CO₂ levels are suspected.
 - Sputum sent for microbiology.
 - A chest X-ray, or more detailed chest imaging, when clinically indicated.
 - Plan venous access, ideally prior to admission and in consultation with the patient/family. Initially, use a totally implantable vascular access device if available or peripheral IV line.
- Consult physiotherapy service for treatment and collection of a sputum sample for microbiological culture and sensitivities.
 - Consult CF dietitians for prompt assessment to allow timely access to appropriate CF diet in hospital, nutritional and dietary needs assessment and supports including enteral feeds, oral supplements, PERT, and other nutritional medications.
 - The plan for each admission should be clearly defined, with indication(s) for the admission, aims, and with therapeutic and patient goals stated and agreed on by the patient/family and team. The treatment plan should be appropriate for the presenting problems and include usual medications, investigations and referrals to specialists as required.
 - For most people with CF admitted to hospital, antibiotic treatment should be commenced without delay.
 - Antibiotic treatment will depend on usual organisms (usually anti-Pseudomonal) and should follow CF centre protocols or guidelines^{6,9}.
 - Discharge planning should begin at this time and develop in accordance with patient progress (see end of section).

Intravenous Access

- Centres should develop a plan for IV access for each person based on knowledge of their history of IV access.
- Options for IV access should be discussed with the patient/family at each admission.
- A peripheral intravenous line may be sited initially for unplanned admissions. A peripherally inserted central catheter (PICC) line, midline, or a central venous catheter (CVC) will usually be arranged during working hours.
- Venous access should only be performed by experienced staff. Centres should have staff with expertise in IV access, and facilities to provide a service for insertion of temporary peripheral or central venous lines as well as implantable vascular access devices (IVADs).
- Needle anxiety/phobia is important to consider. Involvement of a psychologist, or a child-life therapist for children, is recommended to develop individualised procedural action plans, and provide intervention for procedural fears and anxieties.

Medicines and Drug Treatment

- | | |
|--|---|
| <ul style="list-style-type: none"> - Enquire and document carefully each patient's adverse drug reactions and ensure records are up to date. Medication interactions, particularly in the context of CFTR modulators, indications and responses to treatments and patient preferences should be reviewed and discussed with the patient/caregiver. - The use of IV antibiotics should follow hospital and CF-centre guidelines that provide clear information on the selection of drugs, medication doses, and drug level monitoring. - Protocols for the management of antibiotic allergies should be developed. | <ul style="list-style-type: none"> - Patient/caregiver education about CF medications (current, new, or recently changed) and adherence should be provided by a specialist CF pharmacist, where available, or experienced CF medical staff. - Discuss self-management/bedside access to medications, e.g. PERT, where appropriate - Early planning for treatment at discharge and review of progress particularly if continuing IV antibiotics at home. - Education and equipment for nebulised antibiotics and tolerability test for initial dose should be conducted during inpatient stay. |
|--|---|

- When appropriate, the date of the next implanted vascular access device flush should be discussed, and an appointment made.
- Upon discharge, each patient should have a comprehensive, individualised home treatment

plan and allied health therapy plan for maintenance therapy and the management of future exacerbations. This should be written by staff with experience and expertise in CF.

Physiotherapy - Assessment and Treatment

- Access to physiotherapy services experienced in CF should be applied according to the [Australian Clinical Practice Guidelines for Physiotherapy in CF](#) ¹¹.
- Patients should be assessed by a physiotherapist within 24 hours of admission, with airway clearance performed as indicated by the patient's respiratory condition.
- Physiotherapy services should be available on evenings, weekends, and public holidays to enable daily physiotherapy input.
- Physiotherapy treatment includes inhalation therapy, airway clearance, musculoskeletal care, exercise, and management of any co-existing conditions where appropriate.
- Treatment (including frequency of sessions) should be tailored to the individual patient needs, according to age and clinical status.
- Physiotherapy devices to assist with airway clearance, including bilevel positive airway

pressure (BIPAP) and other forms of non-invasive ventilation (NIV) should be available.

- Facilities should be provided for inpatient exercise assessment and provision. Such facilities must consider current infection control guidelines for people with CF and should ideally be performed within the inpatient room or outside the hospital (if appropriate).
- In hospital care will include discharge planning, ongoing education, and review of their home program. If appropriate and available, referral to local physiotherapy or rehabilitation services with experience in CF care for ongoing follow up may be necessary.
- Home based courses of intravenous antibiotics to treat pulmonary exacerbations should, where possible, be supported by physiotherapy sessions in the home as part of a "hospital in the home" program.

Nutrition and Dietetic Therapy - Assessment and Treatment

- Access to dietetic services with experience and expertise in CF is required alongside nutritional assessment and management strategies in accordance with the Australasian [Clinical Practice Guidelines for Nutrition in Cystic Fibrosis](#)¹².
- Access to equipment required to support nutritional assessment, monitoring, goal setting and interventions in the ward setting including calibrated weighing scales.
- Dietetic services available to support timely initiation of, or changes to, nutrition regimens outside usual business hours (including but not limited to provision of enteral feeding supplies and oral nutritional supplementation).
- Policies for the identification, prevention and management of malnutrition should be available in accordance with the Australasian Clinical Practice Guidelines for Nutrition in Cystic Fibrosis¹² and local hospital standards.
- Frequency and breadth of dietetic review during the admission will be determined by the severity of respiratory illness, nutritional status and stability, the nutritional interventions provided and educational and discharge planning needs¹²
- Pancreatic enzyme replacement therapy (PERT), micronutrient status, bowel function, glucose tolerance, CFTR modulator usage (timing, food taken with medication), medical progress and alterations in therapy should be reviewed by the CF dietitian during the admission, with adjustments to therapy being implemented when indicated.
- Energy dense foods and/or oral supplements should be available to supplement the standard hospital diet, and food must be available for patients outside scheduled hospital mealtimes to meet specific nutritional and dietary needs of patients, for example, with diabetes, to support evening CFTR modulator therapy dosing, and in those with reduced appetite requiring frequent, smaller volume meals. Enteral nutrition regimens, including associated PERT and insulin requirements should be documented and reviewed.
- Access to services that manage placement and care of in situ feeding tubes (gastrostomy and nasogastric), support patient and caregiver education, and troubleshoot problems, are required. Communication between gastrostomy placement services and the CF team is necessary prior to any procedures to ensure CF specific issues around anaesthesia, sedation, post operative management of pain and respiratory care are planned and provided.
- The use of parenteral nutrition and monitoring of electrolyte, protein and nutrient balance may be required in selected cases and should be led by an experienced CF dietitian.
- Patients with additional complications (e.g. reduced bone mineral density), may require further dietary support, additional medications and counselling.
- Acute admissions provide the opportunity to provide additional education on nutrition and the appropriate approach to dietary modification.



Discharge Planning

Discharge planning should begin at the start of the admission as part of admission planning and outline the expected duration of the admission and expected discharge date. These details should be revisited throughout the admission to ensure admission goals are met and to ensure patient/caregiver and team satisfaction with progress. Arrangements for continuing treatment should be discussed with the patient and their family. This should include information about nebulised and/or oral antibiotics, airway clearance and nutrition therapy and any changes to medications. Follow-up should be arranged at a specific CF multidisciplinary team outpatient clinic that is appropriate for the patient with respect to their medical and psychosocial needs.

References

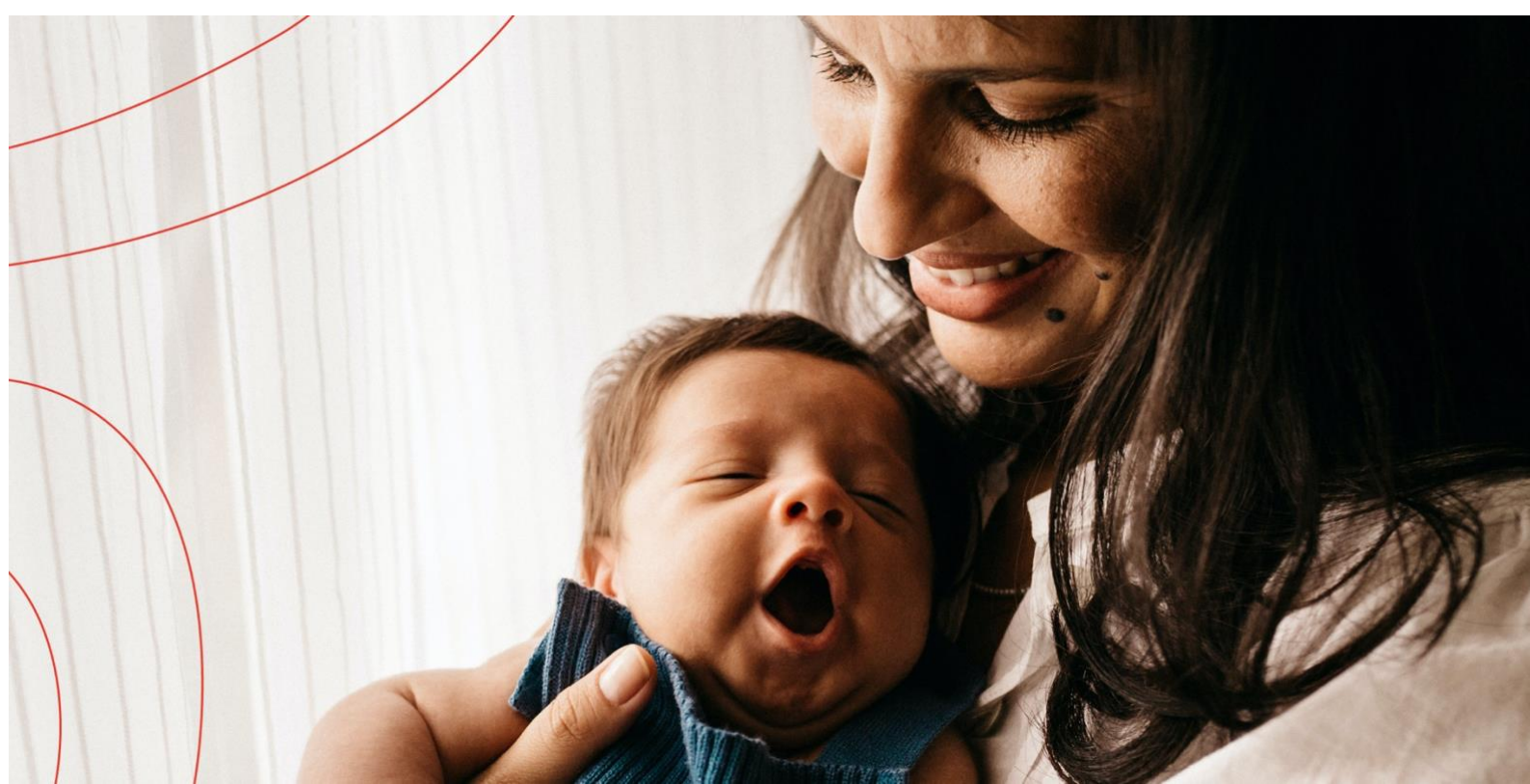
1. Cystic Fibrosis in Australia 2017. 17th Annual Report Australian Cystic Fibrosis Data Registry (2019). Monash University and Cystic Fibrosis Australia, North Ryde, NSW, Australia.
2. Conway, S., Balfour-Lynn, IM et al (2014). "European Cystic Fibrosis Society Standards of Care: Framework for the Cystic Fibrosis Centre." *Journal of Cystic Fibrosis* 13 (2014) S3-22.
3. Cystic fibrosis: diagnosis and management. NICE guideline. Published: 25 October 2017.
4. Standards for the Clinical Care of Children and Adults with cystic fibrosis in the UK, Second edition. (2011). The Cystic Fibrosis Trust, Bromley, Kent, UK.
5. Saiman, L, Siegel, JD et al (2013). "Infection Prevention and Control Guideline for Cystic Fibrosis: 2013 Update. *Infection Control and Hospital Epidemiology*." August (35): S1-S67.
6. Antibiotic Treatment for cystic fibrosis. Third Edition. (2009). The UK Cystic Fibrosis Trust Antibiotic Working Group, Bromley, Kent, UK.
7. The *Burkholderia cepacia* complex. Suggestions for Prevention and Infection Control, Second edition. (2004). The UK Cystic Fibrosis Trust Infection Control Group, Bromley, Kent, UK.
8. Methicillin Resistant *Staphylococcus aureus* (MRSA). (2008). The UK Cystic Fibrosis Trust Infection Control Group, Bromley, Kent, UK.
9. Castellani C, Duff AJA, Bell SC. et al. ECFS best practice guidelines: the 2018 revision. *J. CF* 2018. <https://doi.org/10.1016/j.jcf.2018.02.006>
10. *Mycobacterium abscessus*: Suggestion for infection prevention and control; Interim Guidance. (2013). The UK Cystic Fibrosis Trust *Mycobacterium abscessus* Infection Control Working Group, Bromley, Kent, UK.
11. Button, BM, Wilson, C et al (2016). *Physiotherapy in Australia and New Zealand: Clinical Practice Guideline*. Thoracic Society of Australia and New Zealand, Sydney, Australia
12. Saxby, N, Painter, C et al., (2017) *Nutrition Guidelines for Cystic Fibrosis in Australia and New Zealand*. Thoracic Society of Australia and New Zealand, Sydney, Australia.

Home Therapy

Tonia Douglas, Penny Mitchell



- Standard 1** Home therapy may be considered for the treatment of pulmonary exacerbations in selected patients with CF.
- Standard 2** Protocols for selection and training of patients (and carers), delivery of treatment and monitoring of responses are required.
- Standard 3** Home therapy services should replicate the key components of multidisciplinary inpatient care including nursing, physiotherapy, nutritional and psychosocial assessment, and management.
- Standard 4** Written information of the treatment plan and emergency contact details at the CF Centre should be provided to patients.



Background

Home therapy in this context is defined as the delivery of all aspects of care required for the management of pulmonary exacerbations in the home environment in people with CF. Home therapy for exacerbations has been provided by CF centres in Australia, and internationally, for people with CF for decades and has gained acceptance as an alternative to inpatient care in selected patients. Reported advantages of home therapy compared to inpatient care include:

- a) Less disruption to the daily life of patients and their families
- b) Better quality of life and reduced burden of care
- c) Reduced risk of hospital acquired infection
- d) Treatment is not delayed as may happen when waiting for a hospital bed
- e) Reduced direct health care costs compared with hospitalisations

Evidence

While home therapy offers certain advantages over inpatient care, it remains uncertain whether home therapy is as effective as treatment in hospital for individual patients, and there is uncertainty about the true cost effectiveness^{1,2}. There is a lack of

sufficiently powered, adequately designed, prospective studies comparing the outcome of pulmonary exacerbations treated at home or in hospital. Published studies are (often) single centre, observational studies of heterogeneous design and with differing models of home therapy delivery ranging from self-administered IV antibiotics alone through to multidisciplinary home exacerbation management. Details of patient selection are often unclear.

The available evidence suggests clinical outcomes with home therapy may be comparable to inpatient therapy in highly selected patients and using models of care that include support and supervision from CF team members.

No studies have demonstrated that home therapy is superior to hospital treatment, and several studies have reported inferior outcomes in patients receiving home therapy compared to inpatient care.

In conclusion, the available evidence with which to base recommendations for home therapy is limited and current recommendations stipulate that home therapy should not be considered if the resources and supports to provide care that is *equivalent* to inpatient care cannot be provided by the CF Centre ³.

Adult Studies

Home vs. inpatient care - comparable/non-inferior outcomes

1. In the one RCT ⁴ involving only 17 adult patients home-based therapy was non-inferior to hospital therapy for lung function, and weight and better quality of life.
2. Observational studies report similar lung function (FEV1) outcomes, weight gain, rates of lung function decline and time to next pulmonary exacerbation, and greater patient satisfaction and comfort among patients receiving home therapy ⁵⁻¹¹.
3. Four studies have demonstrated the cost of therapy was reduced both for the family and the hospital for home-based therapy ^{4,6,12,13} whereas the study by Bosworth et al ¹⁴ found that the

reduced costs of treatment (hospitalisation days) were offset by longer treatment courses and more frequent courses of antibiotic therapy.

Home vs. inpatient care - Inferior clinical outcomes

1. Analysis of data from 2773 patients across 75 US CF centres recruited to the Epidemiological Study of Cystic Fibrosis ² demonstrated a higher probability of regaining baseline lung function following pulmonary exacerbations among those treated in hospital, compared to those treated with home therapy. One-year outcomes in patients receiving predominantly home therapy were worse (lower weight and lung function) compared with those who had predominantly hospital-

based therapy¹³. Those who had a mixture of home and hospital therapies were intermediate for both clinical variables. Two

other studies demonstrated lower lung function outcomes and longer duration of antibiotics with home therapy.

Paediatric studies

Home vs. inpatient care - Comparable/non-inferior outcomes

1. Comparable outcomes (FEV1, BMI and safety) between home therapy and inpatient treatment have been reported in single centre observational studies of relatively small cohorts of children^{16,17,18}. Quality of life was reportedly higher among children receiving home therapy and cost savings were observed¹⁸.

Home vs. inpatient care - Inferior outcomes

1. Inferior outcomes with home therapy were reported in a single centre retrospective study of children and young adults¹⁹ over the period 1994-2003. While home and inpatient therapy both significantly improved FEV1, the lung function gains were greater, and the duration of treatment shorter, for those who received inpatient therapy.

Experience and practice in Australia

Home therapy is offered by most Australian CF centres for pulmonary exacerbations ²⁰. There are variations in methods for providing home treatment in Australia and different methods for delivery of home treatment.





Recommendations

The recommendations for provision of home therapy are derived from descriptive studies and consideration of overseas guidelines ³ and represent a consensus of the group (Expert Opinion).

1. Patients for home therapy should be selected to ensure best outcome

Considerations underpinning the decision to provide home therapy for individuals include:

CF team and patient preference and acceptance, the complexity of therapies required, the severity of disease and how sick the patient is currently, associated comorbidities and the patient's social supports and resources. In addition, it is important to ensure there are local resources available to provide treatment in the home that replicates the key services delivered in the inpatient setting (nursing, physiotherapy,

dietetics, psychosocial support etc.). The burden of home therapy for patients and carers and the need for respite or rest is an important consideration, particularly among patients/carers with a high care burden already such as parents of young children or carers for elderly relatives. Inpatient bed pressure is

not a primary indication for home therapy at CF centres.

Contraindications to home therapy include:

- a) Clinical instability that requires regular monitoring (e.g. patients with hypoxaemia, acute hypercapnia, recent major haemoptysis, or pneumothorax).
- b) Psychosocial factors including poor adherence, poor understanding of treatment needs, inadequate practical, financial and/or social supports may reduce the likelihood of success of home therapy.
- c) History of severe allergic reactions to prescribed drugs that have not been successfully controlled by desensitisation.
- d) Poor venous access
- e) Antibiotics that lack pharmacological stability using home delivery devices and dosing regimens.

Relative contraindications include:

- a) Remote geographical location or difficulty returning for review
- b) Very young children
- c) Previous poor response to home therapy
- d) Complex therapy involving multiple antibiotics, or other interventions including investigations, procedures, assessments and/or education that require inpatient specialist services
- e) Complex therapy involving multiple antibiotics, or other interventions including investigations, procedures, assessments and/or education that require inpatient specialist services
- f) Patient/carer preference for inpatient care

2. A standardised protocol for initiating home therapy should be established at each CF centre.

This should include:

- a) Assessment of patient suitability for home therapy through discussions with treating physician and patient/carer and development of standardised referral criteria
- b) Stable venous access, which will usually (but not exclusively) involve a PICC (peripherally inserted central catheter) line, midline catheter placed in the upper arm or IVAD (intravenous vascular access device) (e.g. Port-a-cath®)

- c) First dose of antibiotics to be administered in a hospital
- d) Antibiotics, delivery devices and disposables to be provided by the CF centre. Access to antibiotic delivery devices to be determined by local policy. Protocols for drugs, dosing, and frequency (as per local CF centre policy)
- e) An education program for the patients (and carers where appropriate) co-ordinated by the CF and home therapy teams. Patients should be reassessed periodically for their ability to perform home-based therapy
- f) A written protocol to be provided to the patients (and their family) at the initiation of each episode of home therapy, including details of contact arrangements with the CF team and the home therapy team during work hours and after hours

3. Care and monitoring of patients receiving home therapy should replicate, as close as possible, guidelines for inpatient care.

Models of care for home therapy should be adequately designed and securely funded to ensure patients receive the expertise and services of the CF MDT and quality of care that is equivalent to in-hospital care.

This includes:

- a) Initiation of intravenous antibiotics and CF multidisciplinary team assessment and treatment in hospital where possible, to allow assessment of clinical status, tolerance of intravenous antibiotics (and other therapies), establishment of therapeutic drug levels and multidisciplinary exacerbation management planning tailored to the individual. Management may then be continued during home therapy.
- b) Adequate specialist nursing, physiotherapy, dietetic, and psychosocial support during home treatment of pulmonary exacerbations. Successful treatment of pulmonary exacerbations is not achieved through antibiotics alone and requires multidisciplinary team care. Multidisciplinary intervention for individuals receiving home therapy should replicate inpatient services as closely as possible and ideally, intervention is provided by home visits or via telehealth. Aspects of care may be delivered by the patient or carer where individual capabilities, resources and care burden are acceptable, and progress is closely monitored. Allied health support may be delivered by the local CF team or community service providers experienced in CF care, including the local CF organisation in some locations. Close communication is required between the CF team and contracted service providers.
- c) Monitoring of clinical response to home therapy. This may involve a weekly review of progress by the CF team (Physician, CF

- specialist nurse or other health care worker with expertise in IV therapy and/or CF care) undertaken at the hospital or at the patient's home. Monitoring requires access to spirometry, scales for weight and other clinical assessment equipment. Telehealth may be appropriate for some patients who are at a distance to the CF specialist team, have appropriate IT facilities, access to home spirometry, scales etc
- d) Modification of home therapy based on clinical response and including current microbiology and other investigation results as per CF centre protocol.
- e) Monitoring for drug toxicity is required (e.g. aminoglycoside levels as per CF centre protocol).
- f) Monitoring of venous access including changes of lines and dressings or IVAD as per CF centre protocol.
- g) If a patient is not improving clinically or is unable to adhere to/continue with home therapy, the patient should return to hospital for ongoing care.

4. Patients receiving home therapy should have access to the CF MDT for advice and support.

- a) Easy access to help and advice. Details of 24-hour contact point (e.g. a person via direct telephone number or telephone number of the hospital ward/unit) in case of queries or complications during home therapy.
- b) Details of the supports and services provided by the home therapy service should be provided to the patient

5. Monitoring and audit of home therapy services.

- a) The CF centre should have systems established to allow quality and performance assessments of its home therapy program. Data collection should include objective measures of clinical response, adverse events, complications, and costs.
- b) Home therapy activity and outcomes should be audited regularly by the CF team.

References

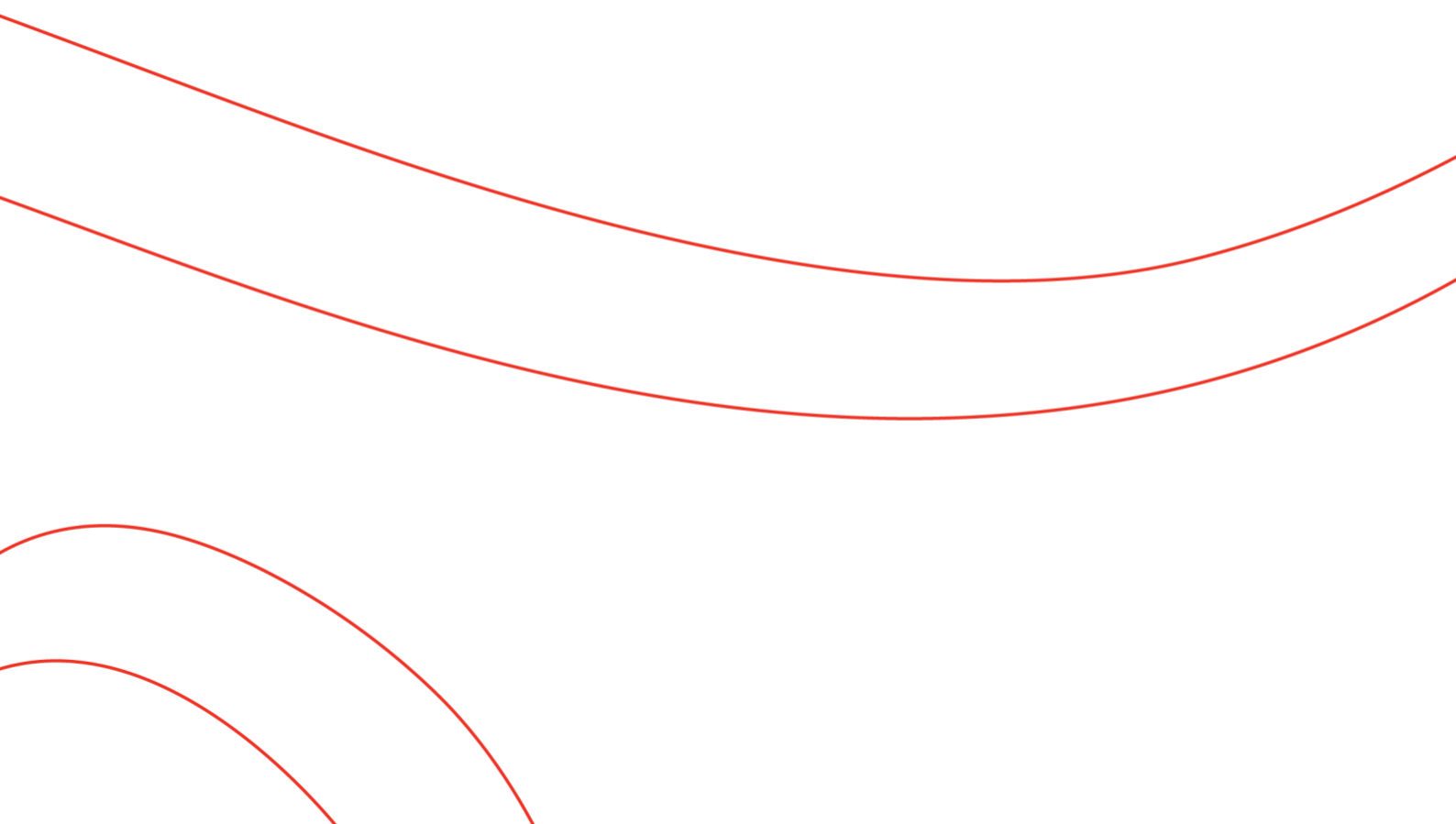
1. Balaguer_A, González de Dios_J. Home versus hospital intravenous antibiotic therapy for cystic fibrosis. Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD001917. DOI: 10.1002/14651858.CD001917.pub4.
2. Schechter M, Van Devanter DR, Pasta DJ, et al. (2018). "Treatment setting and outcomes of cystic fibrosis pulmonary exacerbations". *Ann Am Thorac Soc* 2018; 15:225–233.
3. Flume PA, Mogayzel PJ Jr., Robinson KA, et al Cystic fibrosis pulmonary guidelines: treatment of pulmonary exacerbations. *Am J Respir Crit Care Med* 2009; 180: 802–808
4. Wolter, J. M., S. D. Bowler, et al. (1997). "Home intravenous therapy in cystic fibrosis:a prospective randomised trial examining clinical, quality of life and cost aspects." *Eur Respir J* 10(4): 896-900.
5. Collaco JM, Green DM, Cutting GR, et al. Location and duration of treatment of cystic fibrosis respiratory exacerbations do not affect outcomes. *Am J Respir Crit Care Med* 2010; 182:1137–1143.
6. Donati, M. A., G. Guenette, et al. (1987). "Prospective controlled study of home and hospital therapy of cystic fibrosis pulmonary disease." *J Pediatr* 111(1): 28-33.
7. Saad E.Y, Leung W.M, Smith M.P, Salgado J, Hassan I , Brown N.E. (2018) "Comparison of home and hospital intravenous antibiotic therapy for clinical outcome in patients with a pulmonary exacerbation of cystic fibrosis. Do they always need to be admitted?" *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine*, 2:3, 133-137, DOI: 10.1080/24745332.2018.1461037
8. Strandvik, B., L. Hjelte, et al. (1992). "Home intravenous antibiotic treatment of patients with cystic fibrosis." *Acta Paediatr* 81(4): 340-4.
9. Graff von der Schulenburg, J. M., W. Greiner, et al. (1997). "Economic aspects if the treatment of cystic fibrosis with ambulatory intravenous therapy in comparison with inpatient treatment." *Medizinische Klinik* 92: 626-629.
10. Klettku, U., K. Magdorf, et al. (1999). "Ambulatory vs. inpatients antibiotic therapy in mucoviscidosis patients a controlled study." *Pneumologie* 53: 31-36
11. Riethmueller, J., A. Busch, et al. (2002). "Home and hospital antibiotic treatment prove similarly effective in cystic fibrosis." *Infection* 30(6): 387- 91.
12. Thornton, J., R. A. Elliott, et al. (2005). "Clinical and economic choices in the treatment of respiratory infections in cystic fibrosis: comparing hospital and home care." *J Cyst Fibros* 4(4): 239-47.
13. Thornton, J., R. Elliott, et al. (2004). "Long term clinical outcome of home and hospital intravenous antibiotic treatment in adults with cystic fibrosis." *Thorax* 59(3): 242-6.
14. Bosworth, D. G. and D. W. Nielson (1997). "Effectiveness of home versus hospital care in the routine treatment of cystic fibrosis." *Pediatr Pulmonol* 24(1): 42-7.
15. Esmond, G., M. Butler, et al. (2006). "Comparison of hospital and home intravenous antibiotic therapy in adults with cystic fibrosis." *J Clin Nurs* 15(1): 52-60.
16. Proesmans M, Heyns L, Moons P, Havermans T, De Boeck K. (2009). "Real life evaluation of intravenous antibiotic treatment in a paediatric cystic fibrosis centre: outcome of home therapy is not inferior". *Respir Med*. 2009; 103: 244-250.
17. Com G, Agarwal A, Bai S, et al. Outcomes and Safety of Outpatient Parenteral Antimicrobial Therapy in Select Children with Cystic Fibrosis. *Pediatr Allergy Immunol Pulmonol*. 2019;32(4):149-154. doi:10.1089/ped.2019.1073

18. Chrysochoou EA, Hatziaorou E, Kirvassilis F, Tsanakis J. Home intravenous antibiotic therapy in children with cystic fibrosis: clinical outcome, quality of life and economic benefit. *Hippokratia*. 2016 Oct-Dec;20(4):279-283. PMID: 29416300; PMCID: PMC5788226.
19. Nazer D, Abdulhamid I, Thomas R, Pendleton S. (2006). "Home versus hospital intravenous antibiotic therapy for acute pulmonary exacerbations in children with cystic fibrosis". *Pediatr Pulmonol*. 41: 744-749.
20. Bell, S. C. and J. P. Bunting (2005). Home therapy for people with Cystic Fibrosis in Australia. *Proceedings Sixth Australian Cystic Fibrosis Conference, Adelaide*



Outpatient Care

Peter Wark, Jagdev Singh,
Hiran Selvadurai, Tonia Douglas



- Standard 1** All people with CF should have access to treatment coordinated by a multi- disciplinary team in specialised CF centres.
- Standard 2** People with CF should be reviewed four times a year by the CF specialist team as the current minimum standard, with frequency of individual patient reviews tailored to clinical progress and need.
- Standard 3** Respiratory samples should be collected at least 4 times per year. Oropharyngeal samples and induced sputum should be obtained in those unable to expectorate spontaneously. In symptomatic patients with a negative culture, bronchoalveolar lavage should be considered.
- Standard 4** An annual review, including appropriate tests, should be undertaken and a written report provided to the patient/family and the general practitioner. Goals and plans for the following year should be discussed and agreed upon between the CF team and the patient/carers.
- Standard 5** Policies and procedures that actively promote contemporary infection control guidelines are essential to optimise clinical care in the outpatient setting.
- Standard 6** Telehealth facilities should be available to support equitable and enhanced access to multidisciplinary CF health care for all patients. Standards of clinical practice using telehealth should be equivalent the standards of CF care applied in face-face settings.

Background

Multidisciplinary outpatient care forms the backbone of paediatric and adult CF care and is likely to adopt an even greater role in CF health care delivery as the benefits of CFTR modulator therapies and improved patient survival are realised^{1,18}. The outpatient clinic provides patients and families with access to the CF multidisciplinary team allowing early detection and treatment of CF complications and comorbidities and continued monitoring to evaluate progress and response to treatment. The impact of the global COVID-19 pandemic has seen telehealth emerge as a feasible and acceptable method of CF healthcare delivery in the outpatient setting that has enhanced access to the MDT and is widely endorsed by patients and their families².

Infection prevention and control strategies in CF have evolved in response to the mounting evidence demonstrating the risks of infection through person-to-person pathogen transmission, acquisition from health care settings and environmental exposures^{3,4}. Outpatient environments are increasingly recognised as a potential source of pathogen transmission through contact with contaminated surfaces and airborne particles generated by coughing^{5, 6, 7} and lung function testing⁸. These findings have implications for the rates of air exchanges in outpatient clinics and support the use of face masks⁹ and segregation policies. Segregation policies and a multifaceted infection control approach introduced into CF centres have been shown to effectively limit the transmission of these pathogens^{10, 11} and remain a key facet of outpatient care

Surveillance for respiratory pathogens remains crucial in the management of patients with CF of all

ages. Pulmonary infection drives inflammation and structural lung damage and is associated with worse lung function and poorer clinical outcomes¹². Frequent sampling facilitates timely detection and treatment/eradication of key pathogens such as *Pseudomonas aeruginosa*, which may lead to improved lung function and reduced prevalence of chronic infections¹³.

As health status improves, people with CF are becoming increasingly non-productive of sputum and how we obtain samples that reliably reflect lower respiratory flora remains a challenge. The use of oropharyngeal cultures and the utility of induced sputum is subsequently expanding^{14,15}.

The psychosocial challenges associated with living with CF or caring for a person with CF are significant and lifelong. Rates of anxiety and depression are up to three times higher in adolescents and adults with CF and their carers compared with the general population and are associated with poorer health outcomes, increased health care use and reduced adherence to treatment¹⁶. People and families living with CF experience greater economic and financial burden, marital and relationship strain, and poorer quality of life¹⁷. There is a global recognition of the importance of prevention, screening, and early intervention for mental health problems in patients and carers with CF with published practice guidelines available¹⁶.

Increasing survival and an ageing adult CF population will likely lead to an expansion in outpatient specialist services to address emergent needs and complications such as fertility and obstetric care, cardiovascular and oncology

services¹⁸. Outpatient services will need to evolve to meet the changing needs of the CF population.

Previously published guidelines from international and national sources describe details of the

requirements for an outpatient (OPD) review, staff involvement, timing, and aspects of infection control^{5, 8 19-22}. The recommendations in this section are based on published guidelines and expert opinion and references are given where available.



Experience in Australia

There are 23 CF centres and CF outpatient clinics in Australia, which provided 26,700 clinic encounters in 2019. Prior to the SARS-Cov-2 pandemic, 71% of patients had at least 4 clinic visits in 2019. The highest proportion of outpatient visits were among adolescents aged 12-17 years (79.4%) and lowest (65.4%) amongst those > 30 years (Australian Cystic Fibrosis Data Registry, 2019). During the pandemic, 60% of patients had at least 4 clinic visits in 2020. The highest proportion of outpatient visits were among adults (>18 years, 64%) and lowest (46.9%) amongst those 7 to 11 years ([Australian Cystic Fibrosis Data Registry, 2020](#)). Whilst a decline in the number of clinic visits was observed during the pandemic, the current model of CF MDT outpatient care continues to be well supported by the CF community.

Recommendations for Outpatient Care Personnel, services, and facilities

Guidelines from Europe and North America recommend that the review of patients in an outpatient setting should be undertaken by a multidisciplinary team^{5, 8 19-22}. The 2008 Australian standards of CF care, the European CF guidelines and the UK NICE guidelines all have a consensus agreement that the following health professionals should be available for the outpatient care of patients with CF.

- Respiratory paediatrician/adult respiratory physician with expertise in CF
- Specialist CF Nurse
- Physiotherapists
- Dietitians
- Clinical Pharmacist
- Respiratory Scientist
- Social worker
- Clinical psychologist
- Clinical Microbiologist
- Administrative support officers


Outpatient services required beyond the specialist CF clinic include multiple medical, surgical, subspecialty and allied health disciplines as outlined in the chapter Paediatric and Adult Specialist CF Centres: Facilities, Staffing, and Services. Essential CF outpatient services include pulmonary function/physiology testing, pathology laboratory services (including microbiology, pathology, biochemistry, and molecular biology), diagnostic imaging, endocrinology, gastroenterology and hepatology, clinical genetics, and CF pharmacy services.

Outpatient facilities should be age-appropriate, follow current recommendations for infection control and prevention³ and include access to:

- Appropriately maintained equipment for measurement of weight, length or height and head circumference (babies and young children).
- Sufficient, adequately designed waiting areas, clinic rooms, and treatment/procedure rooms to manage the patient flow and without compromising infection control.
- Sufficient and suitable space to accommodate extended education, counselling and consultation sessions when required.
- Technology and facilities for telehealth consultations should be available.
- A respiratory function laboratory for measurement of lung function (with access to exercise testing facilities) with expert scientists

- appropriately trained for measurement of lung function across the age spectrum of patients attending the clinic.
- Facilities and ability to collect and process respiratory samples for microbiological surveillance and assessment.
- Medical imaging facilities including, but not limited to, computerised tomography (CT) scan, dual energy X-ray absorptiometry (DEXA) scan, ultrasonography services, vascular access support and interventional radiology.
- Facilities and capacity for urgent clinical review should be available.
- Facilities, experienced staff, and equipment should be available for simple procedures such as flushing of central venous access devices and first dose safety observation for inhaled antibiotics.

In Australia, all people with CF receiving PBS subsidised CFTR modulators must be reviewed by the CF specialist clinic every 6 months (including clinical assessment, FEV₁ % measurement) to be eligible for ongoing subsidised treatment.



Frequency of outpatient reviews

There is general agreement across European and North American guidelines that patients should have a minimum of four routine reviews per year. In children with classical CF, all four reviews should be performed by a CF specialist multidisciplinary team with additional reviews as clinically required.

Individual patients may require more frequent reviews as their clinical course demands. For some patients with milder mutations, and/or a low burden of disease, less frequent review by the CF multidisciplinary team may be reasonable and should be determined on a case-by-case basis.

Routine Clinic Visit

Adequate time is required for each patient and family to be reviewed. A structured and protected CF clinic format should be established in centres providing patients with time-efficient access to all health professionals. The following procedures should be included at each clinic:

An age-appropriate history should be taken and recorded. This should include but is not limited to:

1. Pulmonary: questions about cough, sputum production, wheeze, and breathlessness.
The frequency and duration of exacerbations should be recorded, including the use and route of antibiotics. Episodes of haemoptysis should be recorded.
2. ENT: nasal obstruction, sinus pain and postnasal drip questioned.
3. GIT: Abdominal symptoms including diarrhoea, constipation, bloating, symptoms to suggest reflux, abdominal pain.
4. Rheumatology: Joint pain, inflamed joints, use of analgesia.
5. Mental health: symptoms of depression, anxiety, procedural distress and including mental health symptoms in primary carers of children and adolescents. Behavioural issues and developmental concerns in children.
6. Adherence to treatment: barriers to adherence, treatment burden, health perceptions, health literacy.
7. Social and lifestyle: alcohol use, smoking and recreational drug use, relationships and family, school and education, employment, and financial issues.

Clinical assessments including a thorough physical examination and not limited to:

1. Measurement of weight, height (at least annually in adults), body mass index (BMI) and head circumference (≤ 2 years of age on growth charts to determine percentiles and track changes over time. Assessment of pubertal status in children/adolescents is required.
2. Dietitian review and assessment of nutritional status in accordance with the Australian Clinical Practice Guidelines for Nutrition in Cystic Fibrosis ²³. Review of diet, glycaemic control, hydration and salt replacement, pancreatic enzyme replacement therapy, micronutrient levels and supplementation, and use of nutritional supplements. Management, education, and counselling provided as required.
3. Assessment of airway microbiology. Sputum samples (spontaneous or induced) or oropharyngeal specimens from non-productive infants and pre-school children, and older patients where induced sputum cannot be successfully obtained, should be obtained a minimum of 4 times a year. Bronchoscopy and BAL may be used to obtain lower airway samples in non-productive patients as part of microbiological surveillance in some centres.
 - a) Culture of respiratory specimens with appropriate media selective for detection of *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Staphylococcus aureus* and MRSA is required. Respiratory virus and fungal cultures should be undertaken based on clinical suspicion.
 - b) It is important to have mechanisms in place following the procurement of these samples. This should include assessment of respiratory sample culture results by a member of the CF team, communication of results to relevant personnel including patient and families, and implementation of appropriate therapeutic changes and documentation of the communication, results and changes made into the patient's medical record.
4. Physiotherapist review and advice around airway clearance techniques and adjuncts, inhalational therapy, exercise regimens, assessment of continence issues and musculoskeletal reviews.
5. Psychosocial review according to patient and family needs. This should include assessment of mental health and emotional wellbeing, family functioning, coping and adherence, and significant stressors. Support with financial benefits, logistical issues, and welfare may be provided.
6. Medication review to include adherence, tolerance/adverse reactions, dosing, potential drug interactions. Ensure adequate supplies until next review. Reviews should include non-prescribed and complementary therapies.
7. Oximetry in patients with moderate to severe lung disease or acutely breathless.

8. Spirometry should be routinely performed from age 5 years at each clinic visit (and may be attempted in experienced paediatric lung function laboratories from around 3-4 years). Spirometry trends should be made available to clinicians to track longitudinal progress.
9. Blood pressure and urine analysis should be undertaken as clinically indicated and specifically in older adults, patients taking oral corticosteroids, CFTR modulator therapy, or with diabetes mellitus.
10. Relevant investigations (blood tests, urine tests, imaging etc.) as clinically indicated and according to patient progress
11. Assessment of patient and carer health literacy, education needs, capacity and capability for self-management is recommended. Information and education should be tailored to individual needs.

A clinic policy should be in place to identify and contact patients who fail to attend clinic appointments. If a patient does not attend the scheduled clinical appointment, the designated clinic coordinator should initiate a follow up call to the patient/family to identify barriers to attendance and to reschedule another appointment as soon as practicable.

Annual Review

A comprehensive clinical review should be carried out annually (annual review). In addition to the components of the routine visit, the annual review visit should include input from all members of the MDT as well as relevant subspecialties. A summary report of the preceding year should be discussed and provided to the patient/family and general practitioner and/or general paediatrician. It is vital that the MDT and the patient/family discuss and agree upon a management plan and determine goals of care over the next 12 months.

Annual review tests should only be performed during a period of clinical stability. In addition to a thorough physical examination, investigations, and procedures specific to the annual review should include:

1. Assessment and overview of respiratory progress and status

- a) Lung function and exercise capacity: Overall spirometry trend and annual decline should be reviewed. Ideally, trend graphs should be provided to facilitate discussion of respiratory progress with patients and families. Multiple breath washout (MBW) testing may be considered in children where expertise in this technique is available (see the Infants and Children chapter). Exercise capacity is of prognostic significance for patients with CF ²⁴, ²⁵. Assessment of exercise tolerance and aerobic capacity is recommended using tests as appropriate for patient status and clinical standards ²⁶: Cardiopulmonary exercise testing (CPET) in children >8 years and adults. In patients with more severe lung disease, especially being considered for lung transplantation, both the 6-minute walk test and CPET have been validated.
- b) Airway microbiology: Oropharyngeal, sputum or BAL samples should be collected at annual review, as per routine clinic visits. Sputum smear and culture for nontuberculous mycobacteria (NTM) should be performed at least annually, or more frequently in patients with an unexplained deterioration, and in any patient with clinical features suggestive of NTM infection ²⁷. Culture results should be acted on promptly if required.
- c) Chest imaging: Annual chest x-ray is recommended and when combined with a scoring system has been shown to predict pulmonary disease progression in children ²⁸, but is less sensitive to early lung disease and structural changes than a chest CT ²⁹. A CT scan together with a validated scoring system has been shown to predict exacerbation risk for up to 10 years ³⁰ but is associated with a greater exposure to radiation and in young children requires sedation and airway support. The optimum interval for CT imaging remains unclear and requires further longitudinal studies ³¹. In many paediatric settings, biennial CT scanning is performed and in others this varies based on clinical assessment, but it is more typical to perform a chest CT scan at least every five years in children and young people. This has not been defined in adults, but a similar standard would be reasonable. Protocols should minimise radiation exposure. Both inspiratory and expiratory CT images (preferably spirometry guided) should also be obtained with consideration given to using a validated scoring system to compare changes over time.
- d) Assessment of allergic bronchopulmonary aspergillosis (ABPA) status from around age 5 years. Annual blood tests for total serum IgE, *Aspergillus* specific RAST test (or skin prick test for *Aspergillus*) and IgG antibodies are recommended.
- e) A diagnostic sleep study should be performed to diagnose sleep disordered breathing in children and adults, and considered in those with advanced respiratory disease, (FEV₁% <40% predicted and waking SaO₂ <93%). It should be part of the assessment for those requiring supplemental oxygen or

requiring non-invasive ventilation. Review and assessment of home-based oxygen therapy or in-flight oxygen in patients with

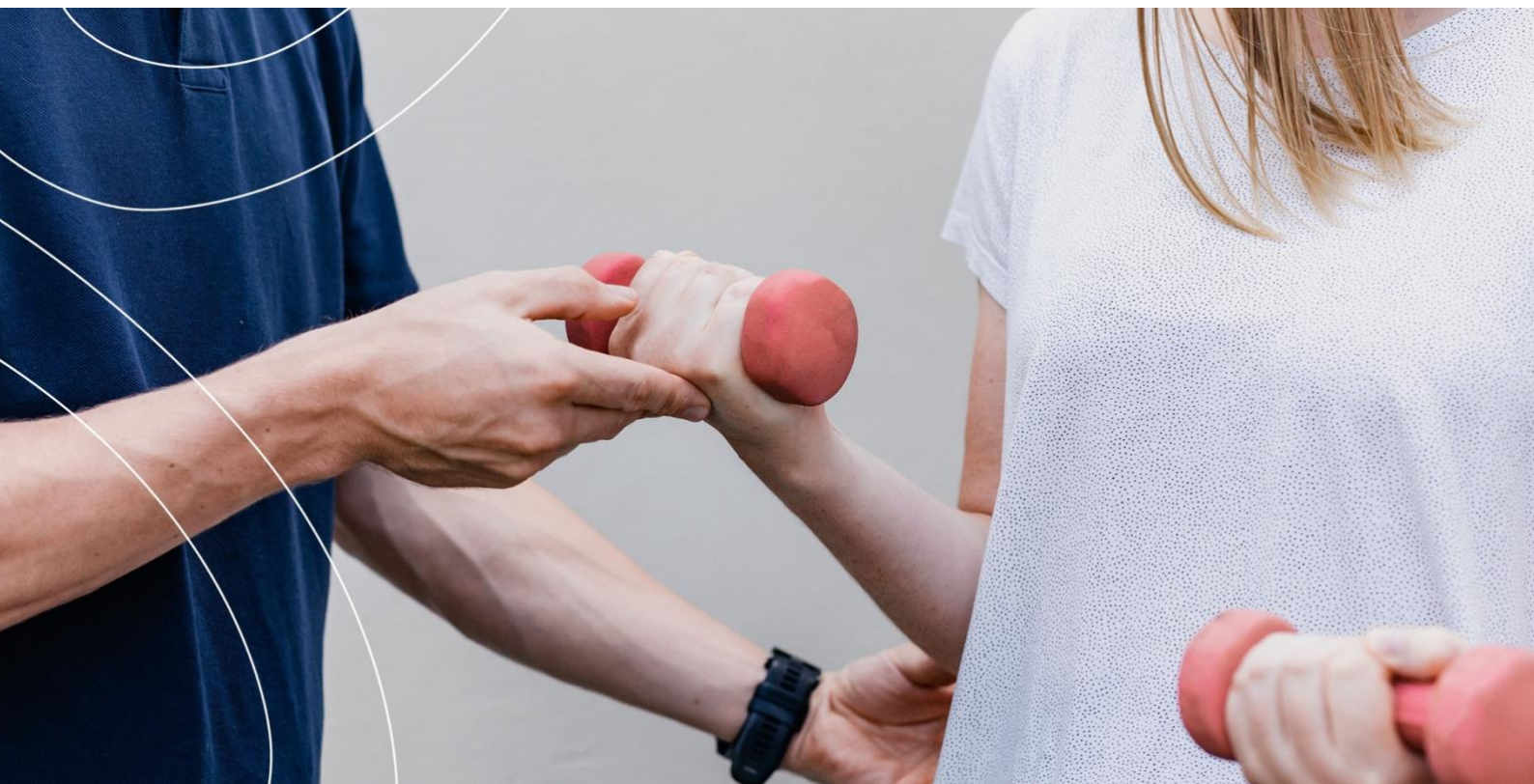
moderate to severe CF-related lung disease may be organised.

2. Assessment of growth and nutritional status in accordance with the Australian Clinical Practice Guidelines for Nutrition in Cystic Fibrosis ²³.

- a) Assessment of growth trends, pubertal progress, (height, weight, BMI, and head circumference for ≤2years only) and identification of undernutrition and at-risk nutritional status.
- b) Consider assessment of body composition for more detailed information regarding nutritional status including fat-free mass.
- c) Consider measurement of luteinising hormone, follicular stimulating hormone and testosterone or oestradiol in adolescents with pubertal delay, along with bone age assessment.
- d) Blood tests for fat soluble vitamins (A, D, E, and K including retinol binding protein to assist in interpretation), FBC, electrolytes and creatinine, liver function tests and clotting profile (hepatic function), iron studies, calcium levels, and fasting or random blood glucose. Consider celiac serology if growth/nutritional concerns. There is insufficient evidence to support routine annual testing of selenium or zinc at the present time.
- e) Consider measurement of urinary sodium (urinary sodium concentrations <10 mmol/L) or calculation of fractional urinary sodium (FENa) to detect salt depletion, particularly in children who are failing to thrive, patients with ileostomy/colostomy, and those with symptoms of fatigue and anorexia ($FENa = \frac{\text{urinary Na} \times \text{plasma creatinine} \times 100}{(\text{plasma Na} \times \text{urinary creatinine})}$ with all parameters as mmol/L). Normal range for $FENa = 0.5\%–1.5\%$ ³².
- f) Develop a nutritional intervention plan with the patient and family for the coming year and address suboptimal growth or nutritional deficiencies.

3. Assessment of glucose homeostasis and bone health

- a) Presently, annual oral glucose tolerance testing (OGTT) for patients aged 10 years or older is recommended. OGTT should be performed in patients during a period of clinical stability. Screening in younger children with symptoms suggestive of glucose intolerance or with unexplained weight loss, growth failure or worsening respiratory status is recommended³³.
- i. Patients diagnosed with CF-related diabetes mellitus (CFRDM) should be referred to endocrinology services (ideally a diabetologist with experience in the management of CFRDM) for surveillance (including 3-monthly HbA1c) and management.
- b) Bone mineral density (BMD) should be assessed annually using DEXA from age 8 years in accordance with clinical practice guidelines ²³.
- i. The frequency for DEXA scanning depends on the previous result, any treatment initiated for low bone density, and emergence of risk factors for osteopenia, osteoporosis, or declining bone density, including poor nutritional status, delayed puberty, corticosteroid use, vitamin D, vitamin K and calcium deficiencies ^{34 35}.
- ii. Briefly, DEXA scanning is suggested every three to five years if BMD is normal (z or T-scores > -1); every two years if moderately reduced (z-score -1 to -2 or T-score -1 to -2.50; and annually if severely reduced (z-score < -2 or T-score < -2.5). Shorter intervals are suggested in those with risk factors for osteopenia/osteoporosis.



4. Physiotherapy assessment and review in accordance with the Australian and New Zealand Physiotherapy Clinical Practice Guidelines ³⁶.

- | | |
|--|---|
| <p>a) Review of inhalation therapy equipment and airway clearance (including equipment and use, and cleaning protocols). Where applicable, servicing of equipment should be conducted by qualified personnel (e.g. spirometers, nebuliser pumps, and respiratory therapy equipment).</p> | <p>specialist musculoskeletal physiotherapist as required.</p> |
| <p>b) Assessment for musculoskeletal complications of CF and associated pain or functional limitation with referral to a</p> | <p>c) Screening and assessment for urinary and faecal incontinence in children and adults and referral to incontinence services for management as required.</p> |
| | <p>d) Development of tailored exercise and airway clearance routines in collaboration with patients and families</p> |

5. Mental health screening for depression and anxiety should be performed for patients (>12 years) and their carer/parents (all children and adolescents), using standardised and validated tools such as PHQ-9 and GAD-7. See Infants and Children Chapter for details on screening in younger children. Documents to support mental health screening are available on the [CFA website](#).

- | | |
|---|--|
| <p>a) Screening may be performed by any member of the CF MDT such as the social worker, psychologist, clinical nurse consultant, or physician who has experience in administering the tool.</p> | <p>c) It is necessary to develop a clear, specific policy which identifies all team members who will ensure the safety of those at imminent risk and next steps while under the care of the CF Centre team.</p> |
| <p>b) A care model of intervention based on the screening results should be developed and implemented prior to initiation of such screening programs. A care pathway should outline the processes for referral to psychological services and include clinician(s) with experience in managing mental health issues, a list of referral sources within the hospital and community and educational resources ¹⁶.</p> | <p>d) Patients with mental health problems identified through screening should be referred promptly to psychological services (hospital or community based) for intervention.</p> <p>e) Parents and carers identified with anxiety/depression should be reviewed by the team social worker and referred to their general practitioner (to access mental health services) or community-based psychology services.</p> |

A broader, more detailed psychosocial assessment should be conducted at annual review and include family functioning, coping and adherence, and financial and economic burdens and benefits, and access to welfare supports.

6. Audiology testing and ophthalmology screening should be considered

- | | |
|---|---|
| <p>a) The Cystic Fibrosis Foundation otolaryngology consensus guidelines³⁷ recommend annual audiology screening for children and adults receiving ototoxic treatments including longer-term macrolide therapy, intravenous and inhaled</p> | <p>aminoglycosides, and treatment for <i>M. abscessus</i>, particularly IV amikacin. Audiology is also recommended prior to, and following, each course of intravenous ototoxic medications in children and adults with CF who already have any hearing loss.</p> |
|---|---|

Audiology/ENT consultative review should also be requested for patients with tinnitus, balance disorders, vertigo and hearing loss or persistent ENT symptoms or abnormal examination (e.g. polyps, epistaxis).

- b) Screening for cataracts should be considered annually for patients receiving

longer-term systemic corticosteroids and those on CFTR modulator therapy. Patients with CF related diabetes should undergo routine screening for retinal microvascular complications beginning five years after diagnosis or from time of diagnosis of fasting hyperglycaemia ³⁸.

7. Sexual and reproductive health should be discussed at least annually and considered in an age-appropriate manner ³⁹.

- a) This should include issues around sexual development, menstrual irregularities, vaginal candidiasis, contraception and safe sex practices, sexually transmitted disease, and family planning (See Adolescent and Young Adult chapter for more details).
- b) Information about fertility, pregnancy (planned and unplanned) and the impact of CFTR modulator therapy should be provided as appropriate with referral to an

obstetrician/gynaecologist as required (see Fertility and Pregnancy chapter for more details).

- c) Women with CF are now reaching menopause and symptom screening should be considered for women from age 40 years. Many of these issues will need to be explored together with the patient's primary care practitioner.

8. Review of medications by the CF pharmacist. Annual review should involve a detailed review of all medications, dosage, and methods of administration to determine whether they are appropriate, and review of non-prescribed medications and complementary therapies. Where access to a pharmacist is limited or not available, the CF physician should undertake this review.

- a) Any changes in therapy should be discussed and clearly documented in both medical notes and on a patient held CF treatment/therapy plan.
- b) Access to CFTR modulator therapies available as indicated through the PBAC should be provided for eligible patients.

Adherence to these therapies should be carefully monitored at each visit and managed.

- c) There should be careful adherence to therapeutic drug monitoring guidelines to prevent drug interactions, toxicity and optimise drug delivery.

Infection Control

General Recommendations for Infection Control in the Outpatient Setting

1. Outpatient clinics should have a local CF-specific infection control and prevention policy informed by published international guidelines^{3,4}. This policy should include details around standard and transmission-based precautions, patient segregation and patient movement, aerosol generating procedures including airway clearance and lung function, and room and equipment cleaning.
2. Infection control policies and procedures must be followed by all members of the CF MDT and by any other health professionals caring for patients with CF in other outpatient settings.
3. All health care professionals in the outpatient setting should practice hand hygiene when caring for people with CF.
4. All contact between patients in the outpatient clinic should be minimised and avoided. Measures to limit patient time in common waiting areas, at reception, in waiting rooms or at the pharmacy should be implemented. As soon as practical patients should be placed in a single clinic room. The patient flow for the clinic should be pre-planned before every clinic session.
5. There should be cohort segregation of CF patients (based on carrier status of organisms). Organisms of particular concern include, but are not limited to *Burkholderia cenocepacia*, *Mycobacterium abscessus*, multi-resistant *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA). Individual clinics need to consider how best to segregate patients to prevent transmission according to the clinic structure and facilities.
6. The psychosocial impact of infection control guidelines needs to be considered and explained to the patients and families to reduce any negative perception.
7. Patients should wear a surgical mask upon entering the CF clinic or the hospital/health facility and use alcohol-based hand gel or wash their hands with anti-microbial soap and water upon entering and leaving clinic rooms and the health facility. This may be difficult for some patients and may not be practical in younger children.
8. Patients should be seen in single clinic rooms with staff rotating into the room. Surfaces should be cleaned in accordance with local hospital cleaning policies between patients.
9. To minimise the spread of airborne pathogens, it is recommended that clinic rooms should provide 4-6 air exchanges per hour (ideally 6 exchanges)⁴⁰. This is usually provided through central ventilation systems with circulation through a HEPA or similar filter. Where this standard is not met, consideration should be made for the use of portable air filtration devices fitted with HEPA filters.
10. A period should elapse between patients occupying rooms to allow for an adequate number of air exchanges to reduce airborne

- pathogens ⁴⁰. This time varies depending on air exchange rate: ~10 minutes for 6 air exchanges per hour and up to 30 minutes for 4 air exchanges per hour.
11. Local infection control policies should be followed during pulmonary function testing.
 - Pulmonary function testing should be performed in a single room with the door closed, or a pulmonary function laboratory using a HEPA filtration system or negative pressure room.
 - Spirometry should be conducted with either portable or integrated high-efficiency particulate air (HEPA) filters.
 - Single use mouthpieces with incorporated bacterial/viral filters should be used where possible, and single use disposable nose clips, attachments and spacers should be used.
 - All equipment needs to be cleaned and disinfected between use.
 - In a pulmonary function laboratory without HEPA filtration, provide sufficient interval between patients with CF for air circulation and cleaning.
 12. Infection control policies should be in place in all locations including patient weighing and measuring areas, common waiting areas such as the nursing or administration desk during check-in as well as bathrooms.
 13. Routine microbiological surveillance should also be adopted to assess the incidence and prevalence of respiratory tract infections in their cohort of patients. CF teams are encouraged to liaise with their respective infection control teams to develop protocols, checklists, and audits and to implement standardised cleaning and disinfecting practices in the clinic ^{10, 41}.

First Outpatient Visit

Following new CF diagnosis

Infants, children, and adults newly diagnosed with CF should be seen by the CF consultant and specialist CF nurse within 1-3 days, and no later than one week, after receiving notification of the diagnosis ^{19, 20}. It is strongly recommended that the CF social worker meets with the family at this time, or soon after the initial visit, to assess parental wellbeing and help with access to psychosocial supports.

Newly diagnosed people should be clinically assessed at this initial visit and management

instigated as appropriate. A CF specialist should discuss the diagnosis with the parents and/or newly diagnosed child/adult. A written, centre specific information pack should be provided to patients and families to take home that includes the process of CF diagnosis, an overview of the condition and its treatment, living with CF and impact on lifestyle, names and contact details of the CF team and State and National CF Associations. Some centres include a short summary of research activities that may be appreciated by patients and families in the weeks following initial diagnosis.

Following the initial visit, a comprehensive clinic visit should be scheduled to introduce the patient and family to the CF multidisciplinary team and begin education and MDT assessment. Referral to genetic services should be considered, and access to psychosocial support during the time of diagnosis is essential.

Transfer from another CF centre

The transferring centre should provide a detailed clinical summary covering all aspects of CF care and include reports from all members of the MDT. This should include copies of recent relevant investigations and sufficient information to understand the patient's clinical status and should be available to the receiving team prior to the patient's first clinic visit. Additionally, the transferring centre is responsible for notifying the Australian CF Data Registry to transfer the patient's data registry details to the receiving centre in a timely manner.

The receiving service should review the diagnosis including genotype, take a detailed history, review correspondence from the referring centre, and perform a physical examination with specific attention to any new changes in symptoms that may have arisen since transfer. Relevant tests, including a respiratory sample may be ordered. A review of all medication, including adherence and administration techniques (including airway

clearance) and other self-management tasks should be assessed. Policies and practices specific to the centre should be discussed and the patient and family/carer should be introduced to the new CF team.

When young adults attend an adult hospital for the first time, parents/carers should be welcomed to attend with them and meet the CF team. Parents/carers and the patient are encouraged to discuss any issues or concerns. The CF physician, preferably accompanied by the CF specialist nurse, should also meet the young adult in a one-to-one consultation, following which, the parents may be invited to spend time with the clinician with or without the young adult.

Rapid access care may help reduce hospitalisations, avoid ED presentations, and improve quality of care for patients⁴².

Rapid review clinic

All CF centres should have capacity for rapid clinical review to allow patients experiencing clinical deterioration, or with acute CF-related issues, earlier access to CF care (outside of routine visits) and timely intervention. Models of care vary, however, patients presenting for rapid review are usually triaged by the CF specialist nurse who then arranges a CF medical consult for investigation, medication changes or escalation in treatment, including hospitalisation. Rapid access care may help reduce hospitalisations, avoid ED presentations, and improve quality of care for patients⁴².

Telehealth clinic

The COVID-19 pandemic endorsed the feasibility and acceptance of telehealth in CF clinics across Australia⁴³ and internationally⁴⁴. Telehealth is the delivery of health care to patients by a range of digital and telecommunication technologies that include videoconferencing and telephone communication. It may occur within the consumer's home or a health facility. The consumer may attend alone or be supported by a health care professional such as a GP. The role of telehealth as part of routine CF care continues to develop, although the outcomes and effectiveness in CF are not yet clear and need to be studied. Clinics delivering telehealth should ensure they have access to IT support, familiarisation, and

training for staff around telehealth platforms, and adequate patient preparation (see [Telehealth Guidelines](#)). Telehealth platforms should be secure, intuitive, and accessible. Patients receiving telehealth should have access to adequate technology to support effective clinical review, consultations, assessment, and education. Where this is not available, telehealth may be conducted at a health facility such as the GP practice. Plans should be in place describing how patients will access prescriptions, complete pathology tests, and how health care workers will access results. Objective measures of patient progress such as growth, lung function and respiratory sampling should be

obtained, and patients should have access to scales for weight measurement, stadiometers for height measurement in paediatrics, sputum pots and OP swabs for respiratory samples and guidance around collection of samples (especially for parents of young children). Home based spirometry may be considered although data about its utility is still emerging. It is important that clinics adhere to spirometry standards when reviewing and interpreting home spirometry, and virtual supervision of spirometry in children is recommended⁴⁵. Multidisciplinary team review via telehealth is recommended including physiotherapy review and assessment of physiotherapy techniques, dietitian review, and psychosocial assessment ⁴⁶. CF clinics should have protocols or guidelines in place

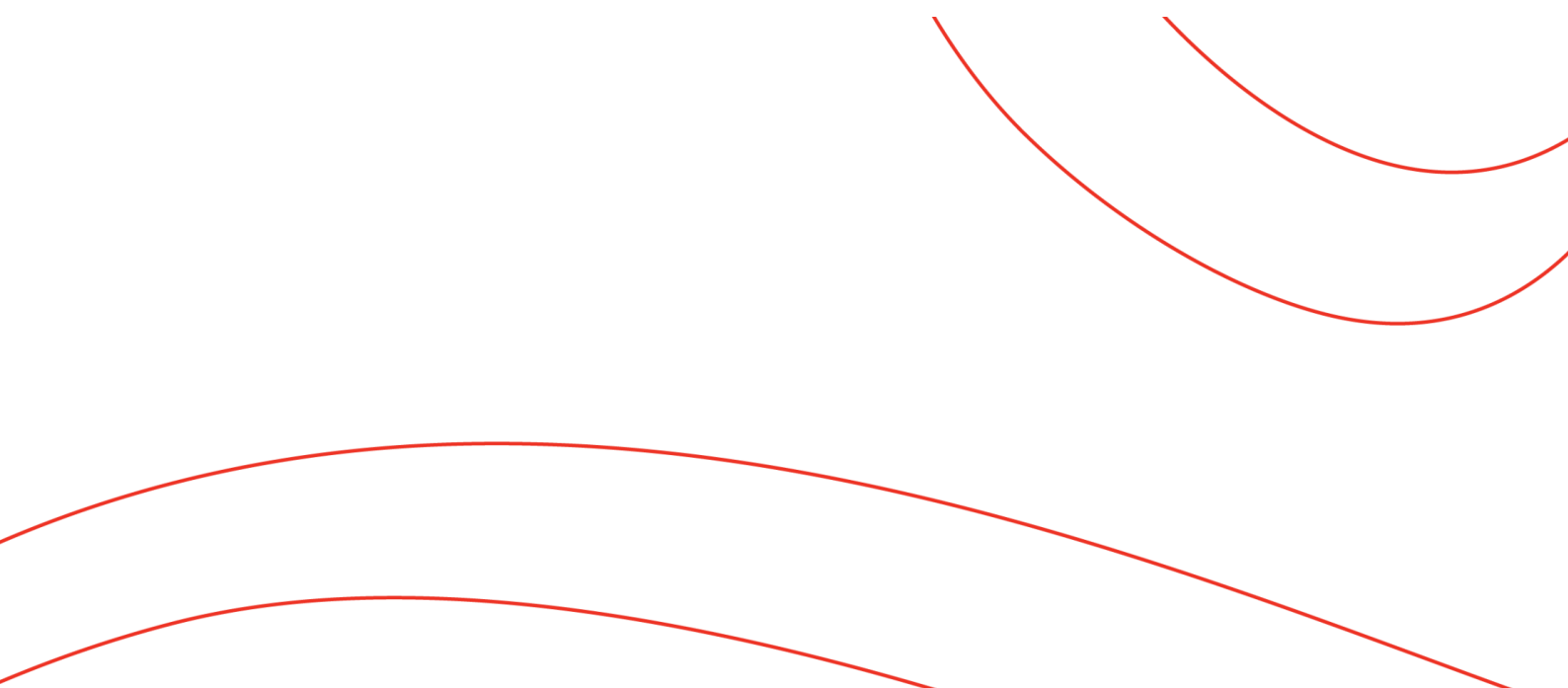
that outline criteria for patient selection, and procedures around telehealth reviews. Training should be provided for both clinicians and patients/carers in the use of telehealth and the associated technology.

There is no consensus or evidence to inform clinicians of the ideal number of telehealth and face-to-face visits in CF at present. Telehealth consultations are not intended to replace face-to-face visits and a balance between telehealth services and face-to-face care within the CF specialist centre must be achieved based on individual patient progress and needs and the resources of the CF centre.

Atypical CF

The availability of more extensive genetic testing has resulted in many more patients being identified with one or more mutations that have an impact on CFTR function. The range of disease severity and system involvement varies. We acknowledge that there is uncertainty around recommendations for these people and their inclusion in a CF clinic is best made on an individual basis in consultation with the patient

and the CF team. In general, adult patients should be reviewed at least annually by a specialist CF centre and/or more frequently according to clinical need. In children, this should be performed 6-monthly or more frequently if there is clinical need. It is preferable that this is done at a time other than the usual CF clinic but with appropriate access to the CF multidisciplinary approach to care.



Other specialist outpatient services

Adults and children with CF should have access to a range of specialist outpatient care for extra-pulmonary complications of CF including endocrinology, gastroenterology and hepatology, ENT, rheumatology, psychology, and clinical genetics services. Models of outpatient care may consider integrating gastroenterology and endocrinology specialists into routine CF outpatient clinics. However, for many centres this remains logistically challenging and there is onus on the CF clinic to coordinate specialist outpatient appointments to minimise care burden and travel for patients and families.

Endocrinology

People with CF should have access to an endocrinology team with experience in the management of CF.

Indications for referral include diagnosis and management of diabetes, abnormal bone mineral density, persistent vitamin D deficiency despite supplementation, delayed puberty, disorders of linear growth, adrenal insufficiency related to corticosteroid use, menstrual irregularities, and hypogonadism.

The prevalence of CFRD increases with age and affects approximately 2% of children, 19% of adolescents, and 40% to 50% of adults³⁸. Management of glycaemic control in patients with CFRD is associated with improved pulmonary function and reduction in pulmonary exacerbations⁴⁷. All patients with CFRD should be seen and regularly reviewed by an endocrinologist experienced in the management of CFRD. The frequency of endocrinology or diabetes team review for patients with CF should be individualised according to patient need, and current guidelines recommend a review 4-times a year^{47, 48}.

Gastroenterology and hepatology

Access to a gastroenterology and hepatology team experienced in the care of people with CF is essential. The frequency of GI review is dependent on the needs of the patient and underlying condition. The following are indications for gastroenterology review in paediatric and adult patients:

1. Failure to thrive or unexplained weight loss
2. Consideration of percutaneous gastrostomy placement and enteral nutrition
3. Liver function abnormalities (persistent), clinical or radiological features of CF-related liver disease

4. Chronic constipation and DIOS
5. Gastro-oesophageal reflux symptoms/disease
6. Recurrent/persistent abdominal pain, bloating, diarrhoea
7. Inflammatory bowel disease, functional gastrointestinal disorders, and small intestinal bacterial overgrowth
8. Bowel cancer
9. Organ transplantation – pre- and post-transplant management of GI complications

Gastroenterology care should include screening for bowel cancer in adults with CF (discussed further in the Ageing with CF Chapter) ⁴⁹. The CF service and GE team should establish a model of care for bowel cancer screening that includes initiation and timing of

screening colonoscopy, ensures clear communication with the service providing colonoscopy and the patient and team, and identifies specific needs of CF patient in relation to preparation for colonoscopy (specifically, around adequate bowel preparation regimens in CF), anaesthesia, and perioperative care.

Genetic services

Continued access to genetic counselling should be available and considered for patients and their families. Siblings of children diagnosed with CF should undergo sweat chloride testing and genotyping. Genetic counselling and fertility clinic access should also be considered in people with CF seeking to start a family.

Communication

Patient Contact Arrangement

Patients and families should have daytime telephone access to contact the CF Centre if required. In addition to in-hours telephone access, centre specific advice about who to contact outside business hours should be clearly outlined to patients and families. In some centres, CF-specific medical personnel may be available to discuss issues by phone directly with families or patients while other centres may recommend patients present to the Emergency Department or another acute medical facility for initial assessment.

Reports

A structured report of the clinic visit, or at the least the annual review should be sent preferably within 14 working days of a clinic visit to the patients, family, and care-givers where appropriate, and

involved medical personnel including the general practitioner ^{50, 51}.

Team communication

Continuity of care and quality improvement will be facilitated through regular weekly meetings by the multidisciplinary team where individual patients and systems issues can be discussed. Ideally, the discussion would involve patients seen in the previous week as well as patients scheduled for review in the following week. All CF specialist centres should have clear lines of communication with role responsibilities for the multidisciplinary team and strategies in place to ensure appropriate referrals and monitoring are undertaken, and results are assessed promptly, with adequate time allocated to team communication in the clinical week.

Exacerbation plan

Patients and caregivers should have an individualised plan for the management of acute exacerbations. This should be individualised and communicated to other medical teams involved, such as the general practitioner, and documented in their local medical records. The exacerbation plan should include signs and symptoms that trigger a change in management, expected response and time frame to the escalation of therapy and further plans in situations of inadequate response. While exacerbation plans are widely used there is no evidence available in CF that assesses the efficacy of exacerbation plans, what components it should include and to whom it should be given ⁵².

Health promotion

Education

Health education that provides disease-specific information about CF and treatment is an important component of outpatient care and is associated with improved self-efficacy and adherence and better health outcomes ⁵³. Regular, developmentally appropriate education of patients, caregivers, and family members should be undertaken, beginning at diagnosis, and continuing throughout the lifespan, and should be tailored to the individual needs of patients and families ^{54 55}. Education should address gaps in understanding and misconceptions around CF and should be available in a range of audio-visual and online material to suit individual preferences and reading ability. Education may include pattern of inheritance and how to access genetic counselling, disease monitoring strategies, treatment and

medication, and infection control measures. Parents and caregivers may seek practical information around preparing for their child's admission to hospital, navigating school, transition processes and transfer to adult services. Adolescents and young adults require and seek information around sexual and reproductive health ⁵⁶, employment choices, benefits, and welfare. Information about new therapies and clinical research trials and disease specific information around transplantation, end of life care may be required ⁵⁷.

Parental decision to disclose their child's CF status to day care or school is a personal one and often involves the wishes of the child. Enquiry around this decision is important to ensure the CF MDT can liaise

with, educate, and inform the school around key aspects of CF. This includes providing information about the child's medication(s), particularly around access to these and help with administration, signs, and symptoms the teacher should bring to the parents' attention, the importance of maintaining hydration and allowances for easy access to the toilet. The attendance of other children with CF at the

same school requires information around segregation and infection control. Teachers should be aware of the potential for school absence due to clinic appointments, illness and admission to hospital and should allow for catch up work. A written school health plan can be provided and is usually developed by the CF nurses and lead CF physician.

Immunisation

All people with CF should receive immunisations according to the standard [Australia immunisation schedule](#). People with CF who are immunocompromised or post lung transplant will need a separate immunisation schedule in discussion with the immunisation clinic. Annual influenza vaccine is strongly recommended for all patients, including children > 6 months of age before the start of winter. Family members of children with CF are recommended to obtain the annual influenza vaccine. Pneumococcal vaccination is recommended with an additional dose of Prevenar 13v at 6 months, and Pneumovax 23v at 4 years of age with a second dose at least 5 years later.

Adolescents and adults with CF are regarded by ATAGI as being at heightened risk of certain preventable bacterial infections. In addition to the standard adult vaccination schedule, it is recommended adolescents and adults receive the 23-valent [pneumococcal vaccination](#) and boosters.

Vaccination against [SARS-CoV-2](#) (COVID-19 virus) is recommended currently for all patients with CF over the age of 5 years and their families.

Immunisations are carried out largely in primary care. The CF clinic should discuss the importance of maintaining vaccinations, making patients aware of vaccinations they are entitled to and encouraging vaccination through their GP.

Dental health

All people with CF should receive regular dental review with assessment of oral hygiene, candidiasis, periodontal disease, and caries, with treatment provided as required. Dental assessments are recommended from age 12 months and 6-monthly into adulthood, according to the needs of the

individual. Dental procedures that require general anaesthesia should be discussed and planned between the dental surgeon, the CF team, and the anaesthetist⁵⁹.

Avoidance of environmental tobacco smoke and hepatotoxins

Approaches to reducing exposure to environmental tobacco smoke (ETS) should be discussed including vaping and the use of different vaping fluids. Increasing reports of e-cigarette, or vaping, product use–associated lung injury (EVALI) throughout the United States is concerning ⁵⁸. Smoking or exposure to environmental tobacco smoke should be openly discussed and strongly discouraged. Patients and carers should be counselled about the health-related risks associated with environmental tobacco smoke

exposure and encouraged to seek assistance to quit smoking.

The multidisciplinary team should consider if the use of other illicit substances and alcohol is occurring and discuss this in a constructive and non-judgemental way with the patient. Advice should be given to avoid additional hepatotoxic insults such as the excess consumption of alcohol, recreational drugs, and prescribed medications.

Research and Clinical Trials

Access to participation in research and clinical trials should be made available regardless of geography for patients eligible for studies. Cooperation between CF specialist centres is required to enable patients to attend other centres to take part in specific trials. Clear communication between clinical and research teams is of key importance.

Shared care arrangements

Outpatient care may be provided by regional/remote health care providers for patients unable to access outreach clinics and those living in remote regions of Australia. Close communication between the CF specialist clinic and regional health care teams is critical to ensure smooth and efficient management and optimal health outcomes for patients. The specialist CF centres should provide regional providers with local policies and guidelines for CF care and detailed patient management plans should be discussed with a general physician/paediatrician. The advent of telehealth has facilitated

communication and consultations with regional teams and patients/caregivers. It is the responsibility of the CF centre to provide as much information to local care providers as possible, especially regarding medication and antibiotic therapy, airway clearance and dietetic advice. In some remote areas a general physician/paediatrician may not be available, and the family GP may manage regular reviews and/or hospital admissions. This situation is not common, and it is strongly recommended that care is delivered with the oversight and support of the CF specialist centre and requires close communication and

collaboration with regional providers. Every effort should be made by local health care providers and the specialist CF centre to ensure people with CF

receiving care in remote locations are able to access allied health services, equipment, and food services.



The role of the general practitioner

The involvement of a GP is recommended for all patients and their families across the lifespan. The GP plays a central role in aspects of management such as coordinating and administering vaccinations, age-appropriate health checks (well child checks, adolescent, and adult health screening), coordinating care in those with mental health problems through mental health care plans, and assisting with access to Medicare funded community-based resources. At all times, GP's must be able to access advice from the CF Centre team and good communication between the

CF centre and the GP is essential in optimising care. It may be useful for a CF Centre to provide general information on the care of patients with CF to the GP. The GP must be kept informed of CF related health decisions, CF health summaries and exacerbation plans. The role of the GP, in general, intensifies during adulthood and involvement may be of paramount importance if palliation is required in end stage disease. The GP is also often the only person who is a constant between paediatric and adult care.

References

1. Bell SC, Robinson PJ, Fitzgerald DA. Cystic fibrosis standards of care, Australia 2008. *Online Mendelian inheritance in Man, OMI McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University, Baltimore* <http://www.ncbi.nlm.nih.gov/omim> 2008
2. Jaclyn D, Andrew N, Ryan P, et al. Patient and family perceptions of telehealth as part of the cystic fibrosis care model during COVID-19. *J Cyst Fibros* 2021;20(3):e23-e28. doi: 10.1016/j.jcf.2021.03.009 (published Online First: 2021/03/30)
3. Saiman L, Siegel JD, LiPuma JJ, et al. Infection prevention and control guideline for cystic fibrosis: 2013 update. *Infection Control & Hospital Epidemiology* 2014;35(S1):s1-s67.
4. Rowbotham NJ, Palser SC, Smith SJ, et al. Infection prevention and control in cystic fibrosis: a systematic review of interventions. *Expert Review of Respiratory Medicine* 2019;13(5):425-34. doi: 10.1080/17476348.2019.1595594
5. Wainwright CE, France MW, O'Rourke P, et al. Cough-generated aerosols of *Pseudomonas aeruginosa* and other Gram-negative bacteria from patients with cystic fibrosis. *Thorax* 2009;64(11):926-31. doi: 10.1136/thx.2008.112466
6. Bryant JM, Grogono DM, Rodriguez-Rincon D, et al. Emergence and spread of a human-transmissible multidrug-resistant nontuberculous mycobacterium. *Science* 2016;354(6313):751-57. doi: 10.1126/science.aaf8156 (published Online First: 2016/11/16)
7. Wood ME, Stockwell RE, Johnson GR, et al. Cystic fibrosis pathogens survive for extended periods within cough-generated droplet nuclei. *Thorax* 2019;74(1):87-90. doi: 10.1136/thoraxjnl-2018-211567
8. Zuckerman JB, Clock SA, Prato BS, et al. Air contamination with bacteria in cystic fibrosis clinics: implications for prevention strategies. *Am J Respir Crit Care Med* 2015;191(5):598-601. doi: 10.1164/rccm.201410-1877LE (published Online First: 2015/02/28)
9. Vanden Driessche K, Hens N, Tilley P, et al. Surgical masks reduce airborne spread of *Pseudomonas aeruginosa* in colonised patients with cystic fibrosis. *Am J Respir Crit Care Med* 2015;192(7):897-9. doi: 10.1164/rccm.201503-0481LE (published Online First: 2015/10/02)
10. Kapnadak SG, Hisert KB, Pottinger PS, et al. Infection control strategies that successfully controlled an outbreak of *Mycobacterium abscessus* at a cystic fibrosis centre. *Am J Infect Control* 2016;44(2):154-9. doi: 10.1016/j.ajic.2015.08.023 (published Online First: 2015/10/08)
11. Ashish A, Shaw M, Winstanley C, et al. Halting the spread of epidemic *pseudomonas aeruginosa* in an adult cystic fibrosis centre: a prospective cohort study. *JRSM short reports* 2013;4(1):1-1. doi: 10.1258/shorts.2012.012018 (published Online First: 2013/01/14)
12. Ramsey KA, Ranganathan S, Park J, et al. Early respiratory infection is associated with reduced spirometry in children with cystic fibrosis. *Am J Respir Crit Care Med* 2014;190(10):1111-6. doi: 10.1164/rccm.201407-1277OC (published Online First: 2014/10/17)
13. Zemanick ET, Bell SC. Prevention of chronic infection with *Pseudomonas aeruginosa* infection in cystic fibrosis. *Curr Opin Pulm Med* 2019;25(6):636-45. doi: 10.1097/MCP.0000000000000616 (published Online First: 2019/08/10)
14. Zampoli M, Pillay K, Carrara H, et al. Microbiological yield from induced sputum compared to oropharyngeal swab in young children with cystic fibrosis. *Journal of Cystic Fibrosis* 2016;15(5):605-10. doi: <https://doi.org/10.1016/j.jcf.2016.01.001>
15. Ronchetti K, Tame J-D, Paisey C, et al. The CF-Sputum Induction Trial (CF-SpIT) to assess lower airway bacterial sampling in young children with cystic fibrosis: a prospective internally controlled interventional trial. *The Lancet Respiratory Medicine* 2018;6(6):461-71. doi: 10.1016/S2213-2600(18)30171-1

16. Quittner AL, Abbott J, Georgiopoulos AM, et al. International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety. *Thorax* 2016;71(1):26-34. doi: 10.1136/thoraxjnl-2015-207488 (published Online First: 2015/10/11)
17. Douglas T, Green J, Park J, et al. Psychosocial characteristics and predictors of health-care use in families of young children with cystic fibrosis in Western Australia. *J Paediatr Child Health* 2016;52(1):34-9. doi: 10.1111/jpc.13011 (published Online First: 2015/10/31)
18. Bell SC, Mall MA, Gutierrez H, et al. The future of cystic fibrosis care: a global perspective. *Lancet Respir Med* 2020;8(1):65-124. doi: 10.1016/S2213-2600(19)30337-6 (published Online First: 2019/10/02)
19. Borowitz D, Robinson KA, Rosenfeld M, et al. Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis. *The Journal of pediatrics* 2009;155(6):S73-S93.
20. Castellani C, Duff AJA, Bell SC, et al. ECFS best practice guidelines: the 2018 revision. *Journal of Cystic Fibrosis* 2018;17(2):153-78. doi: 10.1016/j.jcf.2018.02.006
21. Conway S, Balfour-Lynn IM, De Rijcke K, et al. European Cystic Fibrosis Society Standards of Care: Framework for the Cystic Fibrosis Centre. *Journal of Cystic Fibrosis* 2014;13:S3-S22. doi: 10.1016/j.jcf.2014.03.009
22. McIntosh ID. Health human resources guidelines: minimum staffing standards and role descriptions for Canadian cystic fibrosis healthcare teams. *Canadian respiratory journal* 2016;2016
23. Saxby N, Painter C, Kench A, et al. Nutrition Guidelines for Cystic Fibrosis in Australia and New Zealand. In: Bell S, ed. Sydney: Thoracic Society of Australia and New Zealand, 2017.
24. Nixon PA, Orenstein DM, Kelsey SF, et al. The prognostic value of exercise testing in patients with cystic fibrosis. *N Engl J Med* 1992;327(25):1785-8. doi: 10.1056/nejm199212173272504 (published Online First: 1992/12/17)
25. Pianosi P, Leblanc J, Almudevar A. Peak oxygen uptake and mortality in children with cystic fibrosis. *Thorax* 2005;60(1):50-4. doi: 10.1136/thx.2003.008102 (published Online First: 2004/12/25)
26. Hebestreit H, Arets HGM, Aurora P, et al. Statement on Exercise Testing in Cystic Fibrosis. *Respiration* 2015;90(4):332-51. doi: 10.1159/000439057
27. Floto RA, Olivier KN, Saiman L, et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis. *Thorax* 2016;71(Suppl 1):i1-i22.
28. Rosenfeld M, Farrell PM, Kloster M, et al. Association of lung function, chest radiographs and clinical features in infants with cystic fibrosis. *European Respiratory Journal* 2013;42(6):1545-52. doi: 10.1183/09031936.00138412
29. Mott LS, Park J, Murray CP, et al. Progression of early structural lung disease in young children with cystic fibrosis assessed using CT. *Thorax* 2012;67(6):509-16. doi: 10.1136/thoraxjnl-2011-200912 [published Online First: 2011/12/28]
30. Sanders DB, Li Z, Brody AS. Chest computed tomography predicts the frequency of pulmonary exacerbations in children with cystic fibrosis. *Ann Am Thorac Soc* 2015;12(1):64-9. doi: 10.1513/AnnalsATS.201407-338OC [published Online First: 2014/12/05]
31. Ciet P, Bertolo S, Ros M, et al. State-of-the-art review of lung imaging in cystic fibrosis with recommendations for pulmonologists and radiologists from the "iMAging managEment of cySTic fibROsis" (MAESTRO) consortium. *European Respiratory Review* 2022;31(163):210173. doi: 10.1183/16000617.0173-2021
32. Knepper C, Ellemunter H, Eder J, et al. Low sodium status in cystic fibrosis-as assessed by calculating fractional Na(+) excretion-is associated with decreased growth parameters. *J Cyst Fibros* 2016;15(3):400-5. doi: 10.1016/j.jcf.2015.12.010 [published Online First: 2016/01/19]
33. Middleton PG, Wagenaar M, Matson AG, et al. Australian standards of care for cystic fibrosis-related diabetes. *Respirology* 2014;19(2):185-92. doi: <https://doi.org/10.1111/resp.12227>

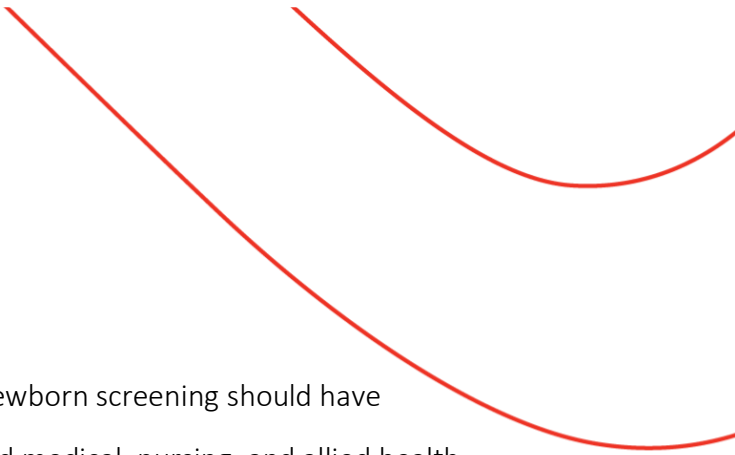
34. Sermet-Gaudelus I, Bianchi ML, Garabédian M, et al. European cystic fibrosis bone mineralisation guidelines. *J Cyst Fibros* 2011;10 Suppl 2:S16-23. doi: 10.1016/s1569-1993(11)60004-0 [published Online First: 2011/06/17]
35. Aris RM, Merkel PA, Bachrach LK, et al. Guide to Bone Health and Disease in Cystic Fibrosis. *The Journal of Clinical Endocrinology & Metabolism* 2005;90(3):1888-96. doi: 10.1210/jc.2004-1629
36. Button BM, Wilson C, Dentice R, et al. Physiotherapy for cystic fibrosis in Australia and New Zealand: A clinical practice guideline. *Respirology* 2016;21(4):656-67. doi: 10.1111/resp.12764 [published Online First: 2016/04/19]
37. Kimple AJ, Senior BA, Naureckas ET, et al. Cystic Fibrosis Foundation otolaryngology care multidisciplinary consensus recommendations. *Int Forum Allergy Rhinol* 2022;12(9):1089-103. doi: 10.1002/alr.22974 [published Online First: 2022/01/29]
38. Granados A, Chan CL, Ode KL, et al. Cystic fibrosis related diabetes: Pathophysiology, screening and diagnosis. *Journal of Cystic Fibrosis* 2019;18:S3-S9. doi: 10.1016/j.jcf.2019.08.016
39. Frayman KB, Sawyer SM. Sexual and reproductive health in cystic fibrosis: a life-course perspective. *The Lancet Respiratory Medicine* 2015;3(1):70-86. doi: [https://doi.org/10.1016/S2213-2600\(14\)70231-0](https://doi.org/10.1016/S2213-2600(14)70231-0)
40. Allen JG, Ibrahim AM. Indoor Air Changes and Potential Implications for SARS-CoV-2 Transmission. *JAMA* 2021;325(20):2112-13. doi: 10.1001/jama.2021.5053 [published Online First: 2021/04/17]
41. Savant AP, O'Malley C, Bichl S, et al. Improved patient safety through reduced airway infection rates in a paediatric cystic fibrosis programme after a quality improvement effort to enhance infection prevention and control measures. *BMJ Qual Saf* 2014;23 Suppl 1:i73-i80. doi: 10.1136/bmjqs-2013-002315 [published Online First: 2014/03/13]
42. McNicholl D, Dickson R, Mulligan E, et al. The experiences of a rapid access respiratory clinic in Northern Ireland. *European Respiratory Journal* 2016;48(suppl 60):OA250. doi: 10.1183/13993003.congress-2016.OA250
43. Shanthikumar S, Moore E, Corda J, et al. Patient and family perspectives regarding the use of telehealth for cystic fibrosis care. *Pediatr Pulmonol* 2021;56(5):811-13. doi: 10.1002/ppul.25262 [published Online First: 2021/01/13]
44. Compton M, Soper M, Reilly B, et al. A Feasibility Study of Urgent Implementation of Cystic Fibrosis Multidisciplinary Telemedicine Clinic in the Face of COVID-19 Pandemic: Single-Centre Experience. *Telemed J E Health* 2020;26(8):978-84. doi: 10.1089/tmj.2020.0091 [published Online First: 2020/05/02]
45. Fettes E, Riley M, Brotherston S, et al. "You're on mute!" Does pediatric CF home spirometry require physiologist supervision? *Pediatr Pulmonol* 2022;57(1):278-84. doi: 10.1002/ppul.25708 [published Online First: 2021/09/29]
46. Cox NS, Alison JA, Rasekaba T, et al. Telehealth in cystic fibrosis: a systematic review. *J Telemed Telecare* 2012;18(2):72-8. doi: 10.1258/jtt.2011.110705 [published Online First: 2011/12/27]
47. Ode KL, Chan CL, Granados A, et al. Cystic fibrosis related diabetes: Medical management. *Journal of Cystic Fibrosis* 2019;18:S10-S18. doi: <https://doi.org/10.1016/j.jcf.2019.08.003>
48. Moran A, Pillay K, Becker D, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Management of cystic fibrosis-related diabetes in children and adolescents. *Pediatr Diabetes* 2018;19 Suppl 27:64-74. doi: 10.1111/pedi.12732 [published Online First: 2018/08/11]
49. Hadjiliadis D, Khoruts A, Zauber AG, et al. Cystic Fibrosis Colorectal Cancer Screening Consensus Recommendations. *Gastroenterology* 2018;154(3):736-45.e14. doi: 10.1053/j.gastro.2017.12.012 [published Online First: 2018/01/01]
50. Melville C, Hands S, Jones P. Randomised trial of the effects of structuring clinic correspondence. *Archives of Disease in Childhood* 2002;86(5):374-75. doi: 10.1136/adc.86.5.374
51. Rawal J, Barnett P, Lloyd B. Use of structured letters to improve communication between hospital doctors and general practitioners. *BMJ: British Medical Journal* 1993;307(6911):1044.
52. Lenferink A, van der Palen J, van der Valk PDLPM, et al. Exacerbation action plans for patients with COPD and comorbidities: a randomised controlled trial. *European Respiratory Journal* 2019;54(5):1802134. doi: 10.1183/13993003.02134-2018

53. Savage E, Beirne PV, Ni Chroinin M, et al. Self-management education for cystic fibrosis. *Cochrane Database Syst Rev* 2014(9):CD007641. doi: 10.1002/14651858.CD007641.pub3 [published Online First: 2014/09/10]
54. Edwards DJ, Wicking K, Smyth W, et al. Information needs of parents of infants diagnosed with cystic fibrosis: Results of a pilot study. *J Child Health Care* 2018;22(3):382-92. doi: 10.1177/1367493518760734 [published Online First: 2018/03/01]
55. Pakhale S, Baron J, Armstrong M, et al. Lost in translation? How adults living with Cystic Fibrosis understand treatment recommendations from their healthcare providers, and the impact on adherence to therapy. *Patient Educ Couns* 2016;99(8):1319-24. doi: 10.1016/j.pec.2016.03.023 [published Online First: 2016/04/03]
56. Frayman KB, Chin M, Sawyer SM, et al. Sexual and reproductive health in cystic fibrosis. *Current Opinion in Pulmonary Medicine* 2020;26(6):685-95.
57. Sawicki GS, Sellers DE, McGuffie K, et al. Adults with cystic fibrosis report important and unmet needs for disease information. *J Cyst Fibros* 2007;6(6):411-6. doi: 10.1016/j.jcf.2007.03.004 [published Online First: 2007/04/25]
58. Zou RH, Tiberio PJ, Triantafyllou GA, et al. Clinical Characterization of E-Cigarette, or Vaping, Product Use-associated Lung Injury in 36 Patients in Pittsburgh, Pennsylvania. *Am J Respir Crit Care Med* 2020;201(10):1303-06. doi: 10.1164/rccm.202001-0079LE [published Online First: 2020/02/06]

Diagnosis of Cystic Fibrosis

Dominic Fitzgerald, Siobhain Mulrennan, Peter Wark,
Tonia Douglas, Peter Middleton, Phil Robinson



- 
- Standard 1** Infants diagnosed through newborn screening should have prompt access to experienced medical, nursing, and allied health CF personnel within a week of an abnormal newborn screening (NBS) result
- Standard 2** Infants with meconium ileus should have their NBS result prioritised
- Standard 3** Newly diagnosed people with CF should be assessed for respiratory symptoms and signs which may require an appropriate respiratory sample collection, antibiotics and/or commencement of airway clearance programs
- Standard 4** Families of newly diagnosed people with CF should have access to genetic counselling services and psychosocial support services
- Standard 5** Individuals and families should have access to up-to-date and relevant educational material about CF from the time of diagnosis
- Standard 6** Salt, electrolyte, and vitamin replacement therapy should be considered in people at diagnosis; particularly those with poor weight gain, evidence of fat malabsorption and those living in geographical areas where hot and humid conditions prevail
- Standard 7** Infants should be assessed for pancreatic insufficiency and enzyme therapy commenced when indicated

Making the diagnosis of cystic fibrosis in neonates

The diagnosis of CF is first considered when newborn screening of the heel-prick blood sample (Guthrie's test) reveals an elevated immunoreactive trypsinogen (IRT) and the presence of at least one mutation of a CFTR allele on genetic testing. Sweat chloride testing follows in addition to confirmation of the presence of mutations in CFTR using a venous blood sample. All states and territories in Australia have a newborn screening (NBS) program which was introduced between 1981 and 2000. Most (Approximately 80%) people living with CF have been diagnosed via newborn screening with an additional 5% diagnosed by 12 months of age ([ACFDR report 2020](#)). Some of those diagnosed in infancy will present with neonatal meconium ileus and may also be detected on newborn screening. A small proportion of infants with meconium ileus

may have a delay in NBS depending upon their clinical condition, although it is vital for this to be performed in the unlikely event that other congenital conditions identified via NBS are present. Approximately 96% of people with CF in Australia were diagnosed before the age of 18 years and the remaining 4% in adulthood (CFA data registry report 2020). It is important that appropriate counselling, support, and education, including accurate, approved internet sites, are provided to the newly diagnosed person with CF and their family members and that a spirit of optimism and hope is conveyed by the CF team. The CF team should also liaise with the patient's community health providers including paediatricians and general practitioners, and notify them of the diagnosis of CF.

CF Newborn Screening (NBS)

All children born in Australia are recommended for screening at birth for CF through a heel prick blood test performed around three days of age. Samples are analysed in accredited state-based screening laboratories in a two-stage procedure¹ first measuring IRT and in those with elevated IRT levels², subsequent genetic testing for the presence of the common CFTR mutations in the population. Some states will repeat the IRT test at 4-6 weeks of age to reduce the number of people needing further diagnostic evaluation. The range of CFTR mutations tested differs in each program and a current comprehensive list of known disease-causing genetic

mutations is available through the [CFTR2 website](#). Some laboratories will require an additional blood test to undertake formal genetic testing at an accredited laboratory.

It is crucial to remember that a small number of infants will not be identified via NBS (usually due to a low IRT; in which case, common CFTR mutations may later be identified), parental choice to forgo NBS, administrative error, or, more commonly, due to the presence of two extremely rare CFTR mutations (generally 'personal' or 'familial' mutations).

Benefits of NBS

Clear evidence exists about the benefits of newborn screening (NBS) for CF in terms of improved nutritional status in young children through to adolescence^{1,2}. Long term benefits for survival in adulthood have also been identified³. Further, as several studies have identified improved outcomes through centre-based care for patients with CF, newborn screening programs should be closely

associated with major CF care centres⁴. Newborn screening for CF means that currently 95% of paediatric diagnoses of CF are made in the first 6 weeks of life. While many infants may be asymptomatic at that time, the introduction of the diagnosis to a family should involve both a clinical assessment of the child and initial education for the family.



Clinical considerations around NBS

Parents/families of infants identified through NBS as having two disease causing mutations, should be contacted by a health professional with knowledge and experience of CF.

Ideally, initial contact with the family should be made by a member of the CF specialist team (usually the CF physician/CF specialist nurse). Where this is not possible, health professionals informing parents of positive NBS results should work closely with the specialist CF team to ensure accurate information is

provided to parents and provide prompt referral of the patient and family to the specialist CF centre. It is important to minimise the time from receiving the notification of a positive NBS, which is highly suggestive of CF, to the initial contact with an experienced CF care team⁵.

Newly diagnosed infants with CF should be reviewed at a tertiary CF specialist centre with paediatric expertise for assessment and parental education.

The complexity of care required for infants newly diagnosed with CF, and the information and psychosocial needs of the parents and family, requires a specialist CF team. Where possible, newly diagnosed infants should be assessed at a paediatric tertiary centre by experienced CF team members, including medical, nursing, and allied health persons.

A CF specialist (usually the treating physician) should discuss the diagnosis with the parents in person, providing information about the disease, CF treatment and the management of their child. A period of education and clinical assessment of the newly diagnosed infant is necessary. A careful assessment of parental capacity and psychological

wellbeing should occur continuously at this time to decide on the pace at which this information is delivered, and clinical testing is performed. Clinical assessment will include, but not necessarily be limited to:

- History and examination including assessment of weight gain and feeding, stool frequency and respiratory symptoms
- Radiological assessment of lungs – usually a chest radiograph (CXR) if clinically indicated
- Blood tests for fat-soluble vitamins (A, E, D; Vit E/lipid ratios), liver function tests (LFTs) and blood chemistry
- Assessment of pancreatic function – faecal elastase sample for children over 2 weeks of age
- Respiratory sample, often upper airway culture, particularly if symptomatic with cough
- Sweat test
- Repeat or extended genotype testing will be required to confirm the newborn screening results in infants and to provide evidence of formal molecular genetic results which will be required for access to CFTR modulators

While the introduction of treatment will reflect clinical need, it may commence at the initial appointment and include:

- Salt/electrolyte replacement therapy
- Vitamin supplementation
- Pancreatic enzyme replacement therapy
- Antibiotic treatment (some centres)
- Airway clearance techniques

Diagnosis after meconium ileus

Approximately 15% of infants with cystic fibrosis will be born with meconium ileus (6,7). Care should be taken to ensure that newborn screening tests are conducted even in sick infants in the NICU. Diagnosis by sweat testing may be technically difficult and not without risk of burns in small, sick neonates⁸. With IRT testing and expedited genetic testing available, sweat testing is less urgent and may be deferred until

Psychosocial support and mental health screening for parents and families should be available at the time of diagnosis and education and may be provided by the CF social worker, CF nurse specialist, and CF psychologist/counsellor as appropriate. Information regarding services and supports available from the local state CF association may be provided.

clinical recovery in sick newborns. Genotyping results will usually confirm the diagnosis of CF. Once the diagnosis of CF is confirmed, education and institution of therapy should start while the infant is still in hospital following treatment of meconium ileus. Assessment of the child and treatment should progress as set out above. Written and on-line educational resources should be provided for

families⁹. These infants should be regarded as being at a higher risk for DIOS throughout life.

Uncertainties around NBS diagnosis.

Infants identified on newborn screening with an elevated IRT, only one identified disease-causing CFTR mutation and a normal sweat chloride (< 30 mmol/L)

These infants should undergo further testing with either (1) a repeat sweat test or (2) a repeat IRT followed by a sweat test if the IRT is still elevated (there is some variability in approach from state to state). The likelihood of having CF is very low if the sweat chloride is < 30 mmol/L and the conclusion is that the child is an unaffected carrier (one parent will be an obligate carrier in this setting). No further testing is undertaken, and the infant has no further

scheduled respiratory follow-up. The family should be informed of the result and be advised that if the child were to develop concerning respiratory symptoms, then a specialist review would be recommended. The family should be offered genetic counselling and consideration of cascade testing where indicated and any siblings with symptoms and signs should be evaluated for CF.

Infants identified on newborn screening with an elevated IRT, only one identified disease causing CFTR mutation and an equivocal sweat chloride (30-59 mmol/L)

In this scenario, there may be a second CFTR mutation identified of uncertain pathogenicity (variant of uncertain significance VOUS:) or no known mutation on the other allele. A second sweat test (in a pathology laboratory accredited for sweat testing and utilising staff experienced in performing sweat tests in young infants) is recommended to confirm the initial result. Repeat sweat testing

concentration should be delivered either by a genetic counsellor or a member of the CF specialist team. Extended genetic mutation analysis, or full genome sequencing, should be considered, and the subsequent assessment of the child and any required treatment should be supervised by a respiratory physician with expertise in children with 'indeterminate' results.

should be considered as a matter of urgency because further delay may cause considerable parental anxiety. Support for the family through this time by an experienced genetic counsellor or CF team member should be available and the family asked to monitor for signs or symptoms of CF. Results of the sweat test and the clinical implication of the chloride

Newborn screening has created an increasing population of infants with initial intermediate/equivocal sweat chloride values, who require follow up through childhood with periodic repeat sweat testing (consider repeating at ages: 6-12 months, 2 years, 5 years, 10 years, and 15 years). Repeat sweat testing will usually provide for four

possible eventualities: (1) Should the child return a sweat chloride greater than or equal to 60mmol/l they will receive a formal diagnosis of CF and no further sweat tests would be required, (2) the child will remain asymptomatic with sweat chloride results on re-test that are in the normal range (and the child is thus an obligate carrier of a CFTR mutation) and no further sweat tests are required, (3) the child develops symptoms, perhaps minimal, and repeated sweat test results remain equivocal, or (4) the child remains asymptomatic with equivocal sweat chlorides. A proportion of young children in this situation will have a diagnosis of CF confirmed over subsequent years on subsequent sweat testing or further genetic analysis¹⁰.

Thus, all children with equivocal sweat chlorides should initially remain under review by a respiratory paediatrician to determine the appropriateness of attention by a wider range of CF care providers (in an established CF clinic). These children are often referred to by a variety of 'labels' including 'CF Screen Positive Inconclusive Diagnosis' (CFSPID)^{11,12}, 'CF transmembrane regulator related metabolic syndrome' (CMS)¹³ or 'Grey CF'^{10,14-16}.

The ability to formally diagnose CF is important for access to multi-disciplinary care and treatments that are reimbursed on the PBS such as dornase alfa and modulator therapies. The use of international CF databases may be helpful in identifying other patients with similar diagnostic challenges (<http://www.genet.sickkids.on.ca/cftr/app>).

Infants identified on newborn screening with an elevated IRT, only one identified disease-causing CF mutation and a diagnostic sweat chloride (≥ 60 mmol/L)

A repeat sweat test in an accredited testing laboratory is recommended and if also positive confirms the diagnosis of CF. Full gene exome sequencing is recommended to attempt to identify the second gene mutation.

Prenatal diagnosis of cystic fibrosis.

This is uncommon but likely to increase in those with a positive family history of CF or those with abnormalities noted on antenatal ultrasounds (e.g. echogenic bowel) who proceed to genetic testing on the foetus. This may also occur with assisted pregnancies using in-vitro-fertilisation (IVF)

and where new programs such as "[Mackenzie's Mission](#)" are being implemented. Families in this setting should be offered genetic counselling and, if desired, an opportunity to meet promptly with experienced CF medical and nursing staff who have been trained in providing prenatal counselling.

Diagnosis of cystic fibrosis in children beyond the newborn period is now a relatively uncommon situation in Australia following implementation of newborn screening for CF in all Australian states and territories over the last 20 years. However, it still occurs, and clinical suspicion remains important for children with significant failure-to-thrive, signs of malabsorption, recurrent chest infections or in children with uncommon presentations such as pancreatitis, severe heat stroke or nasal polyposis. They should be assessed with a physical examination by an experienced CF physician, undergo a sweat test and genetic testing to identify the genotypes ^{11,14}.

Initial education for the family / young person with CF

Once the diagnosis of CF has been made, ample time should be made available for the family to meet with all members of the multidisciplinary CF care team and to begin the process of education and mastery of CF care for their child. Parents and primary carers should meet, preferably face-to-face initially, with their child's physician, the CF physiotherapists, dieticians, social workers, counsellors, and nurses on a frequent basis, tailored to the needs of the parents. On occasion, particularly for those with a newly diagnosed newborn, it may be appropriate for extended family members to be similarly educated at this time. During this time medical assessment of the patient should be completed. It is recommended that patients and families are provided with educational material using both printed⁹ and regularly updated [on-line resources](#) that describe treatment techniques and provide a broader understanding of CF and its

management. People with CF/parents should be provided with directions to access online resources from reliable CF internet sites including CF Australia, [The North American CF Foundation](#) and the [UK CF Trust](#). Where CF Centres have access to community agencies, such as local CF associations, additional support and resources will be available.

A list of contact numbers of members of the CF care team should be provided to the patient/parents/carers following diagnosis. A CF exacerbation action plan and prescriptions for medications should be provided to patients/parents/caregivers. The hazards of environmental tobacco smoke exposure for children with cystic fibrosis should be discussed. Support is available through Quit smoking resources by telephone (13 QUIT or 13 7848) or [on-line](#).



Follow-up

Regular, frequent follow-up after the diagnosis of CF is recommended to review the clinical progress in response to interventions such as pancreatic enzyme replacement therapy, antibiotics, and chest physiotherapy¹¹. In addition, regular review of patient/parental understanding and mastery of CF cares and adjustment to diagnosis is important.

Regular outpatient appointments for review will be made by the CF care team at the hospital. Correspondence to the patient/family's general

practitioner and their local paediatrician (when an established relationship exists) regarding diagnosis and treatment plan should be undertaken. Special care should be taken to ensure those whose domicile is geographically distant to the specialist CF care centre have access to local health care providers who can provide urgent care. For infants, referral to the local child health nurse should be considered. Some paediatric CF centres send copies of medical correspondence to the families.

Diagnosis of cystic fibrosis in the adolescent and adult years

In the year 2020, 10% of new diagnoses of CF were in adulthood, reflecting missed diagnoses in people born in Australia prior to newborn screening, those not detected via NBS programs (particularly in states which previously only tested for a very limited panel of CFTR mutations), or those born overseas. Adolescent and adult CF presentations can vary both in clinical phenotype and onset of symptoms and may be

associated with mutations conferring residual functioning of CFTR ¹⁷. The diagnostic workup of adults and adolescents includes sweat testing, genetic analysis and phenotypic assessment and investigations ¹¹.

Clinical presentation can include any of the following features:

- Congenital absence of the vas deferens in males detected due to infertility or during urological surgery
- Acute pancreatitis (recurrent or an initial episode)
- Chronic rhinosinusitis or nasal polyposis
- Recurrent respiratory infections, bronchitis, or bronchiectasis with persistent colonisation/infection with typical CF pathogens
- Pancreatic insufficiency and malabsorption
- Osteoporosis and low bone mineral density
- Chronic liver disease
- Acute salt depletion or metabolic alkalosis and dehydration

Diagnostic Workup in an adolescent or adult with features of CF

Sweat electrolytes

- Sweat testing should be performed in an accredited laboratory with staff experienced in performing sweat tests in all ages.
- Whilst people with atypical or non-classical CF features often have intermediate sweat chloride results (Cl^- : 30-59 mmol/L) (19), the sweat test is part of the diagnostic algorithm for these individuals¹⁸. The likelihood of a patient with atypical symptoms having CF is highest if the sweat chloride result is in the abnormal range (>60 mmol/L) but is still likely in the intermediate range (30-59 mmol/L) range. However, in some individuals, even a normal sweat Cl^- can be associated with a diagnosis of CF.
- In all instances, it is important to perform the sweat test on more than one occasion.

Genetic screening

- Consultation with a specialist molecular geneticist is indicated for this age group due to the implications for the individual concerned and their immediate and extended family.

- Performing extended genetic analysis accounting for ethnic ancestry of the patient is recommended. Specific mutations analysed for the appropriate population can be useful. Extended CFTR mutation panels and, if considered necessary, whole gene exome sequencing are available in all states of Australia.
- Full CFTR genetic analysis (sequencing) is increasingly available with advances in next generation sequencing technologies. Clinical Genetics and Biochemistry Services attached to CF centres can provide advice on the performing

of gene sequencing to confirm a diagnosis of CF. However, intronic mutations can still be missed despite normal exon sequencing.

- The Clinical and Functional Translation of CFTR Project (CFTR2) has compiled genetic and clinical information on almost 40,000 people living with CF internationally. [The CFTR2 website](#) provides information about specific CFTR mutations, including the impact of clinical features, for health care professionals and people living with CF.

Other phenotypic tests

Review by a CF physician to assess all possible phenotypes is recommended.

There are many other tests that may be considered, depending on the presenting symptoms or signs of the patient, and include, but are not limited to:

- Spirometry, lung volumes and diffusing capacity
- Sputum microbiology
- A high-resolution CT chest for the presence of CF-related lung disease, together with a CT of the sinuses.
- Faecal elastase, liver ultrasound and liver function tests and amylase / lipase.
- Fat soluble vitamin levels should be measured and medical imaging of the abdomen (e.g. liver and pancreas) performed.
- In males, testing for azoospermia may be considered
- Bone mineral densitometry and oral glucose tolerance testing may be considered

The diagnostic criteria for CF (15) are the presence of end-organ changes consistent with CF or a family history and one of the following:

- Two identified CF disease-causing mutations of CFTR.
- an abnormal sweat chloride (>60mmol/L)
- One CF disease-causing mutation of CFTR, clinical features strongly suggestive of CF, (there may be a family history) and a sweat chloride concentration at least in the intermediate range (30-59mmol/L), reflecting CFTR dysfunction.

Management of the adolescent or adult with proven CF at the time of diagnosis

- After a diagnosis of CF has been made, it is recommended that the adolescent/adult receive follow-up by a physician experienced in the management of people with CF. If the adolescent is over 16 years of age, consideration might be given to the immediate referral to an appropriate adult centre so that the young person does not need to transfer their care shortly after such a significant diagnosis.
- Attention should be given to the significant impact of a diagnosis of CF at this age on the advisability or otherwise of a chosen career path or current employment.
- Advantages of a CF centre-based approach include access to the specialist CF team, an opportunity for the recognition and treatment of other complications associated with CF (e.g. specific pulmonary infections), non-specific abdominal pain representing pancreatitis, exploration of possible infertility and genetic counselling for family members.

Management of the adolescent or adult with suspected CF or CF related disorder/CFSPID

- If a diagnosis of CF cannot be made definitively, it is preferable to discuss the situation frankly with the person. An overriding principle to emphasise is that effective clinical treatment is available for most associated conditions such as respiratory, sinus, gastrointestinal tract disease and male infertility even without a formal diagnosis of CF.

References

1. Waters DL, Wilcken B, Irwig L, Van Asperen P, Mellis C, Simpson JM, Brown J, Gaskin KJ. Clinical outcomes of newborn screening for cystic fibrosis. *Archives of Disease in Childhood-Fetal and Neonatal Edition*. 1999 Jan 1; 80(1):F1-7.
2. Castellani C, Southern KW, Brownlee K, Roelse JD, Duff A, Farrell M, Mehta A, Munck A, Pollitt R, Sermet-Gaudelus I, Wilcken B. European best practice guidelines for cystic fibrosis neonatal screening. *Journal of Cystic Fibrosis*. 2009 May 1; 8(3):153-73.
3. Dijk FN, McKay K, Barzi F, Gaskin KJ, Fitzgerald DA. Improved survival in cystic fibrosis patients diagnosed by newborn screening compared to a historical cohort from the same centre. *Archives of Disease in Childhood*. 2011 Dec 1; 96(12):1118-23.
4. Lebecque P, Leonard A, De Boeck K, De Baets F, Malfroot A, Casimir G, Desager K, Godding V, Leal T. Early referral to cystic fibrosis specialist centre impacts on respiratory outcome. *Journal of Cystic Fibrosis*. 2009 Jan 1; 8(1):26-30.
5. Robinson PJ. Management of the infant diagnosed by newborn screening. In Bush A, Geddes DM, Hodson ME (eds). *Cystic Fibrosis*. Cambridge, Chapman and Hall, 2007, 3rd Ed, 117-123).
6. Evans AK, Fitzgerald DA, McKay KO. The impact of meconium ileus on the clinical course of children with cystic fibrosis. *European Respiratory Journal*. 2001 Nov 1; 18(5):784-9
7. Sathe M, Houwen R. Meconium ileus in cystic fibrosis. *Journal of Cystic Fibrosis*. 2017 Nov 1; 16:S32-9.
8. Massie J, Greaves R, Metz M, Wiley V, Graham P, Shepherd S, Mackay R. Australasian guideline: an annex to the CLSI and UK guidelines for the performance of the sweat test for the diagnosis of cystic fibrosis. *The Clinical Biochemist Reviews*. 2017 Nov; 38(3):115.
9. Fitzgerald DA. *The Cystic Fibrosis Passport*. Clareville Press; 2013.
10. Groves T, Robinson P, Wiley V, Fitzgerald DA. Long-term outcomes of children with intermediate sweat chloride values in infancy. *Journal of Pediatrics*. 2015 Jun 1; 166(6):1469-74.
11. Smyth AR, Bell SC, Bojcin S, Bryon M, Duff A, Flume P, Kashirskaya N, Munck A, Ratjen F, Schwarzenberg SJ, Sermet-Gaudelus I. European cystic fibrosis society standards of care: best practice guidelines. *Journal of Cystic Fibrosis*. 2014 May 1; 13:S23-42.
12. Munck A, Mayell SJ, Winters V, Shawcross A, Derichs N, Parad R, Barben J, Southern KW. Cystic Fibrosis Screen Positive, Inconclusive Diagnosis (CFSPID): A new designation and management recommendations for infants with an inconclusive diagnosis following newborn screening. *Journal of Cystic Fibrosis*. 2015 Nov 1; 14(6):706-13.
13. Borowitz D, Parad RB, Sharp JK, Sabadosa KA, Robinson KA, Rock MJ, et al. Cystic Fibrosis Foundation practice guidelines for the management of infants with cystic fibrosis transmembrane conductance regulator-related metabolic syndrome during the first two years of life and beyond. *Journal of Pediatrics* 2009; 155:S106-16.
14. Massie J, Clements B. Diagnosis of cystic fibrosis after newborn screening: the Australasian experience- twenty years and five million babies later: a consensus statement from the Australasian Paediatric Respiratory Group. *Pediatric Pulmonology* 2005; 39:440-6.
15. Krishnananthan T, Pao C. The implications and management of cystic fibrosis screen positive, inconclusive diagnosis patients. *Paediatric Respiratory Reviews*. 2019 Aug 1; 31:21-4.
16. Barben J, Castellani C, Munck A, Davies JC, de Winter-de Groot KM, Gartner S, Kashirskaya N, et al. European CF Society Neonatal Screening Working Group (ECFS NSWG) Updated guidance on the management of children with cystic fibrosis

transmembrane conductance regulator-related metabolic syndrome/cystic fibrosis screen positive, inconclusive diagnosis (CRMS/CFSPID). *Journal of Cystic Fibrosis* 2021 Sep; 20(5):810-819.

17. Nick JA, Nichols DP. Diagnosis of Adult Patients with Cystic Fibrosis. *Clin Chest Med* 37 2016; 47–57.
18. Goubau C, Wilschanski M, Skalická V, Lebecque P, Southern KW, Sermet I, Munck A, Derichs N, Middleton PG, Hjelte L, Padoan R. Phenotypic characterisation of patients with intermediate sweat chloride values: towards validation of the European diagnostic algorithm for cystic fibrosis. *Thorax* 2009; 64: 683-691.
19. Farrell PM, White TB, Ren CL, Hampstead SE, Accurso F, Derichs N. et al. Diagnosis of cystic fibrosis consensus guidelines from the Cystic Fibrosis Foundation. *Journal of Pediatrics* 2017; 181:pp S4-S15.

Appendix 1

Potential conflicts of interest

The following outlines potential conflicts of interest by the members of the steering committee during the past five years:

Tonia Douglas has received consultancy fees from Vertex Pharmaceuticals for educational services and is a sub-investigator on Vertex Pharmaceuticals funded clinical trials.

Siobhain Mulrennan is a principal investigator for a Vertex Pharmaceuticals funded clinical trial.

Peter Wark has received funding in the form of unrestricted research grants from Vertex Pharmaceuticals and Krystal Biotech and has served on advisory boards for Vertex Pharmaceuticals.

Dominic Fitzgerald has been a sub-investigator on Vertex Pharmaceuticals funded clinical trials.

Bernadette Prentice has received a TSANZ/Vertex Cystic Fibrosis Fellowship award and an honorarium from Vertex Pharmaceuticals for educational events.

Jo Armstrong, Katherine Frayman, Mitch Messer, Caz Boyd, Amanda Bearcroft, and Nicki Mileham have no conflicts of interests to disclose.