CYSTIC FIBROSIS Australia

The Thoracic Society of Australia & New Zealand
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Australia 2026

Standards of Care For Cystic Fibrosis

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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, including Deloitte Australia, this document will pave the way for better outcomes for everyone living with cystic fibrosis.

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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 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

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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.

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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 Staphylococcus aureus
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 Enterococcus

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,
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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 year[1].

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 adults[1]. 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 previously[2]. 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]

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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 can 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 discharge[12].

- 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 infection[5-10]. 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 specialities 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. FEV_1 and FVC).

- Oxyhaemoglobin saturation (SpO_2) monitoring, where clinically indicated.

- Arterial or capillary blood gases measured if high CO_2 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.
- Experienced staff should only perform venous access. 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

- 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.
- 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 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 Fibrosis[12] 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 needs [12].
- 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

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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 heterogenous 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 therapy[13]. 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 small cohorts of children[16,17,18]. Quality of life was reportedly higher among children receiving home therapy and cost savings were observed[18].

Home vs. inpatient care - Inferior outcomes

1. Inferior outcomes with home therapy were reported in a single centre retrospective study of children and young adults[19] 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) The CF team should regularly audit home therapy activity and outcomes.

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Outpatient Care

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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 families[2].

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 testing [8]. These findings have implications for the rates of air exchanges in outpatient clinics and support the use of face masks [9] 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 outcomes [12]. 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 infections[13].

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 treatment [16]. People and families living with CF experience greater economic and financial burden, marital and relationship strain, and poorer quality of life [17]. 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 available [16].

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 services [18]. 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 prevention [3] 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, FEV_1% measurement) to be eligible for ongoing subsidised treatment.

Frequency of outpatient reviews

There is general agreement across European and North American guidelines that PwCF should have a minimum of four routine reviews per year. It should be noted that these recommendations do not consider individual changes in clinical status among PwCF following initiation of CFTR modulator therapy. At the time of publication of these Standards, there is insufficient evidence to guide frequency of visits in this setting. Changes to visit frequency in this context should be carefully tailored to the individual, negotiated with the CF team and the person with CF and their caregivers, and guided by the best-available evidence.

In children with classical CF, all four reviews should be performed by a CF specialist multidisciplinary team with additional reviews as clinically required (see Chapter Infants and Children).

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:

a) 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.

b) ENT: nasal obstruction, sinus pain and postnasal drip questioned.

c) GIT: Abdominal symptoms including diarrhoea, constipation, bloating, symptoms to suggest reflux, abdominal pain.

d) Rheumatology: Joint pain, inflamed joints, use of analgesia.

e) 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.

f) Adherence to treatment: barriers to adherence, treatment burden, health perceptions, health literacy.

g) 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:

a) Measurement of weight, height (at least annually in adults), body mass index (BMI) and head circumference (≤2 years of ag on growth charts to determine percentiles and track changes over time. Assessment of pubertal status in children/adolescents is required.

b) 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.

c) 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.

i. 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.

ii. 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.

d) Physiotherapist review and advice around airway clearance techniques and adjuncts, inhalational therapy, exercise regimens, assessment of continence issues and musculoskeletal reviews.

e) 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.

f) 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.

g) Oximetry in patients with moderate to severe lung disease or acutely breathless.

h) 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.

i) 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.

j) Relevant investigations (blood tests, urine tests, imaging etc.) as clinically indicated and according to patient progress.

k) 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 conducted 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, (FEV_1% <40% predicted and waking SaO_2 <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), irons 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 = urinary Na × plasma creatinine × 100/(plasma Na × 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 recommended[33].

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.

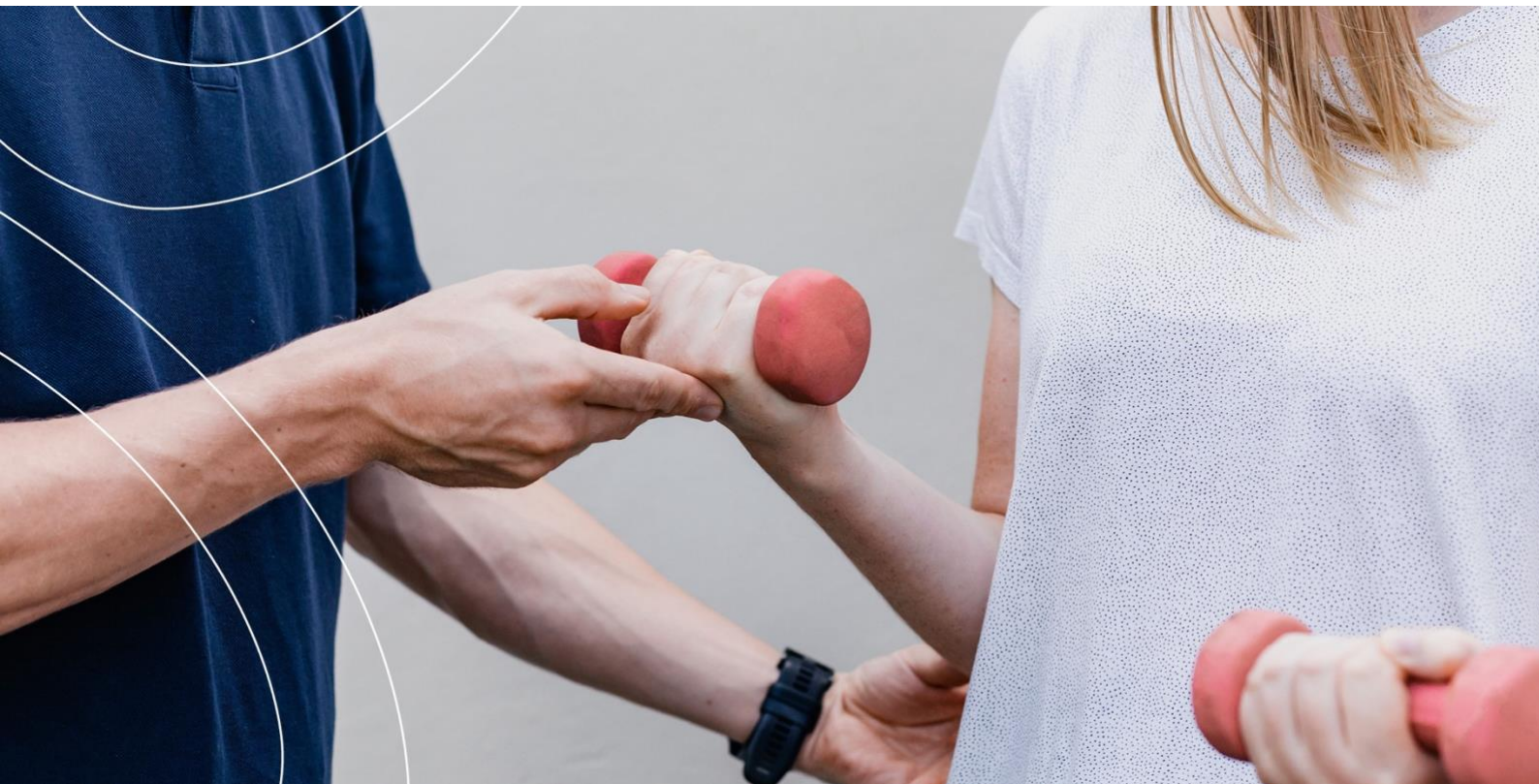
4. Physiotherapy assessment and review in accordance with the Australian and New Zealand Physiotherapy Clinical Practice Guidelines [36].

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).

b) Assessment for musculoskeletal complications of CF and associated pain or functional limitation with referral to a specialist musculoskeletal physiotherapist as required.

c) Screening and assessment for urinary and faecal incontinence in children and adults and referral to incontinence services for management as required.

d) Development of tailored exercise and airway clearance routines in collaboration with patients and families



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.**

   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.

   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].

   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.

   d) Patients with mental health problems identified through screening should be referred promptly to psychological services (hospital or community based) for intervention.

   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.

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.

a) The Cystic Fibrosis Foundation otolaryngology consensus guidelines[37] recommend annual audiology screening for children and adults receiving ototoxic treatments including longer-term macrolide therapy, intravenous and inhaled aminoglycosides, and treatment for *M. abscessus*, 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. 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 patients[42].

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 patients [42].

Telehealth clinic

The COVID-19 pandemic endorsed the feasibility and acceptance of telehealth in CF clinics across Australia [43] and internationally [44]. 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 recommended[45]. 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 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 adults [38]. Management of glycaemic control in patients with CFRD is associated with improved pulmonary function and reduction in pulmonary exacerbations[47]. 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 to consider 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 anaesthetist[59].

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.

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Diagnosis of Cystic Fibrosis

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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 the CF team conveys a spirit of optimism and hope. 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 procedure[1] first measuring IRT and in those with elevated IRT levels[2], 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 identified[3]. 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 centres[4]. 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 collaborate 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 team[5].

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

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.

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 neonates[8]. With IRT testing and expedited genetic testing available, sweat testing is less urgent and may be deferred until 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 families[9]. 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 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 as 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

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 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.

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 analysis[10].

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.

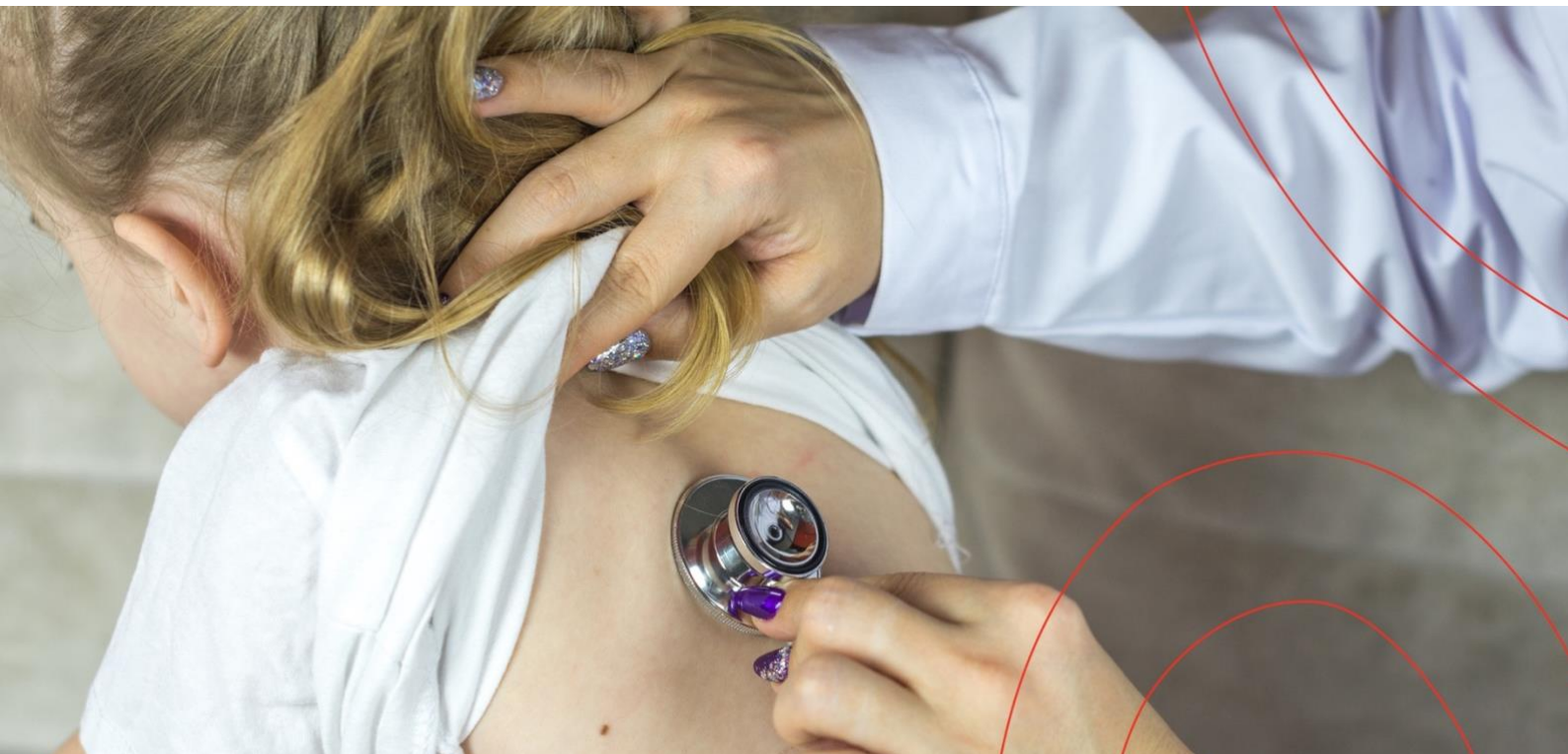
This is uncommon but likely to increase in those with a positive family history of CF or those with abnormalities noted on antenatal ultrasounds (e.g. echogenic bowel) who proceed to genetic testing on the foetus. This may also occur with assisted pregnancies using in-vitro-fertilisation (IVF) and where 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 printed[9] 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 physiotherapy[11]. 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 that previously only tested for a 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 individuals[18]. 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 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 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.

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Infants and Children

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Standard 1 All children should be cared for by a paediatric CF specialist multidisciplinary team and in developmental and age-appropriate healthcare settings that provide family-centred care.

Standard 2 CF care should involve a collaborative partnership with parents/carers and the child based on family and child centred care principals.

Standard 3 Regular clinical assessment by the specialist paediatric multidisciplinary CF team should be provided appropriate to individual needs.

Standard 4 Infants and children should undergo regular surveillance for early CF lung disease using sensitive techniques to facilitate timely interventions.

Standard 5 CF care should include regular surveillance and early intervention for nutritional and growth concerns and for common extra-pulmonary complications of CF that may present in childhood.

Standard 6 Infants and children should have access to effective, up-to-date, evidence-based treatment including approved CFTR modulator therapy, with appropriate monitoring for short- and long-term effects.

Standard 7 Infants and children should receive routine community health and developmental checks and age-appropriate immunisations.

Standard 8 Psychosocial evaluation, support and intervention for children and carers should be available from diagnosis. Mental health and wellbeing screening for children and carers should be routinely implemented.

Background

The childhood years are a critical period where events and exposures in early life shape future physical and psychosocial health across the lifespan (1). Childhood presents, therefore, as an important opportunity to intervene and improve health trajectories and survival for people with CF.

In CF we now understand that early issues such as endobronchial infection and inflammation, poor nutrition, psychosocial adversity, and health behaviours predict worse health outcomes in later childhood and adulthood. Thus, early detection and effective interventions for CF morbidities are crucial and rely on sensitive tools and measures, timely screening, and effective therapies started in early life.

The advent of CFTR modulators will change the landscape of CF in infancy and childhood and we must anticipate that CF care will adapt and evolve for those children benefiting from CFTR therapy. The psychosocial burden of CF and its treatment is significant for families and children, with higher rates of depression and anxiety, reduced quality of life, worse educational achievement, and adverse health behaviours that influence health outcomes (2, 3). As life expectancy increases, there is a greater responsibility to ensure children with CF reach their physical, psychological, and social potential as adults.

Infants and children with CF have unique medical and psychosocial needs that differ from adults. The care provided by a specialist paediatric CF team throughout childhood is associated with the best health outcomes [4, 5].

Evidence

Children receiving CF care in regional or remote areas of Australia that are supported by an outreach MD CF team may have equivalent outcomes to those cared for exclusively in specialist CF centres (6, 7).

Like all children, those with CF should be cared for in an environment that prioritises child and family centred care in a child-friendly environment with facilities and equipment designed specifically for children. Staff providing care for children with CF should have sufficient training and education in paediatric healthcare and the skills required to deliver CF care (8).

Parents/caregivers and families play a key role in their child's CF health care and should be involved as active participants in the CF clinical care team (9, 10). Collaborative partnerships between health providers and parents/caregivers, and later, with the child, improve communication and information transfer and engagement. These achieve improved health outcomes, patient safety and parent/child health experience (39, 40,41).

The best relationships between children, their families and the CF MDT are built on a foundation of mutual trust, respect, and effective communication. This is achieved through understanding and respecting the role of parents/caregivers as both experts in, and advocates for, their child's needs. With parental and later child knowledge and understanding, treatment recommendations should be openly discussed, and a mutually agreed management pathway undertaken. As children mature their understanding of their disease and its treatment will increase which will rightly afford them a greater say in their CF care.

CF lung disease begins in early infancy and often evolves in the absence of any symptoms (11). By age 5-6 years many children have radiologic evidence of suppurative lung disease / early bronchiectasis and some also have lung function abnormalities (11-15). These early changes predict the lung disease trajectory (11-15). Consequently, the importance of conducting regular surveillance with sensitive techniques from an early age and promptly acting

upon abnormal findings cannot be over-emphasised (16, 17).

Detection and prompt management of pulmonary exacerbations in childhood is essential to prevent accelerated decline in lung function and reduce the risk of bronchiectasis (18, 19). Early respiratory infection is associated with increased pulmonary inflammation, lower lung function and progression of bronchiectasis. This highlights the importance of pathogen detection through regular respiratory cultures from early infancy and timely intervention with antimicrobial therapy and pathogen eradication policies (13, 20, 21).

Nutritional status in is a major determinant of health outcomes in CF and better early life growth trajectories lead to higher lung function, fewer pulmonary exacerbations and improved survival (22, 23). Regular surveillance of growth and nutrition, prompt intervention for faltering growth and return to healthy growth indices are essential to ensure the best health outcomes (24, 25). The era of CFTR modulator therapies has brought new challenges related to excessive weight gain and obesity in childhood, with potential adverse effects on future cardiometabolic health. There is a shift in dietary recommendations towards healthy eating and high quality, nutrient dense foods, and a focus on individualised nutritional care for children.

Gastrointestinal symptoms and biochemical liver abnormalities are frequent in childhood (14). Gastrointestinal co-morbidities such as distal intestinal obstruction syndrome (DIOS), constipation, abdominal pain (26), anorexia and gastro-oesophageal reflux (27) are not only prevalent in children with CF but add significantly to the burden of living with CF (14). CF-related liver disease including transient increases in liver enzymes, gall bladder disease, and hepatic steatosis occur commonly in childhood and 5-10% of children will develop multilobular hepatic cirrhosis by adolescence (28). Screening and intervention for these complications remains important as part of routine clinical care and underscores the role of gastroenterology specialists in the care of children with CF.

The clinical benefits of CFTR modulator therapy in younger children with CF are highly anticipated. The arrival of triple corrector therapy [elexacaftor/tezacaftor/ivacaftor] means CFTR modulators are now available for approximately 90% of the CF population, including infants and children. Clinical trials of modulator therapies in infants and children have demonstrated safety and tolerability with significant improvements in lung function, nutritional status, and quality of life and reductions in pulmonary exacerbations and respiratory symptoms (29-33).

It is anticipated that starting CFTR modulators in early childhood may delay or even prevent lung disease and mitigate CF complications, translating into better long-term outcomes and a greater life expectancy (34). Ensuring access to CFTR modulator therapies in childhood is therefore important if the short - and longer-term health benefits are to be fully realised. There are, however, a significant proportion of children unable to tolerate modulator therapies, and approximately 10% of children, based on their CF genotype, for whom no modulator therapies are currently available. Health outcomes for these children will depend on regular, sensitive methods of disease surveillance and timely treatment. They will require ongoing emphasis on early lung disease

detection, monitoring of growth and nutritional status and proactive interventions (35).

The psychosocial impact of CF is enormous. It is experienced by caregivers around the time of newborn screening (NBS) diagnosis and continues well into childhood and adolescence. Diagnosis is associated with shock, denial and parental sorrow that may persist and intensify periodically throughout childhood at significant life/medical events (5, 36).

Adjustment to living with CF may be derailed by maladaptive coping (37) with implications for the health of the whole family and child. Studies show rates of depression and anxiety among parents/caregivers and adolescents with CF are 2-3 times greater than the general population and associated with worse CF-related health outcomes and poor adherence to treatment (2, 38).

Anxiety/depression in the caregiver adversely affects infant and child bonding and doubles the risk of anxiety/depression in adolescents (39). Families of a child with CF may experience psychosocial adversity including financial stress, marital discord and increased rates of parental separation (31). Maternal and child psychological stress and marital discord may increase CF related health-care use (39). Recurrent exposures to invasive procedures and investigations places young children with CF at risk of procedural anxiety that may lead to treatment resistance and avoidance. Behavioural issues around food, and compliance issues around physiotherapy may lead to conflict between the parents and the child and problematic adherence (40). Strategies embedded within routine CF care that focus on prevention, screening and intervention for psychosocial health and wellbeing are essential components of care in infancy and childhood.

Recommendations

1. **Infants and children with CF should have access to an expert, paediatric multi-disciplinary care team:**

The CF MDT should have specialist knowledge and experience in the care of infants and children with CF.

a) CF specialist nurses have a central role in overseeing the daily clinical management of children with CF providing education, support and advice and advocacy for families and children (5, 41). CF specialist nurses coordinate clinical review with relevant CF team members, liaising between patients and families, hospital and community services, and the CF team. CF specialist nurses establish and nurture early relationships with families of newly diagnosed infants and children, paving the way for collaborative partnering and shared decision making.

b) Paediatric CF specialists (currently, these are respiratory paediatricians) should oversee the care of infants and children with CF and are responsible for medical decisions and treatment planning throughout childhood. They should be up to date with current evidence-based therapies, novel treatments targeting early CF disease and clinical guidelines to optimise health outcomes throughout childhood (42). A gastroenterologist with experience in CF is an important member of the CF multidisciplinary team. They will consult on more significant nutritional matters, abdominal concerns [e.g. recurrent or more severe DIOS] and liver disease management. An endocrinologist will be involved from middle childhood where issues with bone health, pubertal delay and CF related diabetes may become evident.

c) Physiotherapists should be engaged in care from CF diagnosis providing education around age and developmentally appropriate airway clearance techniques (43), use of nebulised medications and obtaining respiratory samples for culture to direct treatment. Physiotherapists also assess musculoskeletal health in the growing child and provide advice and management strategies around sport, exercise, and continence. Promotion of self-management in airway clearance through education and support as the child matures is a key role.

d) CF specialist dietitians are needed to evaluate growth, nutritional status, and provide individualised approaches to energy requirements and dietary intake in growing children. Dietitians should be trained in the differing dietary and nutritional requirements of children at different ages and stages of development and be up to date with current CF nutritional guidelines (44). Recognition and prompt intervention for faltering growth,

particularly in the first two years of life, is essential (22) along with surveillance and intervention for accelerated weight gain and obesity. Dietitians are responsible for providing education around early infant nutrition and breast feeding and promoting healthy eating behaviours, positive mealtimes, and nutritient dense foods througout childhood.

e) CF social workers provide a range of important services to families of infants and children with CF. Specifically, CF social workers provide regular psychosocial assessments to assess risk/protective factors around CF care and wellbeing including mental health screening, family functioning, adjustment to diagnosis/grief counselling, parenting roles and parental coping, and significant stressors. CF social workers can help with financial benefits, logistical issues, and welfare support. They provide advocacy and support for families around communication, health literacy and access to health care (45).

f) CF psychologists have a key role alongside social workers and occupational/child life therapists in maintaining and promoting the psychosocial wellbeing of infants, children, and their caregivers. Involvement from CF diagnosis is recommended with ongoing assessment of, and intervention for, emotional, behavioural, and psychological challenges associated with children and their caregivers.

g) Occupational therapists / child life therapists can support and educate families around normal child socio-emotional development, identification and management of child behavioural issues, preparation for medical procedures, school and hospital admissions, development of positive health behaviours including treatment adherence, and socio-emotional health screening.

h) Infants and children with CF have unique age-related physiological, pharmacological, and therapeutic characteristics. Paediatric CF pharmacists are recommended to provide advice and expertise around drug interactions, therapeutic drug monitoring, treatment side effects, adherence, and medication planning in complex regimens. CF pharmacists can help educate and support families in the reconstitution and administration of medications and facilitate easier access to medications through liaison with community pharmacists.

i) Paediatric respiratory laboratory scientists experienced in lung function testing in children are required to provide education and motivational support for children with CF as they master the techniques required to perform reliable respiratory function measures. Facilities and equipment for performance of spirometry, multiple breath washout, body plethysmography and cardio-pulmonary exercise testing (CPET) should be used where available. Home spirometry services are desirable, and testing is best performed under scientist supervision (46).

2. CF care for infants and children should be provided in developmental- and age-appropriate health care settings that provide family and child-centred care.

a) Staff caring for infants, children and adolescents with CF should have sufficient education and training in CF and paediatric illness, and the appropriate skills required to provide holistic patient care(8).

b) Infants and children with CF should be cared for in child-friendly environments with facilities and equipment designed specifically for children.

c) Child and family centred practices and policies should underpin the care of infants and children with CF.

d) Regional clinicians providing care for infants and children with CF must have access to a CF specialist paediatric multidisciplinary team for advice and support. This will include a 24-hour point of access with a CF physician.

e) Development of local, evidence-based CF clinical guidelines policies and protocols for the management of infants, children (and adolescents) with CF are recommended and should be made available to regional CF providers to ensure harmonised and best practice care.

3. CF care should involve a collaborative partnership with parents/caregivers and the child, based on family and child centred care principles

a) A collaborative approach to CF health care involving parents/caregivers as active participants in their child's health care is best practice (10, 47, 48).

b) Partnering with parents and caregivers should begin from the time of diagnosis and be adopted by the whole CF MDT. Collaborative partnering involves delivering CF care through mutually respectful relationships, effective and caring communication, and shared decision-making around CF care.

c) Partnerships with children should evolve as they cognitively develop and physically mature and, over time, enable them to have an equal say in how their care is delivered with opportunities to discuss their health needs, goals, and experiences (49).

d) Regular review of CF treatment and health goals (preferably quarterly) with parents and children as appropriate is recommended.

e) Parents and children should be supported in the development of their health literacy and ability to navigate the health system.

4. Infants and children with CF should receive regular clinical review by the specialist CF multidisciplinary team, tailored to individual needs and progress. Please refer to the Outpatient Care Chapter for more detail

a) Expert consensus currently recommends that infants be reviewed second weekly for the first 3 months of life following CF diagnosis and then monthly until 12 months, with frequency adjusted according to individual needs.

b) Minimum 3-monthly routine MDT clinical reviews are currently recommended for children with CF, with additional visits for periods of ill-health or complications appropriate to need. *It should be noted that this recommendation does not consider individual changes in clinical status among children and infants with initiation of CFTR modulator therapy. At the time of publication, there is no evidence to guide frequency of visits in this setting. Changes to visit frequency in this context should be carefully tailored to the individual child, negotiated with the CF team and the child's caregivers and guided by the best-available evidence (50).

c) Clinical assessments should be tailored to the needs of individual children and their families. Telehealth visits may be considered to ensure equitable access to the CF MDT and to reduce the burden of travel and in-person attendance (See Chapter Outpatient Care). Careful attention to collection of airway samples for culture, measurement of weight and height, and pulmonary function testing is needed around telehealth visits.

d) Clinic visits should include history and physical examination airway clearance techniques and respiratory microbiology, growth and nutrition, psychosocial welfare and developmental progress, treatment plans, care burden and adherence.

e) Annual review of clinical progress by the CF MDT, is required for all children (see Chapter Outpatient Care for details). Progress and subsequent management should be discussed with carers and a mutually agreed treatment plans developed.

f) Age-appropriate respiratory function tests should be performed at each clinic visit where children are able to cooperate.

g) Families and children should receive education and have access to CF resources for up-to-date information on aspects of CF care and supports throughout their time in the CF clinic. The timing of education and support may be tailored to individual needs and linked to key milestones in the child's health care, such as first admission to hospital, starting school, diagnosis of a new CF co-morbdity etc. Health literacy should be supported using plain language, visual aids and technology tailored to individual needs and understanding.

5. Infants and children should undergo regular surveillance for early lung disease and CF complications using sensitive techniques to facilitate timely interventions (51).

a) Airway microbiology, lung function and structural disease must be closely monitored throughout childhood.

i. Microbiological samples (cough swabs, oropharyngeal samples, induced sputum and sputum) should be obtained a minimum of four samples per year and at times of clinical deterioration. Microbiology techniques should enable detection of relevant organisms seen in children with CF including nontuberculous mycobacteria (NTM) (52). Oropharyngeal cultures are frequently used in infants and young children and those not expectorating sputum, although they are insensitive indicators of lower respiratory infection and inflammation(53, 54), and unsuitable for NTM detection(52). For this reason, some paediatric CF centres will prefer to obtain broncho-alveolar lavage (BAL) specimens as part of routine (annual) surveillance for bacterial pathogens in the airways of young children. Induced sputum is feasible in young children, has better pathogen yield and concordance with lower airway pathogens than oropharyngeal specimens, and may be considered in preference to oropharyngeal cultures (where clinic resources permit) particularly in symptomatic children (55). There is consensus on the utility of bronchoscopy with BAL in children with symptoms not responding to treatment or where lower respiratory samples are required to direct management (51).

ii. Spirometry may be attempted from age 3-4 years but is more reliably achieved in a time efficient manner in busy CF clinics from age 5 years. Spirometry should be performed at each clinic visit and during exacerbations. Spirometry trends should ideally be available to clinicians during clinic visits to provide an overview of progress and direct management. Body plethysmography may be considered at annual review from age 8 years whilst formal cardio-pulmonary exercise testing [CPET] may be offered in the mid-primary school years and beyond (56). Multiple Breath Washout (MBW) is a more sensitive measure of early lung disease in children and clinical experience in this technique is increasing (57). There is still uncertainty around what constitutes clinically significant change, which presents a challenge in the routine use of MBW in clinical settings. However, those centres with familiarity and experience in the use of MBW, should consider measuring lung clearance index at annual reviews, particularly if spirometry is normal or unreliable, and using results to track progress (58).

iii. Chest X-ray (CXR) has been the cornerstone of chest imaging in children due to its wide accessibility, minimal requirement for child cooperation and ability to identify acute changes and established disease progression in children. While consensus remains in favour of annual and clinically indicated CXR for these reasons, the role of CXR in routine surveillance is being reconsidered. CXR is relatively insensitive to early, mild disease changes and may delay the detection of bronchiectasis (59). Low-radiation dose chest CT scan is currently the most sensitive method to detect bronchiectasis and early features of CF lung disease (16, 21). The optimal timing and frequency of CT scans in childhood remains unclear (60). Some centres advocate biennial chest scans and others perform chest CT scans every 5 years. The Cystic Fibosis Foundation guidelines recommend chest CT scans, using the lowest radiation dose possible, may be considered every 2-3 years as a substitute to routine annual CXR(51). The frequency of CT chest scans should be tailored to the individual patient and be considered at least once in preschool, school age and adolescence to track the progression of lung disease.

iv. Prompt management of pulmonary exacerbations is essential and involves recognition of symptoms and clinical deterioration and collection of a respiratory sample (OP or sputum) to assess for viral and bacterial pathogens. Treatment should be initiated promptly with oral, inhaled, or intravenous antibiotic therapy depending upon the severity of the exacerbation and guided by previous sputum cultures. Documentation of a clinical and physiologic return to baseline following an exacerbation is important as it is estimated that up to 20% of children fail to achieve their baseline lung function within three months of treatment for a pulmonary exacerbation (18). A clinic review of progress and recovery within 4-6 weeks of treatment of a pulmonary exacerbation is recommended.

b) Surveillance of nutritional status and common extra-pulmonary childhood complications

i. Growth monitoring and screening for malnutrition (under - and over-nutrition) comprise essential elements of regular reviews in the CF clinic with the dietitian (44). Plotting growth parameters [weight, length/height and BMI] on standardised growth charts in the medical record is needed at each clinic visit and conveying these results to families and involved health practitioners is important. Regular dietitian review of dietary content, nutrient quality, eating behaviours, food security, vitamin and salt supplementation and dosing of, and adherence with, pancreatic enzymes is required. Nutritional investigations should be conducted annually (see Chapter Outpatient Care) and when clinically indicated. Excessive weight gain requires review of energy expenditure, adjustments to nutritional requirements and dietary modifications.

ii. CF related liver disease commonly manifests in childhood and may affect up to 40% of young people with CF. Monitoring for liver disease includes regular abdominal examination during routine clinic visits, liver function tests including clotting profile and fat-soluble

vitamin levels measured as part of annual review investigations, and serial abdominal ultrasound scans with doppler imaging to assess liver architecture, biliary system, portal hypertension, and spleen size(61). Infants and children commencing CFTR modulators should have quarterly liver function tests in their first year on therapy as surveillance for drug induced liver injury (62).

iii. Bone health abnormalities may manifest in childhood, particularly among children with poor nutritional status and receiving long-term systemic corticosteroids and can be clinically silent(63). Blood tests for Vitamin D levels are conducted from infancy and deficiency should be corrected with supplementation. Calcium intake should be part of regular assessment by the dietitian. Routine screening of bone mineral density with dual energy X-ray absorptiometry [DEXA] scans begin at age 10 years (64).

iv. CF related diabetes mellitus [CFRDM] occurs with increasing age in CF, affecting approximately 20% of people by the age of transition to adult care. It may begin with impaired glucose tolerance and screening is recommended from the age of 10 years, or younger with suggestive symptoms via an oral glucose tolerance test measuring fasting, and two hour blood sugars, or by elevated fasting or random blood sugars or HbA1c (65, 66). Type 1 diabetes may occur independently of CFRDM, and antibody screening is undertaken to differentiate this aetiology. All children with diabetes require care of a paediatric endocrinologist with expertise in CF related diabetes.

v. Sinus disease, with or without nasal polyps, usually presents during childhood and is often underappreciated and undertreated (67). Screening questions about an allergic disposition, nasal obstruction, mouth breathing, snoring and ear infections are recommended. Referral to ENT specialist services for early intervention is recommended.

vi. Musculoskeletal concerns may present with growth, postural problems, and activity. They are routinely considered by the CF physiotherapist (43). CF related arthropathy of medium sized joints may occur in up to 5% of young people with CF.

vii. Continence problems with bladder and bowel function often occur in young people with CF and may be triggered by cough, laughter, or physical exertion. Managing any constipation/DIOS issues and pelvic floor exercises with programs supervised by physiotherapists may be of benefit. More detailed assessment can be provided by continence experts who may undertake comprehensive continence assessment including diaries and urodynamic studies (43)

6. Infants and children should have access to effective, up-to-date, evidence-based treatment including approved CFTR modulator therapy, with appropriate monitoring for short- and long-term effects.

a) The specialist CF team should be aware of novel therapies and interventions that improve health outcomes through CPD activities, attendance at post-graduate courses and conferences.

b) Evidence-based interventions and therapies that have the potential to improve health outcomes and slow the progression of lung disease should be made available for infants and children when supported by acceptable efficacy, safety, and tolerability data (17, 68).

c) The burden of treatment associated with novel or additional therapies should be considered carefully and discussed with children and families before initiating therapy.

d) CFTR modulator therapy should be considered as a standard of care for all eligible children with appropriate gene mutations in accordance with the Australian Therapeutic Goods Administration approval and prescribing policies.

e) Parents/caregivers and children should receive education and counselling prior to starting CFTR modulator therapy that includes open discussions around clinical expectations, side effects (known and potential unknown), dose administration and monitoring, medication interactions and adherence to the modulator therapies and their existing CF therapeutic regimen. The decision to discontinue existing treatments should be considered on an individual basis in partnership with parents/caregivers, and informed by the best available evidence (50, 69).

f) Screening and monitoring for short- and long-term side effects associated with CFTR modulator therapy is required according to regulatory bodies.

1. Infants and children should receive routine community health checks and age-appropriate immunisations.

a) Infants and children should receive regular health and developmental checks through their general practitioners, community health nurses and general paediatricians. Routine dental checks are also recommended.

b) They should receive age-appropriate immunisations according to the Australian National Immunisation Program (https://www.health.gov.au/health-topics/immunisation/immunisation-throughout-life/national-immunisation-program-schedule).

Annual Influenza vaccine is strongly recommended for all children > 6 months of age before the start of winter. COVID-19 vaccinations are recommended for all children over the age of 6 months with CF as a chronic respiratory condition. Family members of children with CF are recommended to obtain the annual Influenza vaccine and COVID-19 vaccinations. Pneumococcal vaccination is recommended with additional Prevenar 13v and Pneumovax 23v vaccinations as per national immunisation program.

2. Psychosocial evaluation, support and intervention for children and carers should be available from diagnosis. Mental health screening for children and carers should be routinely implemented.

a) Diagnosis of CF in a child is distressing. Parents/carers, especially mothers, are at greater risk of developing anxiety and depression (38). Parental mental health should be monitored and screened at least annually using tools such as GAD-7 or PHQ-9.

b) Children should undergo mental health screening at least annually and as clinically indicated. Children aged 12 years and older may be screened for anxiety and depression using the GAD-7 and PHQ-9 (2). Children younger than 12 years are at risk of anxiety and depression and symptoms may differ to older children, including irritability, withdrawal, agitation, and behavioural disturbance. Younger children should undergo screening for mental health and behavioural issues using age-appropriate measures and tools (70).

c) The emotional health and wellbeing of children should be discussed with parents/caregivers as part of routine CF health care during clinic visits. Children with symptoms of depression/anxiety or other concerns regarding emotional health, behaviour and attachment should be referred to psychology services for evidence-based interventions (2, 70).

d) Children should be monitored for potential neuropsychiatric side effects associated with initiation of CFTR modulator therapies(71).

e) Other psychosocial issues that could arise include difficulties adjusting to the CF diagnosis, poor coping styles, financial stress, housing, substance use, and family violence (37). The CF social worker or psychologist should offer supportive counselling.

f) All members of the family are affected by the diagnosis of CF. Siblings may experience anxiety, low mood, or even feel resentment and anger (72) and may require individual counselling and support.

g) Common tasks that may need support in early childhood include establishing a daily treatment routine, establishing healthy mealtime and sleep habits, and managing any early resistance to medical treatments. Transition periods such as starting day care or school may exacerbate underlying behavioural issues or emotional reactions. This will require input from the CF MDT e.g., occupational therapy or child life therapy around medical procedures. At times, combined intervention from the CF MDT may be needed e.g., dietitian and psychologist around behavioural difficulties with food.

h) Screening and management of procedural fears is recommended from early childhood and behavioural strategies aimed at mitigating procedural distress are recommended(73). Individualised procedural preparation and management plans for children with procedural anxiety or distress should be developed in collaboration with parents and caregivers.

i) Behavioural issues are a challenge in the setting of many chronic illnesses and are not specific to CF. Attentional problems are more common in CF and developmental disorders such as ADHD, autism, and specific learning impairments manifest in childhood and add significantly to the burden of CF care. Enquiry on behavioural issues should be made by all the clinicians in the CF MDT and children experiencing difficulties require referral to hospital or community mental health services for assessment and intervention (70).

j) Engagement of “parents as partners” is crucial for a collaborative relationship between families and CF MDT and for the best health and psychological outcomes for the child with CF (10).

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Adolescents and Young Adults

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Standard 1 Adolescent and young adult (AYA) CF care should be provided in a youth-friendly environment with policies and processes in place to support planned AYA transition to self-management and transfer to adult care.

Standard 2 Health professionals caring for AYA should be familiar with the unique health needs of AYA and have the necessary competencies to provide developmentally appropriate CF care and support health care transition.

Standard 3 AYA should be closely monitored for progression of CF including specific complications of CF that emerge during adolescence and young adulthood, as this is a high-risk period for declining health.

Standard 4 AYA should be reviewed four times a year by the CF specialist team as the current minimum standard (*see Recommendations 4a). Access to care should be facilitated through flexible approaches to appointment times and communication strategies including telehealth.

Standard 5 Barriers to adherence should be regularly assessed to optimise clinical outcomes and interventions to enhance adherence should be provided throughout adolescence.

Standard 6 Psychosocial screening should be undertaken annually as a minimum, and when clinically indicated, by appropriately trained staff. A psychologist and social worker should be involved in the care of AYA to ensure early detection and intervention for psychosocial problems.

Standard 7 AYA should receive age-appropriate CF-specific sexual and reproductive health (SRH) education, information, and counselling.

Standard 8 A structured transition and transfer program for adolescents with CF should be developed through close collaboration between paediatric and adult specialist care teams that extends beyond timing of transfer.

Background

Adolescence and young adulthood, defined as the years from 10-24, is characterised by rapid physical, neurodevelopmental, and socio-emotional changes that create the foundation for future health and social wellbeing [1, 2]. The developmental maturation that occurs across these years has significant implications for young people with CF and their families.

Adolescence brings capacity and opportunities for young people to achieve autonomy and greater engagement in self-care. However, the transition to self-management occurs at varying rates and may fluctuate in response to developmental and lifestyle priorities. This can create new challenges for the CF team, young person, and their caregivers around treatment adherence, and participation in CF care.

Comparison with peers, and sensitivity regarding physical differences (whether real or perceived), increases during this period, and may lead to additional management challenges. Young people with CF-have disease-specific sexual and reproductive health (SRH) needs that should be addressed. Additionally, AYA with chronic disease are at increased risk of mental health problems, substance abuse, and unsafe sexual behaviours compared to young people without chronic illness.

Health outcomes in adolescents and young adults with chronic illness are improved when care is provided in a youth-friendly environment that acknowledges, understands, and responds to the specific developmental needs of AYA [3]. These needs include support around self-management, providing privacy and confidentiality, and acknowledging the role that parents continue to provide in supervision and psychosocial support.

How CF care is received by AYA changes gradually over time, from parent-directed care to parent-supported care, to autonomous engagement in their own health care. Transition programs play a key role in establishing positive health behaviours, supporting self-management, and readiness for transfer to adult services. Young people with CF and their families benefit from formal processes that support timely transfer from paediatric to adult CF services and ensure continuity of care.

Evidence

The human brain continues to develop into the third decade, with specific implications for learning, thought processing and risk-taking behaviour among young people[2]. Brain maturation during adolescence brings "new cognitive skills (including abstract thinking capacities), a clearer sense of personal and sexual identity, and (opportunities) to develop a degree of emotional, personal, and financial independence from their parents"[4].

AYA gradually acquire adult roles and responsibilities, however, there may be conflict between the developmental context of adolescence and young people's motivations to meet the care demands of CF[5]. While negotiating these challenges, AYA should be treated with respect and dignity, recognising that many of the difficulties experienced in accepting CF care (including treatment adherence) reflect normal developmental processes.

Youth-friendly health care is a fundamental aspect of care for all AYA, including those with CF[2, 6]. Youth-friendly services are defined by the WHO (World Health Organization) as services that are "accessible, acceptable, equitable, appropriate and effective"[7]. Improving the availability of, and access to, CF and AYA-specific health care is a key requirement.

Reported barriers to health care access for AYA include inconvenient appointment times, clinic distance, and difficulties accessing youth-specific health information. Accessibility (and equity of access) may be enhanced through flexible appointment times to accommodate education and employment, and by leveraging convenient methods of communication (e.g., secure messaging, telehealth consultations). Providing youth-appropriate health information and support for young people attending the CF clinic also aligns with accessibility. Acceptability refers to treating AYA with respect, in a non-judgemental way, and with particular attention to individual privacy and confidentiality[8], which are highly valued by AYA. Acceptability includes the health setting and providing facilities that are appealing, safe, and clean spaces for adolescents to receive health care[8]. Appropriate and effective care refers to health care that directly responds to the specific needs of AYA (see below) in the context of their CF care and leads to improved outcomes.

Youth-friendly services have been shown to improve engagement and access to health care and health outcomes[6]. There is international recognition that AYA are best cared for in such an environment by staff cognisant of AYA-specific health needs and with the knowledge and skills to effectively engage young people [2, 6, 9]. Providing youth-friendly environments for AYA are internationally endorsed, and AYA specific models of CF care should be considered and implemented within the resources and capacity of the local CF team.

CF teams should have established policies and processes in place to support AYA towards independence, self-management, effective engagement with health services and practitioners, and timely transfer to adult CF care. Policies and procedures that are co-produced with young PwCF and their families, and with adult and paediatric CF centres are endorsed (see section on adolescent transition and transfer to adult care below).

Specific AYA health care needs

Privacy and confidentiality are particularly important for young people [10], who may not feel comfortable sharing concerns or asking questions in the presence of their parents. Their need for privacy and confidentiality may extend to accessing sensitive health information and support, including mental and sexual health, without fear of judgement. The confidentiality of AYA should be assured in the transfer to adult services. For example, some AYA may prefer specific information or historical events to remain confidential. While this may not always be appropriate, the paediatric CF team should negotiate with the young person around what to share with the adult team.

There is an increase in common psychological disorders (e.g., depression, anxiety) with increasing age across adolescence and into young adulthood [2]. The prevalence of depression and anxiety in AYA with CF is higher than the general population, is a predictor of lower quality of life, and is associated with lower rates of adherence and participation in CF treatments, and poorer health outcomes [11]. Reports of neuropsychiatric side effects with CFTR modulator therapies are increasing [12]. Mental health screening for AYA should be implemented as per international recommendations [13] alongside access to evidence-based psychosocial interventions [13]. Confidential discussions around psychosocial issues such as body image [14], bullying, recreational drug and alcohol use, sexual health and fertility[15] underpin efforts to optimise health and well-being [10]. Psychologists and social workers should be active members of the CF team, involved in delivery of mental health screening and available for the assessment and treatment of AYA referred as inpatients and outpatients with psychosocial concerns [16].

AYA with CF are at risk of accelerated decline in lung function [17], coinciding with reduced treatment adherence, particularly to physiotherapy and inhaled therapies [18]. Regular specialist respiratory physiotherapist review is recommended for AYA (see Chapter Outpatient Care) to oversee airway clearance strategies, support adherence to therapies, and facilitate increasing self-management in airway clearance. (National physiotherapy guidelines). Nutritional status also declines in adolescence [19], with potential impacts on pubertal progression, linear growth, and future morbidity and mortality [20, 21]. Close and regular follow up by a specialist CF dietitian as outlined in Chapter Outpatient Care (Clinical Practice Guidelines for Nutrition in Cystic Fibrosis) is a key aspect of care for AYA. The prevalence of comorbidities such as CF-related diabetes, liver disease and chronic respiratory infection with significant pathogens, such as Pseudomonas aeruginosa and non-tuberculous mycobacteria, increase in adolescence [19]. These health issues emphasise the importance of regular clinical reviews for AYA by the CF MDT including respiratory and nutritional progress, routine pathogen surveillance to promote early detection and treatment of pulmonary infection, and screening for CF co-morbidities [22-24].

Sexual and reproductive health (SRH) is a specific health need for AYA and has historically been poorly addressed in CF. Young people with CF

report insufficient knowledge and understanding about fertility, contraception, and family planning, with consequent poor health outcomes [25]. Young people in Australia become sexually active at (mean, SD) 15.0 (1.23) years [26] and pregnancy rates among people with CF are increasing[27]. CF has specific implications for SRH, and the CF clinic has a responsibility to provide AYA with accurate education and information about SRH in an engaging format. Education and counselling around fertility, contraception, safe sexual behaviours, and sexual identity should begin in early adolescence [25] and continue into adulthood as part of routine CF care during clinic visits (see recommendation 7 below). The CF team has an important role in facilitating links between AYA and primary care providers to ensure young people with CF receive age appropriate general SRH care, including screening for sexually transmitted infections (STIs) and cervical cancer (papsmears), human papilloma virus (HPV) vaccination, contraception, and support. Infections such as HPV and herpes simplex virus may have serious implications for AYA with CF receiving immunosuppressive therapy, while Hepatitis B and C and human immunodeficiency virus are contraindications to solid organ transplant.

Adolescent transition and transfer to adult health care

Transition refers to a "purposeful and planned" process and involves attention to the systems that promote AYA's capacity to self-manage their disease and acquire the skills and knowledge needed to successfully navigate the adult world. In contrast, 'transfer' is a more specific term that is used to refer to the change in health care delivery from paediatric to adult services [28]. Formal transition programs that extend beyond a focus on transfer are recommended, though the elements of transition programs that constitute best practice remain unclear.

There is limited data describing specific, objective, and measurable health benefits of transition and transfer programs in AYA with CF [29]. In two published reviews examining studies of transition services, lung function and BMI remained stable and no differences in antibiotic requirements or morbidity were observed among AYA following their transfer to adult CF care [30, 31]. However, there is evidence that a coordinated, formal, and structured transition program results in higher levels of patient satisfaction [32], improved independence [32, 33], reduced anxiety[33], increased self-care and improved advocacy skills[34].

The absence of formal transition and transfer programs risks delays or interruptions to continuity of care [35] and suboptimal communication of medical information between treating MDT, and leaves AYA ill-prepared to access health care and at risk of disengaging with their health and health care teams [36]. Common concerns reported by AYA about transfer include meeting the new team, decline in "care quality" and difficulty in accessing care and information from adult CF services [31]. These concerns are best addressed through a planned and personalised process that involves patients and their families.

Optimal transition processes ensure that healthcare is coordinated and continuous, notwithstanding the change from paediatric to adult services [37].

Recommendations for successful transition include allocating a designated transition lead in the CF clinic, providing opportunities for AYA and their families to meet the adult team in the paediatric setting, orientation tours of adult services, social work involvement, written and verbal handover of information, and opportunities for AYA to speak with other recently-transferred AYA.[36].

Building the AYA's capacity for self-management well before the timing of transfer is critical. AYA will be at varying stages of readiness for transfer at the time of completion of secondary education and an individualised plan is best negotiated according to education and employment demands, family context (e.g., siblings remaining at paediatric centre), personal preference and disease stability. Recommendations around the optimal age of transfer vary, and in practice, most AYA with CF in Australia will transfer by/at age 18 years. Transfer may be delayed in patients during periods of health instability or decline [37] including those who are progressing through the terminal stage of their disease or undergoing complex therapy such as around the time of transplant. Transfer may also be considered earlier (<18-years) in cases where the individual's medical and/or psychosocial needs are better met at the adult service. Some AYA will prefer to have their parents' presence and support continue at the adult service and this preference should be accommodated [38]. Close cooperation between medical care teams enables the transfer of care of AYA in a staged and planned manner, fostering engagement with the AYA in the process and ensuring readiness.

Adolescent and young adult care recommendations

1. **Adolescent and young adult (AYA) CF care should be developmentally appropriate and provided in a youth-friendly environment with policies and processes in place to support planned AYA transition to self-management and transfer to adult care.**

   CF clinics should work towards development of a youth friendly environment for the care of AYA. Youth friendly environments are not solely the remit of paediatric centres and should be provided in the adult setting to support engagement and access to CF care following adolescent transfer:

a) AYA require flexibility around accessing CF care and the CF team should consider, where possible, offering alternative times/days for clinical visits to reduce the impact on education and work commitments. Alternative methods of health delivery such as telehealth consultations and secure messaging may be leveraged to ensure equitable and easier access to care.

b) CF care should be provided in a non-judgemental, personalised, and respectful manner [8]. Privacy and confidentiality should be assured for all AYA.

c) AYA specific health information should be made available to adolescents and young adults through the CF clinic.

d) The CF team should work collaboratively with AYA and their caregivers to support self-management. Planned transition programs that provide developmentally appropriate information and support to AYA and their caregivers around skills and competencies in self-management are recommended[16]. Planned and coordinated transfer processes to adult CF care are required (see recommendation 8 for details)[37, 38].

2. Health professionals caring for AYA should be familiar with the unique health needs of AYA and have the necessary competencies to provide developmentally appropriate CF care and support health care transition[39].

The development of "adolescent-competent" health professionals is internationally endorsed[40, 41] and associated with improved clinical performance and health outcomes. Creating an "adolescent competent work force" should be a key objective of CF services and include as a minimum:

a) Education in the core concepts of adolescent development, AYA health needs, and the process of transition for the entire CF MDT.

b) Provision of training and education for the CF MDT in effective communication and engagement of AYA.

c) Staff providing AYA care in the CF clinic should have knowledge and understanding of policies and quality standards for AYA care and be aware of the legal rights of AYA in the health setting.

3. AYA should be closely monitored for progression of CF including specific complications of CF that emerge during adolescence and young adulthood, noting that this is a high-risk period for declining health.

CF complications and comorbidities increase with age across adolescence and into young adulthood. Poorer outcomes have been identified in young people with CF where screening is not routinely introduced[42]. In addition to routine CF care (see chapter Outpatient Care), specific recommendations for care of AYA with CF include:

a) Assessment of growth and puberty should be undertaken at each clinic visit, including plotting of height and weight on growth charts, and Tanner staging. Early involvement of a gastroenterologist and endocrinologist with expertise in CF is recommended if issues are identified.

b) Annual screening for comorbidities such as CFLD and CFRD[43] is recommended. Assessment of bone mineral density is recommended (see Chapter Outpatient Care). Clinicians should have a low threshold for additional or repeat screening where clinical decline is identified.

c) Nutritional assessment should be undertaken (see Chapter Outpatient Care) with specific attention to optimising growth and nutrition to promote normal pubertal progression, and education around healthy eating behaviours and diet quality[44]. Monitoring for micronutrient deficiencies seen in AYA, especially iron, B vitamins and vitamin D

deficiency, is required. Intervention for accelerated weight gain, particularly associated with CFTR modulators, is required to prevent overweight and obesity. The impact of nasogastric tube (NGT) and percutaneous endoscopic gastrostomy (PEG) feeds on body image and adherence should be considered, and psychosocial support provided as needed. The CF MDT should remain observant for features of eating disorders and restrictive eating patterns and refer individuals for support where appropriate.

d) Mental health screening should be performed at annual review as a minimum (see standard 6.)

e) Monitoring of CF lung disease with lung function testing and microbiological surveillance, including NTM screening, should be undertaken as outlined in Chapter Outpatient Care. Clinicians reporting lung function tests should be mindful of individuals' gender identity when reporting using sex assigned at birth, recognising that transgender patients may not identify with the biological sex listed on reports[45].

4. AYA should be reviewed four times a year by the CF specialist team as the current minimum standard. Access to care should be facilitated through flexible approaches to appointment times and communication strategies including telehealth.

a) At the time of writing, it is recommended that AYA should be seen at least 4 times per year on a 3-monthly basis by a CF MDT[46], and more often as needed (see Chapter Outpatient Care). [47]. * It should be noted that this recommendation does not consider individual changes in clinical status with initiation of CFTR modulator therapy and at the time of publication, there is no evidence to guide frequency of visits in this setting. Changes to visit frequency in this context should be carefully tailored to the individual AYA, negotiated with the CF team and the young person (and caregivers), and guided by the best-available evidence.

b) Preferred persons and contact details for communication and appointments should be established with AYA (i.e., their caregivers or themselves). Enquiry and review of contact preferences as the young person matures is recommended and support around self-management and autonomy provided.

5. Barriers to adherence should be regularly assessed to optimise clinical outcomes and interventions to enhance adherence should be provided throughout adolescence.

a) Regular assessment of participation in CF care by all members of the MDT, including adherence to treatments/therapies, and barriers to adherence[5] during each routine clinic visit is recommended.

b) A non-judgemental approach is recommended to identify adherence difficulties and provide opportunities for AYA to confidentially disclose poor adherence to the CF MDT (they may not wish to tell their parents/caregiver)[6].

c) Evidence-based and tailored interventions to optimise adherence should be implemented as needed[18]. It is important to involve the young person in the development of strategies to improve adherence to ensure they fit with their lifestyle, values, and commitments. Mutually agreed plans that are negotiated between the team, the young person, and caregivers when appropriate, are recommended.

d) Enquiries around access to medications, financial barriers, and time constraints related to educational and work commitments should be made.

e) AYA should receive developmentally appropriate information and education about their CF disease and its management, so they understand why therapies are important and the impact of missed treatments.

f) Temporarily prioritising therapies and simplifying regimens for AYA not managing their treatment burden may need to be considered.

6. Psychosocial screening, including mental health and wellbeing, should be undertaken annually as a minimum, and as clinically indicated, by appropriately trained staff. A psychologist and social worker should be involved in the care of AYA to ensure early detection and intervention for psychosocial problems.

a) Screening for mental health concerns using measures such as the GAD-7 and PHQ-9 is recommended at least annually and as clinically indicated[13] . Screening should be performed by staff appropriately trained in the administration of the screening tools (usually a CF social worker or psychologist) using established referral pathways and procedures (below).

b) Clinics should ensure they have clear procedures and referral pathways for AYA identified through screening with mental health concerns, so individuals receive timely assessment and intervention. These pathways should include guidance for referral to specialist youth mental health services and local and community-based services.

c) A psychologist and social worker should be routinely and regularly involved in the care of AYA with CF with capacity for both inpatient and outpatient assessment and management.

d) Discussions regarding psychosocial, behavioural, lifestyle factors and mental health should occur within the context of routine clinic visits.

e) Information about potential cognitive and mental health side effects of CFTR modulators should be provided for AYA and their caregivers prior to starting modulator therapies. Enquiry around psychological side effects should be made during the first 3-6 months of therapy and routinely in future clinic visits[48] .

f) Time should be specifically allocated for patients to have confidential psychosocial assessments. Measures such as the HEADSS tool (Home & environment, Education & Employment, Activities, Drugs, Sexuality, Sleep, Suicide/Depression) [49] may provide a framework for comprehensive discussions around key aspects of adolescent health.

g) Confidential risk counselling around substance abuse, smoking, self-harm, food restriction and unhealthy eating behaviours should be undertaken. AYA with CF are at particular risk from smoking and vaping, and dieting behaviours, (including PERT, insulin, and aperient manipulation/abuse) that may result in nutritional decline.

h) Community support may be required from local general practitioners, psychologists, and psychiatrists to support AYA with complex issues.

7. Adolescents and young adults should receive age-appropriate CF-specific sexual and reproductive health (SRH) education, initiated at regular intervals by their CF team. CF services should facilitate linkages with primary and tertiary care services to ensure appropriate delivery of SRH care.

a) CF-related SRH education and care is a key responsibility of the CF team. Discussions should begin early with the family, continue though childhood and be introduced to AYA in early adolescence and continue into adulthood. Parents should be informed of sub-fertility associated with CF soon after diagnosis of CF in their child.

b) CF-related SRH information should be provided to AYA at developmentally appropriate times starting in early adolescence and may often coincide with school or community based SRH. Information may include written, verbal, and online resources to supplement in-person education and cover topics such as sexual health, fertility, and counselling services[25,50].

c) Parents may appreciate support and guidance around discussing aspects of SRH with their children and benefit from CF-specific SRH education from the CF team prior to talking with and supporting their child with CF[49]. It is ideal if parents are involved in the timing of SRH discussions (when to being discussions and how often) and are aware of the scope of SRH education.

d) CF-related SRH should include information about puberty, fertility, contraception, sexually transmitted infections and candidiasis, and future pregnancy and assisted fertility as appropriate[25].

e) Contraception should be offered to all sexually active individuals who do not want to become pregnant. Contraception should be discussed during clinic visits with consideration of interactions with CF therapies, and potential side effects.

f) Knowledge of, and counselling around, probable male infertility and reassurance typically of normal sexual function in CF is recommended by age 14 years with subsequent referral of individuals for semen analysis offered as and when appropriate.

g) Linking AYA to specialist and community SRH services may improve access to, and choices around, SRH care[25]. Services may include primary care practitioners, gynaecologists, fertility specialists, genetic counselling, and obstetric services.

8. A structured transition and transfer program for adolescents with CF should be developed through close collaboration between paediatric and adult specialist care teams that extends beyond timing of transfer.

Recommendations for Transition:

a) A structured transition program, developed through close collaboration between paediatric and adult specialist care teams, and including details of transfer to adult services, should be developed, and implemented.

b) A transition coordinator responsible for the process should be identified in each centre[37].

c) The concept of transition to adult services should be raised with parents soon after diagnosis with specific and more active discussions around transition and plans for transfer commencing around secondary school entry (approximate age 12-13 years)[37].

d) Transition programs should begin early in adolescence, be developmentally appropriate and be individualised to support the transitioning adolescent to develop self-advocacy and self-management skills.

e) Transition processes should include transition readiness assessment, educational materials and formal lists of desired self-care skills[36].

f) Every consultation should be viewed as an opportunity to improve the young person's capacity for self-management and independence. Annual review provides an ideal opportunity to assess maturity, increasing age-appropriate understanding of adult CF issues and to identify any specific barriers to transfer of care to an adult setting.

g) AYA should have ample opportunities to develop independence and efficacy around CF self-care.

h) Expectations around seeing AYA for short periods during consultations without parents should be set to gradually promote familiarity and independence[16]. The timing and duration of these one-on-one consultations should be tailored to the individual and commonly start around the age of 13- 14 years. Time spent with the young person alone can be gradually extended over time.

i) The need for increased independence in self-care should be highlighted well before the time of transfer approaches.

j) AYA should have access to information about their adult CF centre, including available staff, facilities, services, and expertise, and include more "adult" services, such as fertility and family planning.

k) Transition processes that support AYA in acquiring the skills, confidence, and capabilities to self-care and successfully engage with the "adult world" should continue after transfer to adult care.

Recommendations for Transfer:

Seamless transfer requires good communication between the young person, caregivers, paediatric and adult medical teams[36]. This may be achieved through education and information addressing concerns and barriers raised about transfer, and regular transition team meetings to discuss AYA approaching transfer. Visits to the paediatric clinic by the adult team to meet the young person with CF and welcoming, youth friendly settings in the adult clinic are endorsed.

a) AYA with CF and their parents/carers should have the opportunity to meet the adult CF team at least once prior to transfer, ideally at the paediatric centre. Telehealth may be used to meet the adult team for rural and regional AYA.

b) Prior to transfer, the adolescent (and their caregivers) should have the opportunity to visit the adult CF Centre if possible.

c) Education should target any concerns expressed about transfer to an adult centre with the opportunity for patients and their families to contact relevant staff of both centres to answer questions.

d) Communication between the paediatric and adult teams should identify the likely time of transfer based on assessment of readiness, patient preference, and age, which should then be negotiated with the young person and family.

e) For regional and rural AYA, transfer of care from a paediatrician to an adult care setting must involve the specialist CF teams.

f) The adult CF team should discuss the expectations and preferences for parent/caregiver involvement in care at the adult centre with the young person and communicate these directly with parents.

g) An appointment date at the adult service should be confirmed before care ends at the paediatric service. Parents/caregivers should be included in transfer planning and appointments[37] according to AYA preferences around autonomy and confidentiality.

h) A comprehensive written summary of medical and social issues and current management should be provided before transfer and shared with the adult team[36] . The summary should provide information from all members of the CF MDT: medical, nursing, and allied health. It may be appropriate to provide a copy of the care summary to the young person.

i) Confidentiality for the AYA should be maintained. Issues discussed in confidence should not be disclosed between care teams or with parents/caregivers without explicit permission from the AYA. Sensitivity is encouraged around what information is and is not shared with the adult care team. Not all information about earlier events and experiences need be shared with the new team.

j) After the AYA's first appointment with the adult CF team, transfer is considered complete, and the AYA is no longer a patient of the paediatric centre.

k) If a young person fails to attend appointments or engage with the adult CF services, the adult CF team should try to contact the young person and their family and offer support around engagement. This may involve the support of relevant health professionals including the GP and paediatric team.

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Fertility, Pregnancy and Preparing for Parenthood

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Standard 1 All young people with CF (PwCF) should be given timely, accurate information and counselling concerning fertility and pregnancy.

Standard 2 Preconception counselling should be offered to all PwCF and their partners well before pregnancy is undertaken. Pre-conception counselling should include CF genetic counselling for both PwCF and their reproductive partners with discussion of the health implications of pregnancy.

Standard 3 Assessment of fertility and appropriate referral to assisted reproduction services should be offered to PwCF who are planning parenthood.

Standard 4 Pre-pregnancy planning should include a detailed medical, nutritional, pharmacological, and mental health evaluation, assessment of glucose homeostasis and pre-pregnancy vaccinations. Access to psychosocial support should be provided as necessary.

Standard 5 Obstetric care should be provided as close as practical to the CF Centre. Care of PwCF during pregnancy should be provided by, or in regular consultation with, specialist CF multidisciplinary teams with experience in providing care for such pregnancies.

Standard 6 During pregnancy, PwCF should be reviewed frequently (minimum monthly) during the first and second trimesters and fortnightly during the third trimester by the CF Multidisciplinary Team to optimise pulmonary and nutritional health.

Standard 7 Clinical care during labour and delivery should be led by the obstetric team, with the CF team providing support. Choices about delivery should be made by the pregnant person and obstetrician.

Standard 8 Postpartum care should be jointly undertaken by the maternity and CF services with special emphasis on physiotherapy, nutritional and psychosocial support with adaptations for those delivering at other hospitals distant from the CF centre. The newborn screening status of the baby needs to be checked especially if exposed to CFTR modulators during pregnancy.

Background

As health and survival improve in people with CF (PwCF) a growing number are considering and embarking on parenthood. Surveys have identified around 70-80% of people with CF plan or desire to become parents indicating the growing importance of education, support and management around family planning and pregnancy in CF care [1].

PwCF should receive life-long management by a CF Specialist Multidisciplinary Team including the management of pregnancy and health during parenthood. Fertility, contraception, and pregnancy should be discussed at an appropriate time before pregnancy is contemplated to optimise both health outcomes of pregnant individuals and the foetus and their health management [1,2]. Preconception genetic counselling and carrier testing should be routinely offered to allow couples access to accurate information and prenatal diagnosis.

Women with CF

Subfertility among women with CF (35%) is higher than the general population (5-15%)[4], although fertility rates are increasing dramatically with the advent of CFTR modulators[5], and information regarding contraception is important for PwCF starting CFTR therapies.

Men with CF

Most (95%) men with CF are infertile because of blockage or absence of the vas deferens, although conception and parenthood can be achieved through in vitro fertilisation (IVF) intervention[6]. Males with CF are seeking earlier and better education and resources around fertility and parenting[7]. Referral for assessment of azoospermia and assisted fertility services are important aspects of CF care.

Conception, Pregnancy and Parenthood

Good respiratory and nutritional status is associated with successful conception and maintaining pregnancy to term[8] and the physical impact of fertility treatment and pregnancy on PwCF needs to be carefully considered prior to embarking on parenthood. The physical and psychosocial impact of parenthood in PwCF requires intensified support before, during, and after the arrival of a newborn. The psychosocial impact of pregnancy and parenthood on PwCF is complex, with both positive and negative experiences.

With appropriate care aimed at optimising physical and psychological health most women will have satisfactory pregnancy outcomes. Preconception lung function is the best predictor of pregnancy outcome and lung health should be optimised prior to pregnancy. Contraception should be discussed and provided to avoid unplanned pregnancies. Drugs commonly used during fertility treatments may have side effects such as nausea, vomiting and abdominal pain, and fertility specialists should consult with the CF team if this occurs. As management during pregnancy is enhanced through combined care by the CF multidisciplinary and obstetric teams, most established adult CF centres have close links with their local obstetric colleagues to co-ordinate the complex care required. As women with CF become healthier it is anticipated that local / private obstetric care will be an option for those with mild lung disease and few comorbidities. Local/private obstetric care may not be near the adult CF unit, and this is an additional reason for specific recommendations to guide obstetric management.

Evidence

Contraception, Genetic Counselling and Fertility

Contraception

Reports that up to 50% of pregnancies in women with CF are unplanned highlight the necessity of counselling regarding contraception [9]. Hormonal contraceptives and barrier methods are acceptable forms of contraception in CF. Combined hormonal contraceptives are most used [9] although information regarding the safety and ideal dosing is limited [10]. Although there are theoretical risks associated with contraceptive use related to comorbidities such as CF related liver disease, CF related diabetes, and implantable vascular access devices, the US Medical Eligibility Criteria for Contraceptive Use (2016) does not recommend against any specific contraceptive method for women with CF [11].

Genetic counselling

Preconception counselling is essential for people with CF embarking on parenthood and should include CF carrier screening of reproductive partners and genetic counselling [8]. Genetic counselling should allow calculation of the risk of conceiving a child with CF and discussions around the carrier status of children born.

Fertility and reproduction

PwCF can enjoy a normal sex life, although fertility is often reduced. Over 95% of males are infertile due to congenital bilateral absence of the vas deferens (CBAVD) and resultant azoospermia [6]. Males with CF have normal hormone levels and produce sperm within the testes so reproductive technology methods are available to assist with conception. These include Percutaneous Epididymal

Sperm Aspiration (PESA), Microsurgical Epididymal Sperm Aspiration (MESA), Testicular Sperm Extraction (TESE) and Testicular Fine Needle Aspiration (TFNA). Once extracted, the sperm can be used for intracytoplasmic sperm injection (ICSI) where a single sperm is injected directly into an ovum.

Subfertility in females has been recognised for many years with a multicentre survey reporting that 35% of women with CF were unable to conceive naturally and required assisted reproductive techniques (ART) compared with 5-15% in the general population [5]. Subfertility in women with CF is thought be multifactorial and can be related to thicker cervical mucus, malnutrition, poor respiratory function, and diabetes [4].

Many females with CF do conceive naturally and the advent of CFTR modulator therapies has seen an increase in fertility rates and pregnancies[12,13]. The impact of CFTR modulator therapies in female

subfertility has been highlighted in reports of spontaneous pregnancies in females with infertility or subfertility, as well as in those not trying to conceive, after a median of 8 weeks post commencement of CFTR modulator[14]. It is therefore important now more than ever that women are counselled regarding contraception options.

If there is difficulty conceiving a child, then techniques such as intrauterine insemination (IUI) and IVF may assist.

Natural history of pregnancy in women with CF

Women with CF who have good respiratory and nutritional status can achieve conception and maintain pregnancy to term with minimal or no long-term sequelae [8]. However, unstable clinical status, reduced lung function and comorbidities can all increase the risk to maternal and foetal health [2,3]. Case series of women with CF have shown increased risk of miscarriage [15], in both early - and mid-pregnancy, with the chance of live birth reduced in mothers with worse lung function [16]. Risks are lower in those with better pre-pregnancy lung function, but there have been successful pregnancies in women with FEV1 <40% predicted [12] and pregnancy management should be individualised rather than based on a specific measure of lung function. As maternal and foetal risks are increased in those with lower pre-conception FEV1, pregnancy in a woman with CF and advanced lung disease can be difficult to manage.

Cohen-Cymberknoh recently published a retrospective cohort of 171 pregnancies in 128 women with CF from 1986-2018 at 10 centres internationally. Confirming previous reports, those with more severe disease had more preterm births and more neonatal complications[16]. When the mothers were divided into mild disease (ppFEV1>60% and BMI>21) and moderate-severe disease (ppFEV1<60% ± BMI<21) groups, overall maternal outcomes were similar. But examination of the lung function changes (during pregnancy to after) showed that the mothers with mild disease had some recovery of the FEV1 “lost” during pregnancy whilst the moderate-severe group lost further lung function after pregnancy ($p<0.05$)[16].

Pancreatic insufficiency and Pseudomonas aeruginosa colonisation appeared to correlate with maternal health decline.

Pre-existing CF related diabetes (CFRD) is an important consideration during pregnancy. A recent analysis of the French CF Registry compared outcomes of pregnancy in women with CF with and without pre-gestational diabetes, noting that the women with CFRD were older at the time of first pregnancy (29 versus 26yrs, $p=0.05$) and had worse lung function (50% versus 67%, $p=0.03$) [17]. There was an increased rate of caesarean section in the women with CF and diabetes compared with women with CF without diabetes (48% versus 21%, $p=0.005$) [17]. However, there was no significant impact on foetal growth or preterm birth and there was no difference in long-term outcomes in the 2 groups. [17]. Recent studies have found rates of pre-existing CF related diabetes of up to 30% with gestational onset diabetes in up to 30% hence up to 60% of pregnancies in women with CF are affected by diabetes [18, 19].

Risks to the foetus

Whilst there has long been an increase in the risk of miscarriage in women with CF having pregnancies, earlier studies did not demonstrate any difference in congenital anomalies [2,3]. However, a recent population study of pregnancies in California 2005-2008 compared the outcomes of pregnancies from mothers with CF with those of the general population. They reported a significantly increased risk of congenital anomalies (14.3% versus 6.4%, p<0.005), which included a trend to increased cardiac anomalies (3.9% versus 0.5%, p = 0.08). [15]. This increase is likely to be multifactorial and include contributions from maternal age, drug exposure, micronutrient deficiency, artificial reproductive techniques, and early-pregnancy hyperglycaemia [15].

Long term maternal outcomes

With regards to longer term maternal outcomes, the US CF patient registry demonstrated that women with CF who reported a pregnancy showed no reduction in overall survival compared with age matched women with CF who did not report a pregnancy[20]. The Epidemiological Study of CF showed that pregnancy and motherhood were linked to increased pulmonary exacerbations and clinic visits but were not associated with accelerated loss of lung function [21]. Recent studies have noted that the advent of CFTR modulator therapy will likely improve outcomes [13].

Loss of lung function

In general, it is expected that women with CF will have a transient reduction in lung function to similar levels observed in pregnant women without CF. However, there are very few studies outlining the relative drop in lung function for women with CF with differing levels of lung function pre-conception. Many studies have compared pregnancy outcomes against pre-pregnancy lung function. In general, higher values of FEV1 pre-pregnancy are associated with better outcomes and complete return of lung function to baseline values after pregnancy [22]. Importantly, long term lung function in women with CF who have had a pregnancy shows a similar change with time to those who have not been pregnant [21].

Currently there is little data concerning the relative outcomes of pregnancy in women colonised with the common CF pathogens, S aureus or P aeruginosa. There are multiple cases of women colonised with Burkholderia species, in particular the Burkholderia cepacia complex, who have had poor outcomes following pregnancy [23,24]. The Brompton group noted a particularly difficult combination of poor lung function (FEV1 < 50%) with Burkholderia cepacia colonisation where maternal mortality was high [25]. At present, there is little information concerning pregnancy in women chronically infected with mycobacterial species, but many of the drugs used to treat these organisms are not recommended for use during pregnancy.

Medications during pregnancy

The European Respiratory Society and Thoracic Society of Australia and New Zealand published a statement on the management of reproduction and pregnancy in airways disease including CF. This statement comprised a review of evidence-based literature and expert opinion with recommendations regarding CF care during pregnancy and advice on medication safety during pregnancy and breastfeeding [8]. Importantly, the development of CFTR modulators [26,27] is already changing outcomes

for people with CF [28]. Nash et al have recently reported the findings of a survey of 64 pregnancies in 61 women and no apparent safety signal was evident [29]. O'Connor et al summarise the occurrence of pregnancy in women following commencement elexacaftor + tezacaftor + ivacaftor in two US CF centres [14]. They reported 14 women who became pregnant on average two months following commencement elexacaftor + tezacaftor + ivacaftor. Although the exact mechanism(s) of improved fertility are not clear, the cohort included subjects with previous infertility or subfertility issues. Seven of the 14 reported that they were "not attempting to conceive". Although this case series did not have controls, it does suggest that elexacaftor + tezacaftor + ivacaftor may be associated with an apparent increased fertility, like ivacaftor [30].

Taylor-Cousar and Jain have recently reported 45 pregnancies exposed to elexacaftor/tezacaftor/ivacaftor, including 41 on elexacaftor + tezacaftor + ivacaftor at the time of conception with a further four commenced during the 2nd or 3rd trimesters [5]. Importantly, elexacaftor + tezacaftor + ivacaftor was withheld in six pregnancies out of concern for unknown foetal risk, but 5 of these 6 were forced to restart therapy following pulmonary decline [5]. Foetal outcomes included four miscarriages during the first trimester, including two women who miscarried following cessation of modulator therapy. Five infants were born prematurely, including one infant born at 25 weeks gestation who died. Congenital anomalies were seen in 2 of the 41 pregnancies exposed at conception. There was one case of trisomy 16 leading to spontaneous miscarriage in a mother with previous miscarriages. The second case, in a mother with uncontrolled diabetes, had multiple severe congenital anomalies leading to elective termination. As the numbers are small, further data collection will be imperative to better balance the risks and benefits elexacaftor + tezacaftor + ivacaftor before, during and after pregnancy. A recent report has demonstrated lens opacities (<1.0mm) in infants exposed to elexacaftor + tezacaftor + ivacaftor who underwent ophthalmological examination [31]. However, the relevance of these <1mm opacities is not clear. A case of pulmonary haemorrhage has also been reported in a neonate born to a woman with CF who used elexacaftor + tezacaftor + ivacaftor during the pregnancy [32].

A case report of CFTR modulator treatment in a woman with CF during pregnancy resulted in a falsely normal newborn screening test in a newborn who was F508del / F508del. The authors hypothesised that in utero exposure to CFTR modulators and through maternal breastmilk may have helped delay or prevent organ damage or dysfunction typically seen in CF [33]. More recently, two cases describing women who were known to be CF carriers who took elexacaftor + tezacaftor + ivacaftor during pregnancy to treat foetal echogenic bowel have been described[34,35].

Recommendations

1. All PwCF should be given timely, accurate information and counselling concerning fertility and pregnancy with access to fertility services and preconception counselling as required

a) Information and education around family planning, contraception and fertility should begin in early adolescence (see chapter Adolescents and Young Adults) and continue into adulthood.

b) All PwCF should have sufficient understanding of their fertility and reproductive health to assist with reproductive and parenting decision and planning.

c) Contraception should be discussed and provided to all PwCF to avoid unexpected pregnancies and allow for appropriate optimisation of CF care prior to pregnancy.

d) Information and resources should be accurate and CF specific; referral to fertility specialists with an interest in CF is recommended for further information, support, or intervention.

e) Enquiry about parenting plans or desire to start a family should be part of routine clinical care for PwCF and may be discussed during routine clinics or annual review.

2. Preconception counselling should be offered to everyone with CF and their partners who are planning on future parenthood, well before pregnancy is undertaken. Pre-conception counselling should include CF genetic counselling for people with CF and their reproductive partners and discussions around health implications related to pregnancy in people with CF.

a) Preconception counselling should be offered to people considering parenthood well before pregnancy is undertaken and should be provided by health professionals with sufficient education and training in CF genetic counselling and CF specific reproductive health and pregnancy, ideally through the CF Clinic [8].

b) Genetic counselling should outline risks of having a child affected by CF (informed by the carrier status of the partner) and obligate CF-gene carrier status, together with options for pre-implantation genetic diagnosis (PIGD) and prenatal CF diagnostic testing (amniocentesis or Chorionic villus sampling). Reproductive options such as sperm/ovum donor, adoption and surrogacy may be discussed.

c) The physical impact of pregnancy and the potential maternal and foetal risks associated

with pregnancy in individuals with CF should be carefully explained, with emphasis placed on the importance of optimising nutritional and pulmonary health and psychosocial wellbeing prior to, and during, pregnancy.

d) The social and psychological impacts of caring for a newborn whilst maintaining CF treatments and living with a chronic health condition should be discussed alongside the importance of developing a strong support system [36].

3. Assessment of fertility and appropriate referral to fertility services should be offered to all PwCF interested in parenthood.

a) Males with CF considering parenthood should be offered semen analysis for azoospermia and referred to fertility specialists to discuss assisted reproductive technologies.

b) All reproductive partners of males with CF considering parenthood should undergo CF carrier screening with next generation genetic sequencing prior to conception.

c) Women with CF unable to conceive naturally after 12 months of trying should be referred to fertility specialists for assessment and consideration of in vitro fertilisation and intrauterine insemination of sperm techniques.

4. Pre-pregnancy clinical assessment should include a detailed medical, nutritional, pharmacological, and mental health evaluation, assessment of glucose homeostasis and pre-pregnancy vaccinations. Access to psychosocial support should be provided as necessary.

a) Prior to pregnancy, everyone should receive pre-pregnancy planning and clinical assessment with emphasis on achieving the best possible respiratory, nutritional, and mental health prior to conception. Planning should include:

I. Evaluation and optimisation of lung health. Spirometry should be performed, and interventions including inhaled therapies, antibiotics, and hospital admission, considered to optimise lung function. Women with low lung function (ppFEV1 <50-60%) should be counselled around the relative risks of adverse maternal and foetal outcomes in pregnancy [16]. Review of physiotherapy and airway clearance techniques is required, and ACT modifications anticipated during pregnancy may be discussed [37]. Respiratory cultures should be collected for treatment of acute and chronic infection, whilst women with chronic B. cepacia infection should be counselled about the potential for adverse pregnancy outcomes [8,38].

II. BMI and nutritional evaluation including assessment of energy requirements, micronutrients, iron status, folate

supplementation, and fat-soluble vitamin levels. Ideally, nutritional status should be optimised before conception.

III. An OGTT should be undertaken pre-pregnancy to assess glycaemic control. Women should be counselled of the risk of gestational diabetes of up to 30% [19]. Pre-conception glycaemic control should be discussed with all women with CF-related diabetes mellitus considering pregnancy and control optimised as part of pregnancy planning.

IV. Review of medications should be undertaken by the CF pharmacist or CF physician and known and unknown risks of medications to the foetus discussed. Discontinuation of CF medications must be balanced by the risk to maternal health and individuals with CF should be informed and supported around decisions to continue or discontinue medicines.

V. Review by the CF psychosocial team should include screening for depression and anxiety in persons with CF and their partners and referral for psychological management as required. Assessment of social supports, financial status and access to benefits and welfare are recommended with information around accessing help.

VI. Pre-pregnancy vaccinations are recommended as per the Australian Immunisation handbook: https://immunisationhandbook.health.gov.au/contents/vaccination-for-special-risk-groups/vaccination-for-women-who-are-planning-pregnancy-pregnant-or-breastfeeding.

b) Using a pre pregnancy checklist can potentially aid optimisation of preconception health [13].

c) Pregnancy is not recommended in those with severe lung disease, especially those with pulmonary hypertension, significant liver disease, poor nutritional status, and in women with poorly controlled CF-related diabetes.

5. Obstetric care should be provided as close as practical to the CF Centre and care of pregnant PwCF should be provided by, or in regular consultation with, specialist multidisciplinary teams with experience in providing care for such pregnancies.

Pregnancy is best managed when it is a planned event and where there is close collaboration between the medical and obstetric teams.

a) During pregnancy PwCF should be referred to a specialist obstetric team/maternal-foetal medicine team with experience in CF pregnancy.

b) Early referral is recommended with first obstetric appointment between 12 and 16-weeks' gestation.

c) Individuals with CFRD should be seen in a combined obstetric-endocrinology clinic as soon as possible following conception [8,39].

d) Antenatal care will require close collaboration between obstetric team, the CF team, the GP, and endocrinology team in the case of CFRD or gestational diabetes mellitus. Women with CF should be counselled regarding the need for increased clinic visits and monitoring during pregnancy.

6. Pregnant women with CF should be reviewed frequently (minimum monthly) during the first and second trimesters by the CF MDT to optimise pulmonary and nutritional health and fortnightly during the third trimester. Where possible, visits to the obstetric and CF teams should be co-ordinated with good communication between the teams, especially if not in the same hospital.

a) Pregnant individuals should be reviewed in a multidisciplinary CF clinic at least monthly for the first and second trimesters, increasing to every two weeks or more frequently as necessary in the 3rd trimester [8].

b) More frequent follow-up during pregnancy should be undertaken in those with more severe pulmonary disease and with complex co-morbidities.

c) Regular contact should be maintained between the antenatal clinic/service and the CF and other specialist teams throughout pregnancy, and where possible, appointments should be co-ordinated to avoid excessively burdening the patient.

d) Nutritional health:

I. Women should typically gain 10 - 12kg in weight during pregnancy [13]

II. If weight gain is suboptimal and nutritional status cannot be optimised by a high energy diet alone, the use of oral nutrition supplements or enteral nutrition support may be required to ensure sufficient energy intake and adequate weight gain during pregnancy.

III. Education should be provided about minimising the risk of infections which are potentially harmful to the foetus (e.g., listeriosis, toxoplasmosis and salmonellosis) through correct food handling techniques.

IV. Information should be provided on alcohol, caffeine and fish and mercury consumption parallel to that for the general population [3].

V. Fat soluble vitamins and other supplements should continue during pregnancy to maintain normal levels of all vitamins [3]. Regular measurements of fat-soluble vitamins A (to monitor for retinol toxicity), D and E should occur at first assessment after confirmation of pregnancy and at the beginning of the second and third trimester [40], with dose reduction if necessary.

VI. Iron studies should be reviewed at 20 weeks' gestation to assess the need for supplementation if deficiency is developing with close monitoring of supplementation tolerance and gastrointestinal symptoms particularly constipation. [3,40].

VII. Glucose homeostasis should be closely monitored via OGTT performed pre-pregnancy, repeated at 12-16 weeks and 24-28 weeks in all women with CF with referral to an Endocrinologist as necessary [39,41].

e) Pulmonary health:

I. The transient fall in lung function during pregnancy should be explained to all women. Maintenance therapies (mucolytics, inhaled antibiotics, etc.) should be continued where safe to do so.

II. Prompt detection and treatment of pulmonary exacerbations with appropriate and safe antibiotics is recommended in accordance with general guidelines [42]. Close monitoring to ensure return to pre-baseline FEV1 and health status is important. Women may be counselled on the potential for more frequent hospital admissions and treatment with antibiotics during pregnancy [21].

III. Physiotherapy should continue throughout pregnancy with modifications to ACT and exercise according to individual needs. A high degree of individualisation is required as there are no studies confirming the "best option". It is important to liaise closely with pregnant women to identify an effective and achievable regimen which may be modified as pregnancy progresses.

IV. Reflux increases during pregnancy [3] and adjustments to physiotherapy regimens may be necessary including avoidance of head-down posture, performance of ACT prior to small meals.

V. Regular airway clearance and exercise should be an established routine before the pregnancy and maintained through the pregnancy, with modification as necessary, including avoiding contact sports [37,43].

f) Pregnancy leads to increased stress on the pelvic floor, especially in the third trimester, and may result in urinary leakage. Women with CF are encouraged to perform pelvic floor exercises including during coughing with ACT. If concerns persist referral to a specialist physiotherapist should be made.

g) Consideration of medication safety during pregnancy (and lactation) is required and therapies required for maternal health should be balanced by risks to the foetus or breast feeding newborn [8]. All medications should be reviewed against existing drugs and lactation databases. Open discussions around continuation or discontinuation of CFTR modulator therapies based on current evidence are recommended

7. Clinical care during labour and birth should be led by the obstetric team, with the CF team providing support. Choices about birth should be made by the pregnant person based on individualised information provided by the obstetrician.

There are no published studies specifically addressing intrapartum management in women with CF and the obstetric specialist team should lead care alongside the anaesthetist, with the CF MDT providing support and advice around CF care. Vaginal birth, in the absence of other obstetric contraindications, is highly desirable to minimize post-partum complications [44].

Most applicable guidelines recommend obstetric and anaesthetic evaluation prior to pregnancy or in early pregnancy, to develop a detailed and individualised management plan for birth with the pregnant person including:

a) Place and mode of birth including potential for elective birth to ensure specialist teams are available and modifications to second stage of labour to ensure the expulsive phase of labour is not prolonged.

b) Appropriate maternal-foetal monitoring during labour (e.g., oxygen saturation monitoring)

c) provision of necessary pulmonary interventions (e.g., inhaled therapies, physiotherapy and assistance with sputum clearance may be required by some women during labour, supplemental oxygen as required)

d) Analgesia and anaesthesia considerations including epidural analgesia and avoidance of systemic opioids and general anaesthetic where possible.

e) Invasive and non-invasive maternal monitoring after birth [3]. Adequate maintainance of hydration, nutrition, and blood glucose control should be optimised during labour and birth in women with CF [3].

Anaesthetic considerations include:

I. Ensuring adequate pain relief to reduce anxiety and maternal stess. Early epidural analgesia is the preferred method and can be extended into safe regional anaesthesia in the case of an emergency cesarean section, avoiding the need for airway management and assisted ventilation [45].

II. Avoidance of systemic opioids where possible in favour of epidural to avoid suppression of cough and ventilation and reduce risks of bowel obstruction.

III. For women with more severe CF, assisted ventilation strategies such as BIPAP may be considered with appropriate ICU support. Hypoxia, hypercarbia and respiratory acidosis occur more readily in women with more severe pulmonary disease [18].

IV. Oxygen therapy should be provided to maintain normal saturations as per standard care

8. Postpartum care should be jointly undertaken by the maternity and CF services with special emphasis on physiotherapy, nutritional status, and psychosocial support.

The post-partum period is a challenging time for women with CF as they recover from birthing, adjust to the demands of parenthood, and balance their own CF care needs with those of their newborn and potentially, their other children or dependants. The first 12 months post-partum may be associated with decline in health in mothers and fathers with CF due to these increased demands [46]. Therefore, review and optimisation of treatment regimens, nutritional support, exercise prescription and psychosocial assessment should be conducted soon after delivery and reviewed regularly thereafter.

a) Following delivery, adequate pain relief, oxygen therapy (if required), inhalation therapy and early mobilisation should be considered and prioritised after a caesarean section.

b) Breastfeeding can successfully be undertaken by a mother with CF, however, observation of nutritional status and the impact of fatigue on physical and mental health should be closely monitored. It is also necessary for new mothers with CF to maintain all aspects of CF care during this time Breastfeeding advice should be offered to new mothers by a lactation consultant and strategies to meet increased energy requirements during breastfeeding should be provided by the specialist CF dietitian. All medications should be reviewed against existing drugs and lactation databases. Mothers should be supported in their choices around infant feeding and formula feeding may be preferable for those unable to maintain adequate nutrition or too exhausted/time poor to breast feed.

c) Post-natal and CF clinic appointments should be streamlined where possible to reduce the burden of clinic attendance. Clinics may consider telehealth visits and flexible clinic times to make attendance and access to care easier for new mothers.

d) Post-natal domestic support may be offered to women where available, for example via local CF charities and government-based carer support services, to allow for time to attend to CF treatments including inhalation therapy, airway clearance, and physical exercise. The CF social worker may have a pivotal role in facilitating access to social supports for new parents.

e) Screening for maternal post-natal depression and anxiety using tools such as the Edinburgh Postnatal Depression Scale (EPDS), PHQ-9 and the DASS should be performed as soon as the first antenatal visit (4-6 weeks) and repeated at intervals during the first year according to individual need [47,48]. Established referral pathways for mothers to access psychological interventions should be identified. Screening for paternal anxiety and depression should also be regularly performed.

f) The US and European CF associations now recommend that infants born to mothers with CF taking elexacaftor + tezacaftor + ivacaftor during pregnancy are screened for CFTR mutations directly, given the potential for false negative newborn screening results[33].

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Lung Transplantation in cystic fibrosis

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Standard 1 Transplant discussions should occur early to facilitate timely referral to a specialist transplant centre, allowing person/people with (Pw) CF and their caregivers opportunity to make informed decisions, address modifiable barriers to transplantation, and to optimise clinical status prior to transplant.

Standard 2 Transplant evaluation throughout the pre-, peri-and post-transplant periods should involve multidisciplinary assessment by medical (CF, transplant specialists and extra-pulmonary CF subspecialists), nursing, physiotherapy, dietetic, pharmacy and psychosocial teams.

Standard 3 CF specific infection prevention and control policies should be implemented across all services caring for people with CF undergoing transplantation in accordance with national and international guidelines.

Standard 4 Psychosocial evaluation and access to evidence-based interventions for PwCF and their caregivers should be provided early and regularly throughout the pre-, peri- and post-transplant periods to optimize transplant candidacy and longer-term health outcomes.

Standard 5 Children and adolescents should be co-managed by specialist teams with expertise in paediatric CF care and transplant care, in close consultation with the paediatric specialist multidisciplinary CF team to address issues unique to CF.

Standard 6 A structured adolescent transplant recipient transition and transfer process to a suitable adult shared care model should be in place.

Standard 7 Close communication and aligned policies and protocols should be established between the specialist transplant and CF centre with agreed shared care arrangements in the pre, peri and post -transplant periods.

Background

Cystic Fibrosis has historically been one of the leading indications for lung transplantation in children and young adults. For patients with advanced CF lung disease, lung transplantation continues to be the definitive treatment when maximal medical therapy can no longer maintain adequate respiratory function and quality of life. Transplant offers advantages in both increased survival and quality of life (1) and is of major importance for PwCF with advanced lung disease established before the advent of modulator therapies, those with progressive disease despite maximal intervention, and for individuals who are ineligible for, or unable to tolerate, modulator therapy.

International registry data have consistently shown that people with CF achieve some of the best post–lung transplant survival outcomes among all transplant indications, with median survival exceeding 9 years in many contemporary series. In 2019, CF accounted for 15% (9,674) of all lung transplants and adult CF Lung Transplant Recipients (CFLTRs) had the best survival among all pre-transplant diagnostic groups (2).

The advent of CFTR modulator therapies has resulted in unprecedented improvements in health for PwCF, including those with advanced lung disease. These welcome improvements have seen global reductions in transplant referrals, reduced waiting list mortality, and fewer PwCF referred for urgent transplantation (3-5). Rates of lung transplant among PwCF in the US have fallen from 13% to1% since the introduction of Elexcator/tezacaftor/ivacaftor (ETI) in 2019 (6). The ACFDR reports a decrease in transplants in Australia from approximately 40 people in 2015 to just 3 people in 2024. (3)

Lung transplant referral and assessment guidelines have recently been developed by the American Cystic Fibrosis Foundation (1) and endorsed by the International Society for Heart and Lung Transplantation (ISHLT)(7). These documents, along with expert consensus, underpin the Australian standards for transplant care and have informed the recommendations in this chapter. Whilst the widespread use of highly effective CFTR modulator therapy may lead to changes in predictors of survival and modifications to referral and listing criteria, the principles outlined in this chapter are likely to remain relevant.

The international reduction in numbers of CF lung transplants underscores the importance of centralised expertise in transplant care and maintenance of skills and knowledge. In Australia, transplant programs will continue to play an essential role in CF care, although the timing of referral, listing and selection of candidates is evolving. The CF transplant model of care must evolve toward a lower-volume, higher-complexity model that sustains multidisciplinary expertise despite reduced procedural numbers. This relies on close collaborative partnerships between the CF and transplant multidisciplinary teams providing long-term expert care across the stages of transplantation. (1, 7, 8).

This chapter provides contemporary and evidence-based standards and recommendations for lung transplant care in people with CF in Australia.

Australian Experience

There are four specialist lung transplant centres in Australia and one specialist paediatric lung transplant centre at the Alfred Hospital in Victoria. Rates of lung transplantation in CF are decreasing in Australia in line with international trends reflecting the impact of modulator therapies and improved health outcomes in the CF population. In 2024, three bilateral lung transplants were performed in adults with CF, with 46 individuals assessed for transplant and 8.7% of these waitlisted. (3).

The Alfred Hospital is the only dedicated paediatric lung transplant service in Australia. This single national service arose due to the rarity and complexity of paediatric transplantation. The program combines paediatric expertise with a large adult lung transplant service and works collaboratively with local paediatric CF centres with respect to post-transplant care. Many paediatric CF centres nationally benefit from close collaboration with their local adult specialist transplant centres (where available) in the care of older adolescents undergoing transplant, although models of care vary.

Recommendations

Transplant discussion should occur early to facilitate timely referral to a specialist transplant centre, allowing PwCF and their caregivers opportunity to make informed decisions, address modifiable barriers to transplantation, and to optimize clinical status prior to transplant

All people with Cystic Fibrosis (PwCF) should have the opportunity to regularly discuss lung transplantation with their CF team, especially if there is no CFTR modulator option available or no evidence of sustained improvement despite CFTR modulator commencement. Some PwCF may not wish to discuss transplantation repeatedly and this should be respected.

a. Routine CF clinical care should include early regular discussions about disease trajectory and potential treatment options including transplantation to normalise the concept. These discussions should start well in advance of the need for referral

I. If not already introduced, discussions about transplantation should occur for all PwCF when their FEV1 is less than 50% predicted and /or on identification of clinical concern including rapid FEV1 decline.

b. Recommendations for lung transplant referral include

I. individuals with progressive severe lung disease despite maximal medical therapy resulting in symptoms that impact activities of daily living / quality of life.

II. Individuals for whom the risk of death within two years is considered high without transplantation (7).

c. Timely referral for transplantation assessment in PwCF is essential. ISHLT consensus statement (7) recommends referral when:

I. FEV1 < 30% predicted in adults (or <40% predicted in children)

II. FEV1 < 40% predicted in adults (or < 50% predicted in children) and any of the following:

- Six-minute walk distance < 400 meters
- PaCO2 > 50 mmHg
- Hypoxemia at rest or with exertion
- Pulmonary hypertension (PA systolic pressure > 50 mmHg on echocardiogram or evidence of right ventricular dysfunction)
- Worsening nutritional status despite supplementation
- 2 exacerbations per year requiring intravenous antibiotics
- Massive haemoptysis requiring bronchial artery embolization
- Pneumothorax

III. FEV1 < 50% predicted and rapidly declining based on pulmonary function testing or progressive symptoms

IV. Any exacerbation requiring positive pressure ventilation

V. Special consideration should be given to women, especially those younger and smaller in stature, for earlier referral due to poorer survival data and added complexity for transplantation.

d. In the event of a precipitous decline leading to an urgent inpatient referral for transplant, candidates should be assessed using similar frameworks to other candidates with every effort undertaken

to complete a full and comprehensive evaluation. ECMO bridge to transplant in select patients may be considered by transplant centres with this expertise but should not be regarded as a standard of care.

e. Modifiable barriers to lung transplant should be identified early and actively addressed where possible. Such barriers include, but are not limited to, nutritional status, infection, diabetes control, renal impairment, liver disease, poor adherence, mental health status, substance abuse, psychosocial and geographic factors (7, 9). It should also be acknowledged that such barriers do not preclude referral for transplantation.

I. Psychosocial factors, especially adherence and mental health, are important determinants of post-transplant outcomes and are potentially modifiable risk factors. Psychosocial interventions aimed at improving adherence and mental health are required (see later section).

F. Treatment with CFTR therapies should not prevent referral for those who meet referral guidelines, including those who recently commenced treatment (4, 10, 11).

Transplant evaluation throughout the pre-, peri-and post-transplant periods should involve multidisciplinary assessment and management by medical (CF, transplant specialists and extra-pulmonary CF subspecialists), nursing, physiotherapy, dietetic, pharmacy and psychosocial teams.

Assessment for suitability for lung transplantation is a multidisciplinary process that includes assessment of severity of lung disease, nutritional status, presence of comorbidities and psychosocial circumstances. The timing of a comprehensive evaluation for transplant will be dependent on the transplant providers' assessment of potentially modifiable risk factors, the individual's disease trajectory, and the likelihood of prolonged wait for suitable donor organs (which will be influenced by sex, height and HLA sensitisation amongst other factors).

a. All PwCF should be cared for by a specialist lung transplant multidisciplinary team with knowledge and experience in the care of PwCF. CF expertise may be provided by the referring CF centre, the transplant institutions affiliated with the CF centre, or the transplant service if expertise and resources permit (1).

b. All PwCF undergoing transplant should have regular contact with the transplant nurses/transplant coordinator for education, information and support around transplant processes and stages (prior to and post transplantation). Transplant nurse coordinators play a key role as liaison between the person with CF and the transplant team and ensure patient care is coordinated across the MDT (multidisciplinary team).

c. Assessment and management of individuals by a CF specialist dietician should occur to optimise nutritional status and body mass index (BMI) prior to and post-transplant. Malnutrition is an important and potentially modifiable risk factor for transplant outcomes in those with CF. Low BMI is a predictor of lung function decline and mortality (12), although more recent evidence suggests satisfactory outcomes in PwCF transplanted with a BMI <17kg/m2(17).

d. A specialist transplant pharmacist with experience in cystic fibrosis is recommended to manage complicated medication regimens, including therapeutic drug monitoring, and provide PwCF education and counselling around medication use, adherence, interactions and side effects.

e. Assessment of aerobic capacity, strength, mobility and airway clearance techniques by a specialist CF physiotherapist is recommended pre- and post-transplant to inform individualised pulmonary rehabilitation programs that aim to improve survival and function.

f. Access to CF subspecialists with transplant knowledge and expertise is required to prevent and manage extra-pulmonary risk factors and complications. These include infectious disease (see later in chapter), nephrology, endocrinology, gastroenterology, fertility, dermatology and mental health subspecialists (see later in chapter).

I. Consultation with infectious disease specialists in the pre-, peri- and post-operative period is recommended to assist in the treatment of respiratory pathogens and implementation of IP&C policies.

II. Assessment and management of CF related diabetes by endocrinologists is recommended, with regular diabetes screening for those without CFRD prior to transplant and close monitoring for diabetes in all individuals post-transplant. A focus on optimal diabetes control is essential in the peri-operative period and is associated with improved survival (13). A lower threshold for transplant referral and listing for those with diabetes should be considered (7).

III. Regular bone density evaluation with appropriate management and treatment of osteopenia and osteoporosis pre, peri and post-transplant is advised.

IV. Gastroenterology expertise is required to screen and monitor CF liver disease (CFLD), and in the management of post-transplant GI complications including gastroparesis and GI dysmotility, DIOS and constipation. Screening for colorectal cancer should continue due to the increased risk of bowel cancer in the CF population which is further increased by lung transplantation (14).

V. Screening for chronic rhinosinusitis symptoms is recommended prior to transplant and referral to Ear nose and throat (ENT) specialists required for those with symptomatic sinus disease (15).

VI. Discussions around fertility, conception and pregnancy should occur with all women of childbearing age prior to, and after, transplantation in accordance with ISHLT guidelines (16). Expertise provided by reproductive endocrinologists, feto-maternal medicine specialists and genetic counsellors is recommended.

VII. Mental health conditions including anxiety, depression and other diagnoses should be evaluated and managed in consultation with psychiatry, psychology and psychosocial experts.

CF specific infection prevention and control policies should be implemented across all services caring for people with CF undergoing transplantation in accordance with national and international guidelines.

The Cystic Fibrosis Foundation (CFF) and the ISHLT (1, 7) recommend that CF and transplant programs implement infection and prevention and control (IP&C) across all CF services in accordance with their guidelines (17). Individuals with CF who are awaiting lung transplantation may have chronic respiratory infection with pathogens (including *Burkholderia cepacia complex*, *non-tuberculous mycobacteria* species or *fungi).* Pathogens may be resistant to antimicrobials, considered potential contraindications to transplantation (18-21) and may influence health outcomes post-transplant (22). Culture surveillance prior to transplantation in addition to culture of operative samples are important strategies to guide peri-operative antimicrobial management.

a. CF care teams should collaborate with their institution's IP&C team to implement the recommendations in these guidelines and have procedures in place to mitigate the risk of transmission and acquisition of CF pathogens in all PwCF.

b. PwCF and their families undergoing transplant should be educated about IP&C and empowered to utilise strategies that prevent transmission of pathogens, regardless of culture results (1, 17, 23, 24)

c. Health care workers (HCWs) caring for PwCF undergoing transplant must take appropriate precautions to prevent transmission of potential pathogens in accordance with international CF IP&C guidelines (1, 17, 23, 24).

d. A multidisciplinary, consultative approach including infectious diseases, microbiologists and respiratory specialists to guide management based on the patient's clinical condition, respiratory function and relevant radiological findings is recommended.

e. Non-invasive bacterial, fungal and AFB respiratory cultures should be obtained by the transplant or CF centre every 3 months (more if clinically indicated) in actively waitlisted transplant candidates.

f. Retrospective studies examining peri-operative antimicrobial strategies suggest that ideal treatment is composed of susceptibility-targeted antimicrobials where an agent with acceptable toxicity is available (1, 17). Where this is not possible, the use of previously effective antimicrobials should be considered.

g. Intra-operative bacterial, fungal and AFB culture sampling of the native lung is recommended at the time of transplantation, although optimal sampling strategy is unclear. Published strategies include peripheral sputum samples prior to surgery, intra-operative bronchoalveolar lavage prior to explantation, large airway swabs and/or native lung tissue sampling (1).

h. In the post-transplant period, prompt diagnosis and treatment of symptomatic respiratory tract infection is essential. Sputum culture at the time of infection, in addition to prior culture results, should be utilised to guide antimicrobial management. The utility of routine sputum cultures in asymptomatic

individuals following transplantation is uncertain and no specific management recommendation regarding the use of antimicrobials for asymptomatic bacterial airway isolated can be made.

i. The CF Foundation recommends that all CF transplant centres obtain and review centre-specific quarterly surveillance reports of the incidence and prevalence of respiratory tract pathogens at their centres, to be reviewed in collaboration with IP&C teams and microbiologists (17)

Psychosocial evaluation and access to evidence-based interventions for PwCF and their caregivers should be provided early and regularly throughout the pre-, peri- and post-transplant periods to optimize transplant candidacy and longer-term health outcomes.

Psychosocial (PS) assessment and intervention is an essential part of care for PwCF and their caregivers throughout the transplant journey (25). PwCF undergoing transplant experience significant PS challenges during their care. Psychological distress, uncertainty and anxiety, social isolation with deteriorating health status and increasing care burden are common in the pre-transplant period. PwCF may also experience grief as a response to the transition to a new treating team and new medical regimens. In the post-transplant period, affective disorders are common with studies reporting depression in up to 63% of cardiothoracic transplant recipients in the first few years after transplant (26).

Anxiety and panic disorder and post-traumatic stress disorder related to the surgery and intensive interventions are common. Experiences post-transplant include a sense of loss of agency, identity, adjustments, guilt and sadness for the donor family, and fear of transplant rejection (25). There may be significant re-evaluation of expectations around physical recovery and anticipated return to “normal life” after transplant as PwCF adjust to life as a transplant recipient. Families caring for young people with CF who present for transplant assessment have often had a host of experiences that will influence their functioning post-transplant. Family dysfunction, stress and burn out are recognised. Adolescent transplant candidates may experience challenges around treatment adherence, autonomy, and risky behaviours that threaten transplant success. PS factors including mental health and adherence are important determinants of transplant outcomes warranting careful and broad psychosocial assessment and management (25, 26).

a) A stable, experienced psychosocial team, ideally embedded within the larger multidisciplinary transplant team, should be available to support PwCF and their carers through the challenges of transplant.

b) Early introduction of PwCF to the PS team for pre-transplant assessment and ongoing regular monitoring of PS health is recommended. This allows sufficient time for trust and rapport building, facilitating psychological safety and containment for the

PwCF. It also ensures timely screening and intervention for risk factors associated with transplant outcomes and quality of life (27, 28). It is desirable that the clinicians who perform the psychosocial assessments are part of the broader multidisciplinary lung transplant team.

c) There should be close collaboration between the referring CF team, the lung transplant team, and psychosocial health specialists to ensure a comprehensive PS assessment is completed.

d) Key psychosocial domains recommended for assessment in PwCF (26) are:

   I. Risk factors associated with poor post-transplant outcomes and reduced survival including treatment adherence, mental health history, substance use history (29).

   II. The candidate's knowledge, understanding and capacity to engage in decision making about transplant. This includes cognitive status, capacity to give informed consent, knowledge and understanding of current illness, knowledge and understanding of current treatment options.

   III. The candidates personal, social, and environmental resources and circumstances, including strengths and supports that may mitigate identified risks. Including coping strategies, emotional reactions to illness, social supports, social history, legal issues, exposure to traumatic events, and concurrent life stressors.

   IV. Consideration should be given to the patient's end of life wishes and concurrent referral to palliative care for co-management of symptoms and support (30, 31)

e) A family centred approach to assessment in children and adolescents is needed with careful consideration of both child/adolescent recipients and their caregivers including; developmental status and educational functioning, capacity for decision making and consent, knowledge and understanding of transplant processes, social and family supports available to manage the complex demands of transplantation, mental health and family stability (32).

f) Involvement of the PS team in admissions to hospital for any procedure or exacerbation of health following transplant is recommended to address psychological and social distress (33)

Children and adolescents should be co-managed by specialist teams with expertise in paediatric CF care as well as transplant care and in close consultation with the paediatric specialist multidisciplinary CF team to address issues unique to CF.

Lung transplantation in children with CF is rare and complex, especially since the advent of CFTR modulators (34). There are specific considerations in children and adolescents, including the smaller size of the lung allograft needed (and thus donor scarcity) and the significant impact of graft size on transplant outcomes, longer wait times and higher mortality pre-transplant, and surgical challenges related to smaller anatomy. Consequently, early discussion of potential candidates with a specialist paediatric lung transplant centre is essential prior to referral (7, 35).

a. Guidelines outlining indications for lung transplant referral for children with CF should be considered (36) and early discussions with the transplant specialists to clarify candidate suitability and referral are strongly endorsed. Referral of children and adolescents for transplant is recommended when

    - FEV1 is less than 50% predicted and rapidly declining (defined as >20% decline in 12 months).
    - FEV1 is less than 50% predicted with markers of shortened survival
    - FEV1 is less than 40% predicted.

b. All children in Australia aged 4-16 years should be referred to the specialist paediatric lung transplant team (37, 38). In Australia, this is to the Alfred Hospital, Melbourne, Victoria.

c. Children and adolescents have unique health care needs related to their developmental, cognitive, emotional and psychosocial needs. They are best cared for in a child/adolescent friendly environment (see **Chapters on Infants and children and Adolescents and young adults).**

d. Psychosocial assessment and intervention are a cornerstone of paediatric CF transplant care and all children and adolescents with CF and their families should receive psychosocial support throughout the transplant process. Specific focus on optimising adherence to treatment is needed to improve transplant outcomes among adolescents.

e. Clear lines of communication between CF and transplant teams are needed and this should occur irrespective of geographical location (see section below).

f. Educational resources provided to children and families should be age and developmentally appropriate, CF specific, and include information for caregivers. Educational material should be tailored to individual needs using a variety of media and resources.

A structured adolescent transplant recipient transition and transfer process to a suitable adult shared care model should be in place.

A structured approach to transition and transfer to adult care is critical for adolescent and young adult (AYA) lung transplant recipients who are at significantly increased risk of graft loss during a period of potential instability in health care access and or delivery. In a recent analysis of International Society and Heart and Lung Transplant Registry data, AYAs (aged 10-24 years) had a 10% lower 3-year survival than adults (aged 25-34 years), despite fewer co-morbidities and more favourable donor and transplant characteristics (39) . This is mirrored in data from other solid organ transplant populations, describing a peak incidence of graft failure between 17-21 years (39-43).

The aetiology of poorer transplant outcomes during adolescence-young adulthood is multifactorial, although the principal drivers are medication and treatment non-adherence, chronic graft rejection, and psychosocial risk factors active during the transition to adult care. Rates of non-adherence are highest during adolescence with the period of transition from paediatric to adult care exerting a further detrimental effect (44, 45).

a. A structured transition and transfer program should be developed and implemented by the transplant centre in collaboration with the paediatric and adult CF centres. A structured approach supports greater AYA engagement with the receiving adult centres, better adherence to transplant and CF care and reduced morbidity/mortality(46, 47). In the transplant setting the consequences of non-adherence and disengagement with healthcare teams are greater with potentially catastrophic outcomes.

b. Dual transfer processes to both the adult transplant and adult CF centre are necessary and should run in parallel with designated AYA transfer coordinators identified to lead the process at each centre. See **Chapter AYA** for details on transition and transfer standards of care.

c. Transition and transfer processes should provide uninterrupted health care across all facets of transplant care, which is AYA-centred, age and developmentally appropriate, flexible and comprehensive (47).

    I. Given the complexity of dual transfer to both adult transplant and CF services, individualised transition programs with graded transfer processes tailored to the individual AYA needs should be considered. This may offer greater opportunity for AYA to acquire necessary self-care skills across a range of complex treatment regimens and allow familiarisation and engagement with new adult teams.

    II. Proactive support for AYA around the competing priorities of normal adolescent socio-emotional development and complex transplant and CF treatment regimens is strongly recommended.

d. Psychosocial factors are strongly associated with adherence to treatment in adolescence

(48) and therefore special attention to psychosocial health must be given during this period.

Close communication and aligned policies and protocols should be established between the specialist transplant and CF centre with agreed shared care arrangements in the pre-, peri- and post-transplant periods.

A co-ordinated shared care model across the pre-, peri- and post-transplant periods is important for people with cystic fibrosis given the multisystem nature of CF. It is noteworthy that PwCF who undergo their first lung transplant in a transplant centre with a dedicated cystic fibrosis care centre on site have a 33% reduction in risk of death or re-transplantation compared to those transplanted without onsite CF care (49). Benefits of a shared care model include continuity of care for the non-pulmonary complications of CF, improved communication between CF and transplant teams, and sharing of expertise (8).

a. Shared care models should include clear and open forms of communication between the CF centre and the transplant centre (8). These include regularly scheduled meetings, educational sessions for both teams, a pre- and post-transplant MDT handover, an accessible contact list of transplant team and CF MDT members.

b. Aligned policies and protocols across CF and transplant centres should be developed to ensure standardisation of care

c. Roles and responsibilities of the CF and transplant care teams should be clearly defined. PwCF should have clear pathways around whom to contact for issues and advice.

d. All PwCF should be offered resumed care with the specialist CF MDT within 6-12 month following transplantation particularly if they live a distance from the transplant centre

e. Regular cross disciplinary meetings for individual patient management and transplant team updates should be facilitated.

f. Close monitoring and management of transplant recipients for extra-pulmonary complications such as diabetes is required in the post- transplant period to optimise outcomes.

g. Prescribing of CFTR modulators pre- and post-transplant should be undertaken by practitioners skilled in the prescription and monitoring of these medications. CFTR modulator use in PwCF post lung transplant may have beneficial impacts on the non-pulmonary manifestations of CF (50, 51).

h. Models of shared care should be patient and family centred and responsive to the expertise and resources of both the CF and transplant teams.

i. Specialist pharmacy expertise is recommended as an integral part of shared care models to support therapeutic drug monitoring, management of medication interactions and dosing, and to provide support for PwCF with complex medication regimens.

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FRAMEWORK FOR CF CARE

The CF CENTRE: Patient-Centred Care, Services and Staffing

The Framework for CF Care sets out a nationally consistent approach to delivering high-quality, equitable, and coordinated care for all Australians living with cystic fibrosis (CF).

Developed collaboratively with clinicians, researchers, and the CF community, it outlines best-practice standards across clinical management, mental health, data-driven improvement, and access to emerging therapies.

The Framework ensures that every person with CF, regardless of where they live, receives the same level of comprehensive, multidisciplinary support throughout their life, helping to improve outcomes and quality of life across the CF community.

Read the Framework Here: https://www.cysticfibrosis.org.au/wp-content/uploads/2026/10/Framework-for-CF-Care-V2.pdf

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.