CYSTIC FIBROSIS

Introduction

Cystic fibrosis (CF) is one of the most common genetic diseases in European populations. It results from mutations affecting a gene that controls a chloride channel in cell membranes called the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is essential regulating salt and water movements across cell membranes [1].

Absent or reduced functioning of CFTR results in thickened secretions in a number of organs, including the lungs and digestive system. In the lungs, the airways become clogged with thick sticky mucus, which slows the clearance of bacteria, leading to frequent infections and scarring of the airways. In about 85% of cases, ducts in the pancreas also become blocked, leading to problems with digestion and intestinal malabsorption. In infants this may result in failure to thrive, while older children and young people may become malnourished. Other complications include male infertility; CF related diabetes, which in older patients may require daily insulin injections; chronic liver disease and portal hypertension; joint problems; and psychological problems arising from having to cope with a severe long-term medical condition [1].

The outlook for people with CF has improved steadily over the past two decades, largely as a result of earlier diagnosis, more aggressive treatment, and the provision of care in specialised centres [2]. In the US, the median predicted survival for those with CF increased from 25 years in 1975, to 37 years in 2008, and the length of survival is directly correlated with the decade of birth [3]. People born with CF today are expected to live into their sixth decade [2,3].

In New Zealand, babies are routinely screened for CF as part of the Newborn Metabolic Screening Programme [4]. Screening involves a heel prick blood spot test that measures immunoreactive trypsinogen (IRT). A very high IRT concentration suggests pancreatic injury consistent with, but not necessarily specific to, CF [2]. In older children and adults, the diagnosis is made when a clinical history suggestive of cystic fibrosis is accompanied by biochemical and genetic markers of CFTR dysfunction. This typically includes a sweat test, which looks for an elevated concentration of chloride in sweat [2].

People with CF benefit from treatment in specialised CF centres which have a dedicated multidisciplinary team and an emphasis on frequent visits, periodic testing and monitoring adherence to therapy [3]. Those centres which see patients more frequently, obtain more cultures, and use more oral and intravenous antibiotics, have been shown to achieve better lung function than centres with less aggressive approaches to care [2]. A range of other therapies are also available, and reviews of a number of these are summarised in the evidence-based review table at the end of this section.

The following section reviews hospitalisations for children and young people with any mention of CF in any of their first 15 diagnoses, as well as mortality for those with CF listed as the main underlying, or as a contributory cause of death.

Data Source and Methods

Definition

1. *Hospital admissions for children and young people aged 0–24 years with cystic fibrosis listed in any of the first 15 diagnoses*
2. *Mortality in children and young people aged 0–24 years with cystic fibrosis listed as the main underlying cause of death, or as a contributory cause*

Data Source

1. National Minimum Dataset

Numerator: Hospital admissions for children and young people aged 0–24 years with cystic fibrosis (ICD-10-AM E84) listed in any of the first 15 diagnoses.

2. National Mortality Collection

Numerator: Mortality in children and young people aged 0–24 years with cystic fibrosis (ICD-10-AM E84) listed as the main underlying cause of death, or as a contributory cause.

Denominator: Statistics New Zealand Estimated Resident Population (projected from 2007).

Notes on Interpretation

Note 1: This analysis focuses on hospital admissions and mortality for children and young people with cystic fibrosis listed in any of the first 15 diagnoses, or as the main underlying or a contributory cause of death. The rationale for looking beyond the primary diagnosis was the need to highlight the full spectrum of health issues experienced by those with cystic fibrosis, and their consequent requirement for acute health services.

For example, during 2008–2012, while around 84% of hospitalisations for children and young people with cystic fibrosis had cystic fibrosis listed as the main reason for admission, a significant minority were admitted for infectious and respiratory diseases, digestive system problems, or other reasons. Further a review of the secondary diagnoses of those admitted with a primary diagnosis of cystic fibrosis found that a significant proportion were also for infections, respiratory, or digestive system complications.

Note 2: If no mention of cystic fibrosis was made in any of the first 15 diagnoses, these cases were not included, even if the patient had been assigned a diagnosis of cystic fibrosis on a previous admission.

New Zealand Distribution and Trends

Distribution by Primary and Secondary Diagnosis

Primary Diagnosis: In New Zealand during 2008–2012, 83.7% of hospitalisations in children and young people with cystic fibrosis listed in any of their first 15 diagnoses, had cystic fibrosis listed as the primary reason for admission. The remainder of admissions were for a variety of infectious and respiratory diseases, digestive system problems and other issues (**Table 1**).

Secondary Diagnosis: Of those children and young people with cystic fibrosis listed as the primary diagnosis, the majority (92.6%) also had a secondary diagnosis. Of these, unspecified acute lower respiratory tract infections were the most frequent secondary diagnosis listed, with a range of other infectious (e.g. pseudomonas, *staphlycoccus aureus*, aspergillosis), respiratory (e.g. bronchiectasis, pneumonia) and other (e.g. diabetes and pancreatic problems) conditions also making a contribution (**Table 2**).

Distribution by Age

In New Zealand during 2008–2012, hospitalisations for children and young people with cystic fibrosis were relatively evenly distributed across the age range, although a small peak was evident during adolescence. Mortality however, was more common amongst those in their late teens and early twenties, with 20 young people having cystic fibrosis listed as the main underlying cause of death, or as a contributory cause, during 2006–2010 (**Figure 1**).

Table 1. Hospital Admissions in Children and Young People Aged 0–24 Years with Cystic Fibrosis by Primary Diagnosis, New Zealand 2008–2012

Primary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	Admission Rate per 100,000 Population	% of Admissions in those with Cystic Fibrosis
Cystic Fibrosis				
Cystic Fibrosis with Pulmonary Manifestation	1,226	245.2	16.06	44.1
Cystic Fibrosis with Intestinal Manifestation	58	11.6	0.76	2.1
Cystic Fibrosis with Other Manifestation	878	175.6	11.50	31.6
Cystic Fibrosis Unspecified	164	32.8	2.15	5.9
Total Cystic Fibrosis-Related Diagnoses	2,326	465.2	30.46	83.7
Respiratory System Diseases	90	18.0	1.18	3.2
Factors Influencing Health Service Contact	86	17.2	1.13	3.1
Diseases Digestive System	57	11.4	0.75	2.1
Complications Surgical Medical Care	47	9.4	0.62	1.7
Infectious and Parasitic Diseases	37	7.4	0.48	1.3
All Other Diagnoses	137	27.4	1.79	4.9
Total Other Diagnoses	454	90.8	5.95	16.3
Total	2,780	556.0	36.41	100.0

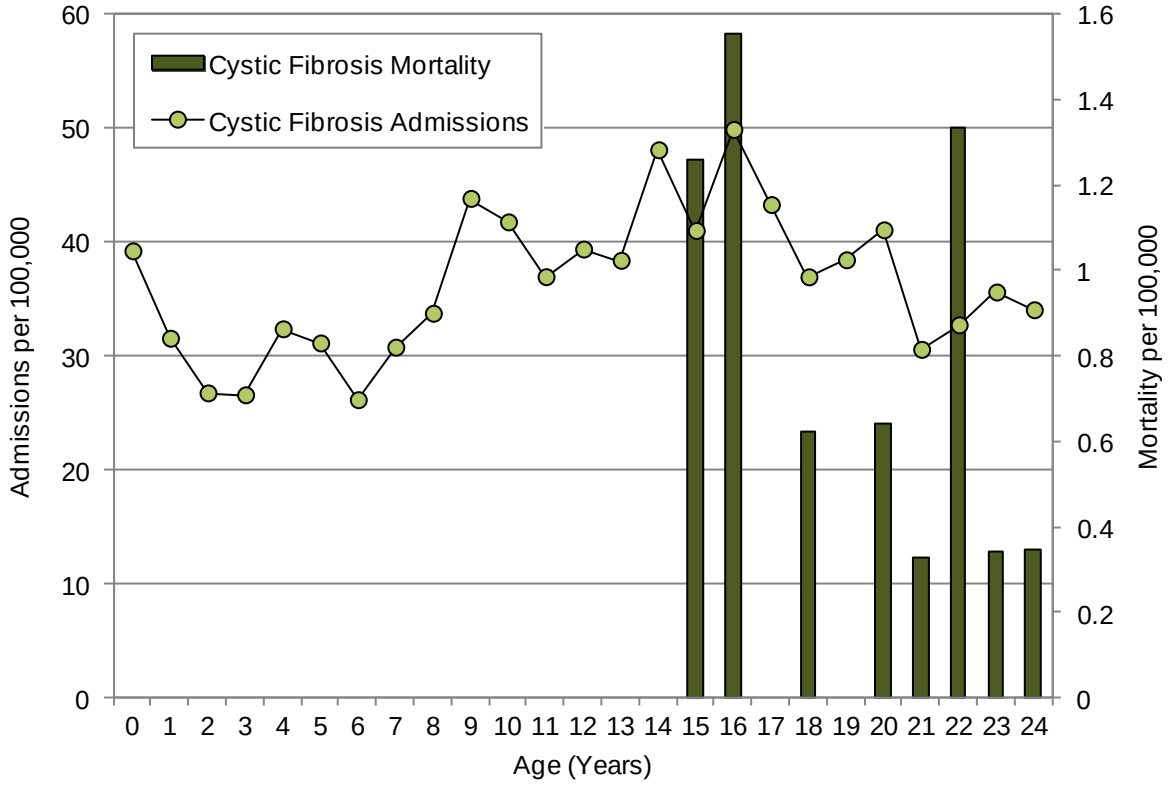
Source: Numerator: National Minimum Dataset, hospital admissions by primary diagnosis for children and young people with cystic fibrosis listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Table 2. Secondary Diagnosis in Children and Young People Aged 0–24 Years Hospitalised with Cystic Fibrosis as a Primary Diagnosis, New Zealand 2008–2012

Secondary Diagnosis	Number of Admissions: Total 2008−2012	Number of Admissions: Annual Average	% of Admissions with Cystic Fibrosis as a Primary Diagnosis
Secondary Diagnosis in Admissions with Cystic Fibrosis as a Primary Diagnosis			
Acute Lower Respiratory Infection Unspecified	588	117.6	25.3
Bronchiectasis	274	54.8	11.8
Influenza and Pneumonia	56	11.2	2.4
Acute Upper Respiratory Infections	54	10.8	2.3
Other Respiratory System Diseases	123	24.6	5.3
Pseudomonas Infection	207	41.4	8.9
Aspergillosis	133	26.6	5.7
Staphylococcus aureus Infection	112	22.4	4.8
Other Infectious and Parasitic Diseases	113	22.6	4.9
Specific Diseases of Pancreas	117	23.4	5.0
Other Diseases Digestive System	81	16.2	3.5
Diabetes Mellitus	68	13.6	2.9
Other Diagnoses	227	45.4	9.8
No Secondary Diagnosis	173	34.6	7.4
Total	2,326	465.2	100.0

Source: Numerator: National Minimum Dataset, hospital admissions by secondary diagnosis for children and young people with cystic fibrosis listed as their primary diagnosis; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Figure 1. Hospital Admissions (2008–2012) and Mortality (2006–2010) for New Zealand Children and Young People with Cystic Fibrosis by Age



Source: Numerator Admissions: National Minimum Dataset, hospital admissions for children and young people with cystic fibrosis listed in any of the first 15 diagnoses; Numerator Mortality: National Mortality Collection, Deaths with cystic fibrosis listed as the main underlying or a contributory cause of death; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Distribution by Ethnicity and Gender

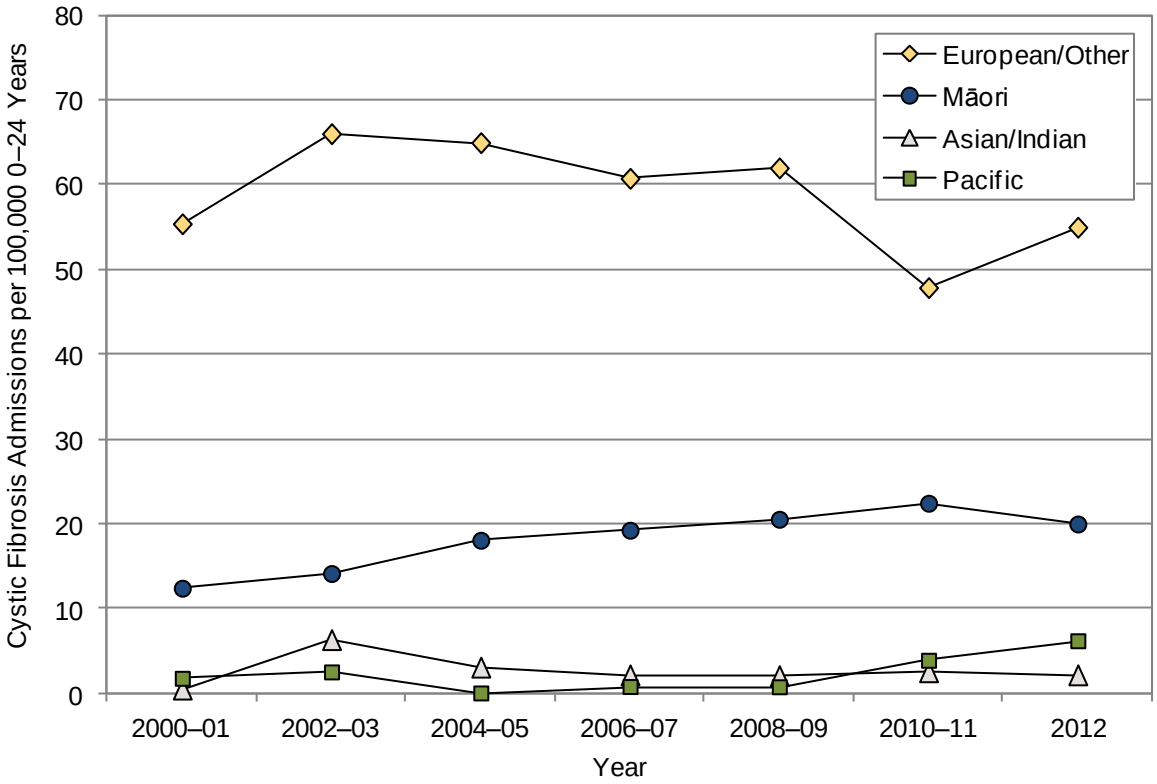
In New Zealand during 2008–2012, hospital admissions for children and young people with cystic fibrosis were *significantly* higher for females than for males. Admission rates were also *significantly* higher for European/Other > Māori > Pacific and Asian/Indian children and young people (**Table 3**). Similar ethnic differences were seen during 2000–2012 (**Figure 2**).

Table 3. Hospital Admissions for Children and Young People Aged 0–24 Years with Cystic Fibrosis by Ethnicity and Gender, New Zealand 2008–2012

Variable	Rate	Rate Ratio	95% CI	Variable	Rate	Rate Ratio	95% CI
Cystic Fibrosis							
Prioritised Ethnicity				Gender			
Asian/Indian	2.25	0.04	0.03–0.06	Female	39.02	1.00	
European/Other	54.88	1.00		Male	33.92	0.87	0.81–0.94
Māori	21.13	0.39	0.35–0.43				
Pacific	3.12	0.06	0.04–0.09				

Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with cystic fibrosis listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007); Note: Ethnicity is Level 1 Prioritised; Rate is per 100,000 population

Figure 2. Hospital Admissions for Children and Young People Aged 0–24 Years with Cystic Fibrosis by Ethnicity, New Zealand 2000–2012



Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with cystic fibrosis listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007); Note: Ethnicity is Level 1 Prioritised

South Island DHBs Distribution and Trends

South Island Distribution

In the South Island during 2008–2012, 21 Nelson Marlborough, 5 South Canterbury, 62 Canterbury, 3 West Coast, 16 Otago and 8 Southland children and young people were hospitalised with a diagnosis of cystic fibrosis. Admission rates per 100,000 in Nelson Marlborough, South Canterbury, Canterbury and Southland were *significantly* higher than the New Zealand rate, while in the West Coast and Otago rates were not *significantly* different (**Table 4**).

South Island Trends

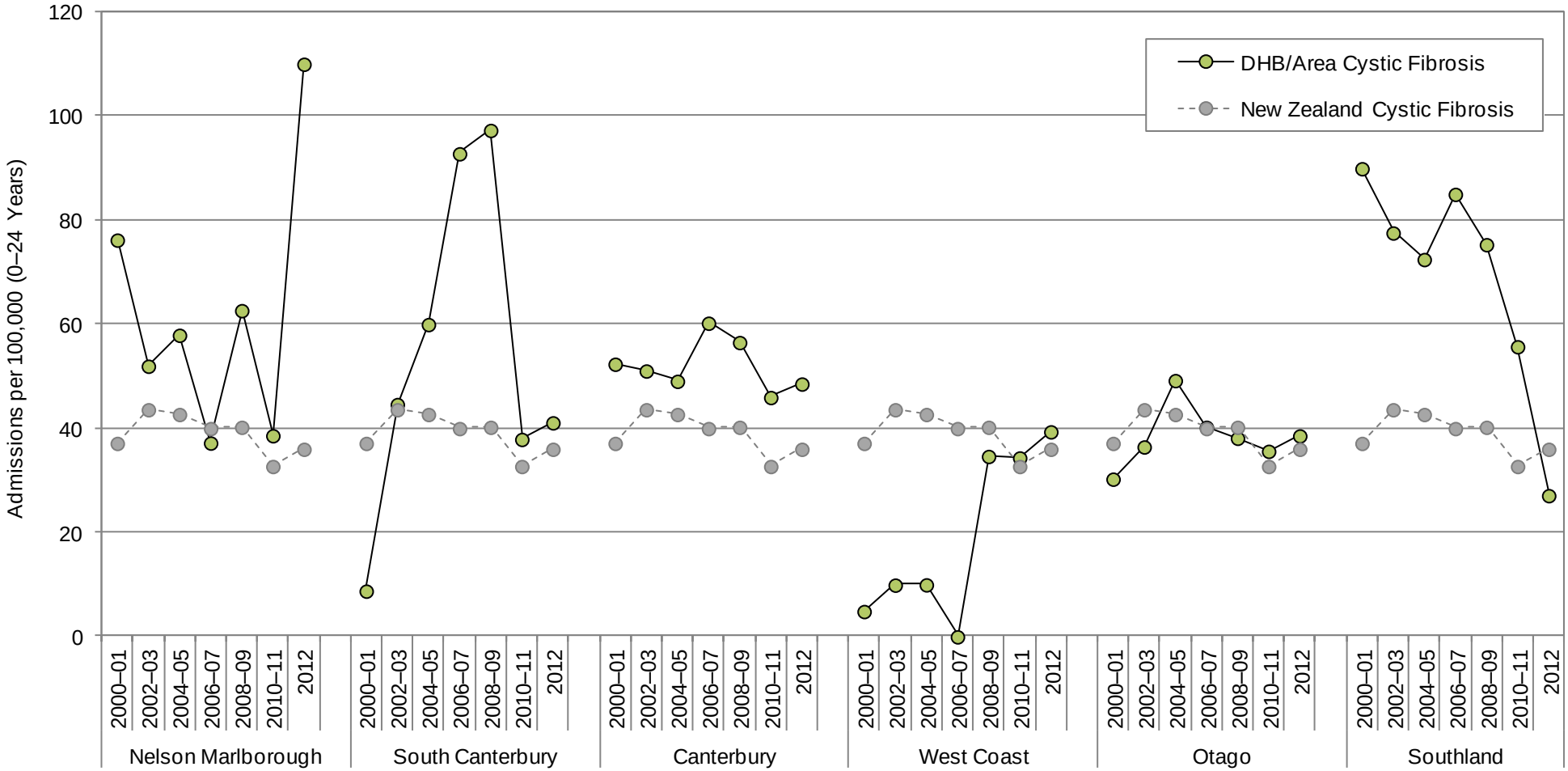
In the South Island DHBs during 2000–2012, large year to year variations (likely as a result of small numbers) made individual DHB's trends in admission rates difficult to interpret. However admissions in Canterbury were higher than the New Zealand rate throughout 2000–2012, while rates in Nelson Marlborough, South Canterbury and Southland were higher for the majority of this period (**Figure 3**).

Table 4. Hospital Admissions for Children and Young People Aged 0–24 Years with Cystic Fibrosis, South Island DHBs vs. New Zealand 2008–2012

DHB/Area	Total Number of Individuals 2008−2012		Total Number of Admissions 2008−2012	Average Number of Admissions per Individual per Year	Admission Rate per 100,000 Population	Rate Ratio	95% CI
	A*	B*					
Cystic Fibrosis							
Nelson Marlborough	21	21	133	1.27	62.57	1.72	1.44–2.05
South Canterbury	4	5	53	2.12	62.23	1.71	1.30–2.24
Canterbury	59	62	422	1.36	50.74	1.39	1.26–1.54
West Coast	3	3	18	1.20	35.51	0.98	0.61–1.55
Otago	12	16	125	1.56	37.26	1.02	0.86–1.22
Southland	8	8	106	2.65	57.82	1.59	1.31–1.93
New Zealand	351		2,780	1.58	36.41	1.00	

Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with cystic fibrosis listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007); Note: A*: Each individual only counted once in DHB in which they first reside (i.e. DHB total = NZ total); B*: Each individual counted once in each DHB in which they reside (i.e. the sum of DHB totals exceeds New Zealand total); Rate Ratios are compared to New Zealand rates and have not been adjusted for population demographics

Figure 3. Hospital Admissions for Children and Young People Aged 0–24 Years with Cystic Fibrosis, South Island DHBs vs. New Zealand 2000–2012



Source: Numerator: National Minimum Dataset, hospital admissions for children and young people with cystic fibrosis listed in any of the first 15 diagnoses; Denominator: Statistics NZ Estimated Resident Population (projected from 2007)

Local Policy Documents and Evidence-Based Reviews Relevant to Cystic Fibrosis

In New Zealand there are a small number of publications of relevance to cystic fibrosis. **Table 5** briefly summarises these, along with a number of guidelines and evidence-based reviews which consider these issues in the overseas context.

Table 5. Local Policy Documents and Evidence-Based Reviews Relevant to Cystic Fibrosis

New Zealand Guidelines and Useful Web Sites
Standards of Care for Cystic Fibrosis in New Zealand Group, Medical Advisory Committee of Cystic Fibrosis Association of New Zealand. 2011. **Standards of Care for Cystic Fibrosis in New Zealand** Cystic Fibrosis Association of New Zealand. http://www.cfnz.org.nz/wp-content/uploads/Standard-of-Care-NZ-2011.pdf This document sets out minimum standards of care for people with Cystic Fibrosis (PWCF) in New Zealand regardless of where they live. It recognises that New Zealand does not have the population to support the types of specialist CF centres found overseas. It recommends that care be provided at a clinic at a hospital near the home of the PWCF with additional at least annual reviews provided by a regional CF centre. It details the requirements for local and regional CF clinics in terms of facilities, services and staffing. It highlights the need for communication and cooperation between PWCF, their local clinic and the regional CF centre for this model of shared care to work effectively.
Cystic Fibrosis Association of New Zealand. http://www.cfnz.org.nz/ The website of the Cystic Fibrosis Association Of New Zealand has a number of useful publications aimed at parents, patients and teachers, which are available for download here: http://www.cfnz.org.nz/our-services/library/downloads/ . They are arranged under the following headings: Ages & Stages, Exercise, Infection Control, New Diagnosis, Nutrition, Travel, Treatments & CF related disorders, Care in New Zealand, CFANZ Annual Reports, and Other.
International Guidelines
Cystic Fibrosis Trust. **Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the U.K.** Second Edition 2011. https://www.cysticfibrosis.org.uk/media/82070/CD_Standards_of_Care_Dec_11.pdf These U.K. guidelines are intended for clinicians and other allied health professionals, service commissioners and providers, parents and carers of children with CF, older children and adults with CF, and their families. They are not an evidence-based guideline but rather a consensus document setting out best practice for cystic fibrosis care. They state that all patients with CF should be under the direct supervision of a Specialist CF Centre serving a minimum of 100 patients but that some child patients can receive some of their care from a Network CF Clinic which has clear lines of communication with a Specialist CF Centre at all levels. The guidelines set standards of care for: clinical care by specialist multidisciplinary teams; measures to prevent cross-infection from other patients; monitoring of lung function, microbial surveillance and treatment of airway infections; chest physiotherapy; nutritional support; identifying and managing other CF manifestations and complications; psychosocial support; transition to adult care; and transplantation, palliative care and end-of life care. The U.K. Cystic Fibrosis Trust has also produced guidelines on pharmacy standards in CF care, physiotherapy, laboratory standards for processing microbiological samples, antibiotic treatment, methicillin resistant *Staphylococcus aureus,* bone mineralisation, *Pseudomonas* infection, the *Burkholderia cepacia* complex, CF related diabetes, nutritional management of CF, and nursing management of CF. These can be found here: https://www.cysticfibrosis.org.uk/about-cf/publications/consensus-documents.aspx .
Cystic Fibrosis Australia. **Cystic Fibrosis Standards of Care Australia**. 2008 http://www.cysticfibrosis.org.au/media/wysiwyg/CF-Australia/PDF_files/CFA_Standards_of_Care_journal_31_Mar_08.pdf These guidelines are the first such guidelines to be published in Australia. The ten chapters cover facilities and staffing, services, newly diagnosed children, newly diagnosed adolescents and adults, outpatient care, inpatient care, home therapy, transition care, outreach services and care, transplantation and end of life care and the role of the CF organisations. Each chapter includes a literature review and provides guidelines for clinical care as well as specifying the requirements for facilities, staffing and services. Where evidence from the literature is referred to it is graded according to the National Health and Medical Research Council guidelines.

Guidelines from the American Cystic Fibrosis Foundation http://www.cff.org/treatments/CFCareGuidelines/

These guidelines are produced under the direction of The Cystic Fibrosis Foundation Guidelines Steering Committee the members of which represent various stakeholders including the different health disciplines providing care for people with CF as well as members of the CF community. The recommendations in the guidelines are informed by the systematic reviews performed by investigators at The Johns Hopkins University who perform explicit assessment of evidence and grade it according to the grading system developed by the U.S. Preventive Services Task Force.

Mogayzel PJ, Jr., Naureckas ET, Robinson KA, et al. 2013. **Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health**. American Journal of Respiratory & Critical Care Medicine, 187(7), 680-9

Tangpricha V, Kelly A, Stephenson A, et al. 2012. **An update on the screening, diagnosis, management, and treatment of vitamin D deficiency in individuals with cystic fibrosis: evidence-based recommendations from the Cystic Fibrosis Foundation**. Journal of Clinical Endocrinology & Metabolism, 97(4), 1082-93

Moran A, Brunzell C, Cohen RC, et al. 2010. **Clinical care guidelines for cystic fibrosis-related diabetes: a position statement of the American Diabetes Association and a clinical practice guideline of the Cystic Fibrosis Foundation, endorsed by the Pediatric Endocrine Society**. Diabetes Care, 33(12), 2697-708

Guidelines from the American Cystic Fibrosis Foundation http://www.cff.org/treatments/CFCareGuidelines/

Flume PA, Mogayzel J, Peter J, Robinson KA, et al. **Cystic Fibrosis Pulmonary Guidelines: Pulmonary Complications: Hemoptysis and Pneumothorax.** Am. J. Respir. Crit. Care Med. 2010:201002-0157OC

Flume PA, Mogayzel PJ, Jr., Robinson KA, et al. **Cystic Fibrosis Pulmonary Guidelines: Treatment of Pulmonary Exacerbations**. American Journal of Respiratory & Critical Care Medicine 2009; 180(9):802-8.

Flume PA, Robinson KA, O'Sullivan BP, et al. **Cystic Fibrosis Pulmonary Guidelines: Airway Clearance Therapies**. Respiratory Care 2009; 54(4):522-37.

Borowitz D, Robinson KA, et al. Cystic Fibrosis Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis. Journal of Pediatrics 2009; 155(6 Suppl):S73-93.

Borowitz D, Parad RB, et al. **Cystic Fibrosis Foundation Practice Guidelines for the Management of Infants with Cystic Fibrosis Transmembrane Conductance Regulator-Related Metabolic Syndrome During the First Two Years of Life and Beyond**. Journal of Pediatrics 2009; 155(6 Suppl):S106-16.

Farrell PM, et al. **Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report**. Journal of Pediatrics 2008; 153(2):S4-S14.

Stallings VA, Stark LJ, Robinson KA, et al. **Evidence-Based Practice Recommendations for Nutrition-Related Management of Children and Adults with Cystic Fibrosis and Pancreatic Insufficiency: Results of a Systematic Review**. Journal of the American Dietetic Association 2008; 108(5):832-9.

LeGrys VA, et al. **Diagnostic sweat testing: the Cystic Fibrosis Foundation guidelines**. Journal of Pediatrics 2007; 151(1):85-9.

Comeau AM, et al. **Guidelines for implementation of cystic fibrosis newborn screening programs: Cystic Fibrosis Foundation workshop report**. Pediatrics 2007; 119(2):e495-518.

Cantin AM, White TB, Cross CE, et al. **Antioxidants in Cystic Fibrosis. Conclusions from the CF Antioxidant Workshop, Bethesda, Maryland, November 11-12, 2003**. Free Radical Biology & Medicine 2007; 42(1):15-31.

Aris RM, Merkel PA, Bachrach LK, et al. **Guide to Bone Health and Disease in Cystic Fibrosis.** Journal of Clinical Endocrinology & Metabolism 2005; 90(3):1888-96.

Yankaskas JR, Marshall BC, Sufian B, et al. **Cystic Fibrosis Adult Care: Consensus Conference Report**. Chest 2004; 125(1 Suppl):1S-39S.

Saiman L, Siegel J, Cystic Fibrosis F, et al. **Infection Control Recommendations for Patients with Cystic Fibrosis: Microbiology, Important Pathogens, and Infection Control Practices to Prevent Patient-to-Patient Transmission.** Infection Control & Hospital Epidemiology 2003; 24(5 Suppl):S6-52.

Stevens DA, Moss RB, Kurup VP, et al. **Allergic Bronchopulmonary Aspergillosis in Cystic Fibrosis--State of the Art: Cystic Fibrosis Foundation Consensus Conference**. Clinical Infectious Diseases 2003; 37 Suppl 3:S225-64.

Borowitz D, Baker RD, Stallings V, et al. **Consensus Report on Nutrition for Pediatric Patients with Cystic Fibrosis**. Journal of Pediatric Gastroenterology & Nutrition 2002; 35(3):246-59.

Sokol RJ, Durie PR. **Recommendations for Management of Liver and Biliary Tract Disease in Cystic Fibrosis. Cystic Fibrosis Foundation Hepatobiliary Disease Consensus Group**. Journal of Pediatric Gastroenterology & Nutrition 1999; 28 Suppl 1:S1-13.

Yankaskas JR, Mallory GB, Jr. **Lung Transplantation in Cystic Fibrosis: Consensus Conference Statement**. Chest 1998; 113(1):217-26.

Cystic Fibrosis Foundation. **Use of Pancreatic Enzyme Supplements for Patients with Cystic Fibrosis in the Context of Fibrosing Colonopathy.** CF Foundation Consensus Statement, March 1995.

Kerem E, et al. **Standards of care for patients with cystic fibrosis: a European consensus**. Journal of Cystic Fibrosis 2005; 4(1):7-26. http://www.elsevier.com/framework_products/promis_misc/2005.pdf

This concise (20 page) publication aims to provide a consensus on standards of care for CF patients in Europe. It is the result of the 2004 European Consensus Conference organized by the European Cystic Fibrosis Society which took place in Artimino in Italy, and involved 36 experts in Cystic Fibrosis. It details the necessary infrastructure for a CF centre (serving a minimum of 50 patients), the minimum standards for routine evaluation and assessment of patients, the management of complications and the documentation of results in a standard database. The appendix covers a series of 35 “important questions” the answers to which include a grading of the evidence on which they are based. A table explains the grading system used.

The European Cystic Fibrosis Society has produced the following guidelines and reports on issues related to optimising patient care and CF team work, which can be downloaded here: https://www.ecfs.eu/ecfs_guidelines .

Colombo C, Littlewood J. 2011. **The implementation of standards of care in Europe: state of the art**. Journal of Cystic Fibrosis 10 Suppl 2 S7-15.

Sermet-Gaudelus I, Bianchi ML, Garabedian M, et al. 2011**. European cystic fibrosis bone mineralisation guidelines.** Journal of Cystic Fibrosis 10 Suppl 2 S16-23.

Colombo C, Ellemunter H, Houwen R, et al. 2011**. Guidelines for the diagnosis and management of distal intestinal obstruction syndrome in cystic fibrosis patients.** Journal of Cystic Fibrosis 10 Suppl 2 S24-8.

Debray D, Kelly D, Houwen R, et al. 2011**. Best practice guidance for the diagnosis and management of cystic fibrosis-associated liver disease.** Journal of Cystic Fibrosis 10 Suppl 2 S29-36.

Sands D, Repetto T, Dupont LJ, et al. 2011. **End of life care for patients with cystic fibrosis.** Journal of Cystic Fibrosis 10 Suppl 2 S37-44.

Nobili RM, Duff AJ, Ullrich G, et al. 2011. **Guiding principles on how to manage relevant psychological aspects within a CF team: interdisciplinary approaches.** Journal of Cystic Fibrosis 10 Suppl 2 S45-52.

Castellani C, Southern KW, Brownlee K, et al. 2009. **European best practice guidelines for cystic fibrosis neonatal screening.** Journal of Cystic Fibrosis 8(3) 153-73.

Also on the same site are guidelines relating to the coordination of clinical research, travelling with CF, neonatal screening for CF, management of pregnancy in women with CF and issues related to small and medium sized enterprises and the development of new therapies for CF.

The European Cystic Fibrosis Society (which publishes the Journal of Cystic Fibrosis) has also published a number of consensus documents which have been developed at meetings of leading workers (typically with about 30 participants) in the particular topics. These publications do not discuss the details of research studies but all the information and recommendations contained in them are very well referenced. These publications can be downloaded here: https://www.ecfs.eu/publications/consensus_reports .

Heijerman H, et al. **Inhaled medication and inhalation devices for lung disease in patients with cystic fibrosis: A European consensus**. Journal of Cystic Fibrosis 2009; 8(5):295-315.

Mayell SJ, et al. **A European consensus for the evaluation and management of infants with an equivocal diagnosis following newborn screening for cystic fibrosis**. Journal of Cystic Fibrosis 2009; 8(1):71-8.

Castellani C, et al. **Consensus on the use and interpretation of cystic fibrosis mutation analysis in clinical practice**. Journal of Cystic Fibrosis 2008; 7(3):179-96.

Edenborough FP, et al. **Guidelines for the management of pregnancy in women with cystic fibrosis**. Journal of Cystic Fibrosis 2008; 7 Suppl 1:S2-32.

Doring G, et al. **Clinical trials in cystic fibrosis**. Journal of Cystic Fibrosis 2007; 6(2):85-99.

Malfroot A, et al. **Immunisation in the current management of cystic fibrosis patients**. Journal of Cystic Fibrosis 2005; 4(2):77-87.

Doring G, et al. **Early intervention and prevention of lung disease in cystic fibrosis**: a European consensus. Journal of Cystic Fibrosis 2004; 3(2):67-91.

Sinaasappel M, et al. **Nutrition in patients with cystic fibrosis: a European Consensus**. Journal of Cystic Fibrosis 2002; 1(2):51-75.

Doring G, et al. **Antibiotic therapy against Pseudomonas aeruginosa in cystic fibrosis: a European consensus**. European Respiratory Journal 2000; 16(4):749-67.

Cochrane Reviews with Good Evidence for Clinical Decision-Making
Warnock L, Gates A, van der Schans CP. 2013. **Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis**. Cochrane Database of Systematic Reviews(9). Chest physiotherapy to clear mucus from the airways is an established part of the treatment for CF. This review considered the effectiveness and acceptability of chest physiotherapy compared to no treatment or spontaneous cough alone. The authors identified eight cross-over studies (96 participants) which met their inclusion criteria. They stated that the enormous heterogeneity in the treatment interventions and the way outcomes were measured precluded any meta-analysis. They concluded that, in the short term, airway clearance techniques increase mucus transport but there was no evidence which could be used to draw conclusions about the long term effects of these techniques.
Cheng K, Ashby D, Smyth RL. 2013. **Oral steroids for long-term use in cystic fibrosis**. Cochrane Database of Systematic Reviews(8). Based on a review of three RCTs (354 participants) of long term (>30days) oral steroid therapy, the authors of this review concluded that oral corticosteroids at prednisolone-equivalent dose of 1 to 2 mg/kg alternate days seem to slow progression of lung disease in CF but that benefits should be weighed against occurrence of adverse events. They stated that no further trials of this therapy are expected so this review will no longer be regularly updated.
Johansen KH, Gotzsche PC. 2013. **Vaccines for preventing infection with Pseudomonas aeruginosa in cystic fibrosis.** Cochrane Database of Systematic Reviews(6). Almost all patients with CF eventually become colonised with *Pseudomonas aeruginosa*. This bacterium produces a biofilm which surrounds the bacterial colonies within the lungs and protects them from host defence mechanisms and antibiotics. The constant frustrated efforts of the immune system to clear the large bacterial colonies results in leakage of toxic enzymes from neutrophils which cause further lung damage. Because it is almost impossible to eradicate *P. aeruginosa* infection once it becomes established an effective vaccine would be very beneficial. This review included three RCTs of vaccines aimed at reducing infection with *P. aeruginosa*, with 483, 476 and 37 patients respectively. No data was published from one of the large trials and the company involved has stated that the trial failed to confirm results from an earlier study and that it had suspended further clinical development of the vaccine. The other large trial reported a relative risk (RR) of chronic infection of 0.91 (95% confidence interval 0.55 to 1.49). The small trial also reported a RR close to one. In the large trial one patient died in the observation period (from acute lymphatic leukaemia, considered to be unrelated to the vaccine), and there were four severe adverse events registered in the vaccine group compared to one in the control group. The authors concluded that the use of vaccines against *P. aeruginosa* cannot be recommended.
Thaker V, Haagensen AL, Carter B, et al. 2013. **Recombinant growth hormone therapy for cystic fibrosis in children and young adults**. Cochrane Database of Systematic Reviews(6). Children and young people with CF often have malnutrition and delayed growth which is not sufficiently improved with nutritional supplementation. This review aimed to evaluate the effectiveness and safety of recombinant human growth hormone therapy in improving lung function, quality of life and clinical status of children and young adults with CF. It included four RCTs (161 participants in total). The authors concluded that recombinant growth hormone therapy, compared to no treatment, is modestly effective in improving height, weight, lean tissue mass and functional vital capacity (one measure of lung function), but not quality of life or overall clinical status.
Lands LC, Stanojevic S. 2013. **Oral non-steroidal anti-inflammatory drug therapy for lung disease in cystic fibrosis.** Cochrane Database of Systematic Reviews(6). This review included five RCTs (334 participants aged five to 39 years; maximum follow up of four years). Three of these, all comparing ibuprofen to placebo, were deemed to be of good or adequate methodological quality. Based on combined data from the two largest ibuprofen trials, the authors concluded that high-dose ibuprofen can slow the progression of lung disease in people with CF, particularly in children.
Moran F, Bradley JM, Piper AJ. 2013. **Non-invasive ventilation for cystic fibrosis**. Cochrane Database of Systematic Reviews(4). This review included seven RCTs with 106 participants in total. The authors concluded that non-invasive ventilation via face mask may be useful as an adjunct to other airway clearance techniques, especially in people with CF who have difficulty expectorating sputum and that non-invasive ventilation, used in addition to oxygen, may improve gas exchange during sleep to a greater degree than oxygen therapy alone in those with moderate to severe disease. They noted that these beneficial effects have largely been demonstrated in single treatment sessions with small numbers of participants. They stated that the impact of this therapy on pulmonary exacerbations and disease progression remains uncertain and that further research involving adequately powered long term RCTs is needed.

Daniels T, Mills N, Whitaker P. 2013. **Nebuliser systems for drug delivery in cystic fibrosis.** Cochrane Database of Systematic Reviews(4).

There are many different types of nebuliser systems that are used to deliver medications to people with CF. This review aimed to evaluate these systems in regard to their effectiveness, safety, burden of treatment and patient adherence to nebulised therapy. This review included 20 studied which were RCTs or quasi-RCTs (1936 participants in total). The authors stated that there is variability in performance between the different nebuliser systems and that newer technologies such as adaptive aerosol delivery and vibrating mesh technology are superior to conventional systems in terms of treatment time, deposition as a percentage of priming dose, patient preference and adherence. They also stated that long-term RCTs of these technologies are needed to determine patient-relevant outcomes (such as quality of life and burden of care), safe and effective dosing levels of medications, clinical outcomes (such as hospitalisations and need for antibiotics) and an economic evaluation of their use.

Southern KW, Barker PM, SolisMoya A, et al. 2012. **Macrolide antibiotics for cystic fibrosis.** Cochrane Database of Systematic Reviews(11).

This review included ten studies (959 participants). Five studies with a low risk of bias examined six months' treatment with azithromycin vs. placebo and demonstrated consistent improvement in FEV_1 over six months (mean difference at six months 3.97% (95% confidence interval 1.74% to 6.19%; n = 549 from four studies). Patients treated with six months' azithromycin were about twice as likely to be free of pulmonary exacerbation at six months: odds ratio 1.96 (95% confidence interval 1.15 to 3.33). They also had had a greater weight gain and a reduced need for oral antibiotics but those who followed a once-weekly high dose regimen had more frequent gastrointestinal adverse events. Azithromycin treatment was associated with reduced identification of *Staphylococcus aureus* on respiratory culture but also a significant increase in macrolide resistance. The authors concluded that: there was evidence of improved respiratory function after six months azithromycin therapy; beyond six months the benefits were less clear although the reduction in pulmonary exacerbations persisted; azithromycin therapy appeared safe although the emergence of macrolide resistance was a concern. They stated that a multi-centre long term trial of azithromycin treatment is needed.

Smyth AR, Walters S. 2012. **Prophylactic anti-staphylococcal antibiotics for cystic fibrosis.** Cochrane Database of Systematic Reviews(12).

Some centres give children with CF prophylactic antibiotics from the time of diagnosis, usually an antibiotic which is active against *Staphylococcus aureus*, such as flucloxacillin. There are concerns that such long-term prophylaxis might lead to the emergence of antibiotic resistance and increased likelihood of colonisation with *Pseudomonas aeruginosa*. There are also short-term adverse effects such as diarrhoea or oral candidiasis (thrush). This review included four RCTs with a total of 401 participants aged zero to seven years at study enrolment. The authors noted that overall the studies were of poor quality. They concluded that anti-staphylococcal antibiotic prophylaxis, when commenced in infancy and continued up to six years of age, leads to fewer children having isolated of *S. aureus* but that the clinical importance of this finding is uncertain since there was no difference between the prophylaxis and the no-prophylaxis groups in infant or conventional lung function measures, nutrition, hospital admissions, additional courses of antibiotics or adverse effects. There were also no differences between groups in the number of isolates of *P. aeruginosa*, though there was a trend towards a lower cumulative isolation rate of *P. aeruginosa* in the prophylaxis group at two and three years and towards a higher rate from four to six years (although this last finding was based on data from only one study since none of the other studies had more than three years of follow up). Since all the reviewed studies lasted for six years or less, no conclusions could be drawn about the long-term effects of prophylaxis.

Smyth RL, Walters S. 2012. **Oral calorie supplements for cystic fibrosis.** Cochrane Database of Systematic Reviews(11).

From the results of three trials (131 participants in total) lasting one month or more, the authors of this review concluded that "oral calorie supplements do not confer any additional benefit in the nutritional management of moderately malnourished children with CF over and above the use of dietary advice and monitoring alone. While nutritional supplements may be used, they should not be regarded as essential."

Ng MS, Francini AJ. 2012. **Drug therapies for reducing gastric acidity in people with cystic fibrosis.** Cochrane Database of Systematic Reviews(4).

Gastric acid-reducing agents have been used as an adjunct to pancreatic enzyme therapy to improve fat absorption and gastro-intestinal symptoms in people with CF. This review included 16 RCTs or quasi-RCTs with a total of 256 participants. One trial found that these therapies improved gastro-intestinal symptoms such as abdominal pain, seven trials reported significant improvement in measures of fat malabsorption and two trials reported no significant improvement in nutritional status. Only one trial reported on measures of respiratory function and one trial reported an adverse effect (of misoprostol). The Cochrane reviewers did not identify any trials assessing the effectiveness of gastric acid-reducing agents for improving quality of life or survival or reducing complications of increased gastric acidity (e.g. heartburn or gastric ulcers). They concluded that there is limited evidence that these agents are associated with improvements in gastrointestinal symptoms and fat absorption but insufficient evidence to determine whether they are associated with improvement in nutritional status, lung function, quality of life, or survival.

Burrows EF, Southern KW, Noone PG. 2012. **Sodium channel blockers for cystic fibrosis**. Cochrane Database of Systematic Reviews(3).

The defective gene causing CF normally codes for a protein called the cystic fibrosis transmembrane conductance regulator (CFTR) which is responsible for the movement of salt across cell membranes. CFTR is a chloride channel but it also plays apart in reducing the activity of the epithelial sodium channel (ENaC). In CF the absence of CFTR leads to increased activity of ENaC leading to excessive absorption of sodium and water which leads to dehydration of the airway surface liquid resulting in sticky mucus that is difficult to clear and a lung environment that is very susceptible to infection. This review aimed to determine whether topical administration of drugs that block sodium transport improve lung function in people with CF. The authors identified five RCTs (with a total of 226 participants) of amiloride (a short-acting sodium channel blocker) vs. placebo. A meta-analysis of results from three six-month studies indicated a mean difference between the intervention and placebo groups in relative change in forced vital capacity over six months which was significant and favoured the placebo group (weighted mean difference −1.51%; 95% confidence interval −2.77 to −0.25), although there was significant heterogeneity between the studies. One two-week study showed that hypertonic saline with amiloride pre-treatment did not result in a significant improvement in respiratory function or mucus clearance, compared to hypertonic saline with placebo pre-treatment. There were no significant differences identified in other clinically relevant outcomes. The authors concluded that there was no evidence that topical administration of short–acting sodium channel blockers improves respiratory function in people with CF and some limited evidence that they may cause deterioration in lung function, especially when delivered before hypertonic saline.

Bradley JM, Moran F. 2012. **Physical training for cystic fibrosis.** Cochrane Database of Systematic Reviews(7).

This review aimed to determine whether a prescribed regimen of physical training produces improvement or prevents deterioration in physiological and clinical outcomes in CF compared to no training. The authors identified seven RCTs or quasi-RCTs meeting their inclusion criteria (with a total of 231 participants). They stated that there was some limited evidence from both short and long term studies that aerobic or anaerobic physical training has a beneficial effect on primary outcomes (exercise capacity, strength and lung function) although improvements are not consistent between studies. They reported that the studies in the review were mostly of small size and limited duration with incomplete reporting which limited the conclusions that could be drawn from them. They noted that most people with CF are already offered physical training as part of their care package and there is a lack of evidence to discourage this. They stated that further research is needed to assess the benefits of exercise programmes comprehensively and to determine the relative benefits of aerobic exercise, anaerobic exercise or a combination of both for people with CF.

Prayle AP, Hurley MN, Smyth AR. 2012. **Percutaneous lines for delivering intravenous antibiotics in people with cystic fibrosis.** Cochrane Database of Systematic Reviews(7).

This review aimed to compare long intravenous lines (percutaneous lines) with short intravenous lines with regard to lifespan of the line, ease of insertion, complication rates of the line and patient satisfaction in people with CF receiving intravenous antibiotics. Two randomised studies with a total of 67 participants were included in the review and both were considered to have potential for bias in several domains. One study with 20 participants found that long lines lasted longer than short lines and were preferred by participants. The other study with 47 participants found no difference in line lifespan or participant preference when comparing two different long intravenous lines (the Hydrocath and Vygon EC). Neither study was adequately powered to detect differences in rates of serious line complications. The authors concluded that there was some evidence that long line are superior to short lines in terms of line lifespan and patient satisfaction but no evidence that any one type of long line is better than any other.

Smyth AR, Bhatt J. 2012. **Once-daily versus multiple-daily dosing with intravenous aminoglycosides for cystic fibrosis.** Cochrane Database of Systematic Reviews(2).

People with CF who have lungs colonised with the bacterium *Pseudomonas aeruginosa* often need multiple courses of intravenous aminoglycoside antibiotics for the management of pulmonary exacerbations. This review aimed to compare the effectiveness and safety of once-daily versus multiple-daily dosing of intravenous aminoglycoside antibiotics. It included four RCTs (328 participants) comparing once-daily to thrice-daily dosing. The results of these studies indicated no significant difference between treatment groups in: FEV_1, mean difference 0.33 (95% confidence interval −2.81 to 3.48); FVC, mean difference 0.29 (95% CI −6.58 to 7.16); % weight for height, mean difference −0.82 (95% CI −3.77 to 2.13); body mass index, mean difference 0.00 (95% CI −0.42 to 0.42); or in the incidence of ototoxicity, relative risk 0.56 (95% CI 0.04 to 7.96). The percentage change in creatinine significantly favoured once-daily treatment in children, mean difference −8.20 (95% CI −15.32 to −1.08), but showed no difference in adults, mean difference 3.25 (95% CI −1.82 to 8.33). The authors concluded that once- and three-times daily aminoglycoside antibiotics appeared to be equally effective for the treatment of pulmonary exacerbations of CF and that for children, but not adults, once-daily dosing was associated with less nephrotoxicity.

Shamseer L, Adams D, Brown N, et al. 2012. **Antioxidant micronutrients for lung disease in cystic fibrosis.** Cochrane Database of Systematic Reviews(7).

Persistent airway infection in people with CF leads to progressive lung damage which is due, in part, to oxidative stress stemming from both the infectious agent and the body's inflammatory immune response. It is thought that supplementation with the exogenous anti-oxidant micronutrients, vitamin E, vitamin C, β-carotene and selenium, also known as free-radical scavengers, may be helpful in maintaining the oxidant-antioxidant balance in people with CF. This review aimed to synthesise the existing knowledge about the effect of vitamin C, vitamin E, β-carotene and selenium in CF lung disease. The authors identified four RCTs and one quasi-RCT which compared vitamin C, vitamin E, β-carotene and selenium (individually or in combination) to placebo or standard care but only three trials (87 participants) had data suitable for analysis. Data from two trials indicated anti-oxidant supplementation did not produce improvement in lung function. One trial reported significant improvement in quality of life favouring control, mean difference −0.06 points on the quality of well-being scale (95% confidence interval −0.12 to −0.01). Based on two trials, selenium-dependent glutathione peroxidase enzyme levels significantly improved in favour of both combined supplementation, mean difference 1.60 units per gram of haemoglobin (95% CI 0.30 to 2.90) and selenium supplementation, mean difference 10.20 units per gram of haemoglobin (95% CI 2.22 to 18.18). Levels of all plasma antioxidants, except vitamin C, significantly improved with supplementation. The authors concluded that the evidence regarding the clinical effectiveness of anti-oxidant supplementation in CF appeared to be conflicting. Limited data from few trials indicates that antioxidants appear to decrease both quality of life and oxidative stress. They stated that further RCTs examining clinically important outcomes and elucidation of a clear biological pathway of oxidative stress in CF are necessary before any firm conclusions can be drawn regarding effects of antioxidant supplementation.

Halfhide C, Evans HJ, Couriel J. 2011. **Inhaled bronchodilators for cystic fibrosis.** Cochrane Database of Systematic Reviews(5).

Inhaled bronchodilators are commonly used by people with CF to treat wheeze and breathlessness. This review aimed to evaluate the effectiveness of these agents in people with CF. There were eighteen RCTs or quasi-RCTs, with 369 participants in total, meeting the review inclusion criteria. All but two used a cross-over design. Meta-analysis of study results was not possible. The trials were heterogeneous with varied conclusions. In three out of five trials, in the short term, compared to placebo, long-acting beta-2 agonists increased FEV_1 and FEF25%– 75% in participants known to have bronchodilator responsiveness, but they produced inconsistent results in long-term trials. Four trials assessed ipratropium, a short-acting anticholinergic, vs. placebo. Results from these trials indicated no consistent effects on lung function tests in either the short or the long term. There were no trials of fenoterol, formoterol or tiotropium. The authors concluded that it was not possible to fully determine the effectiveness of inhaled bronchodilators in CF since a meta-analysis could not be done but that short and long-acting beta-2 agonists can be beneficial both in the short and the long term in individuals with demonstrable bronchodilator responsiveness or bronchial hyper-responsiveness. They found no evidence for the use of fenoterol, formoterol or tiotropium and so they stated that the use of these agents in people with CF cannot be supported.

Ryan G, Singh M, Dwan K. 2011. **Inhaled antibiotics for long-term therapy in cystic fibrosis.** Cochrane Database of Systematic Reviews(3).

This review aimed to examine the evidence that inhaled antibiotics reduce the frequency of infectious exacerbations and improve lung function, quality of life and survival for people with CF. It also aimed to examine the adverse effects of such treatment. The review included nineteen RCTs or quasi-RCTs, with a total of 1724 participants, which compared an antibiotic with placebo or usual treatment over a period of between one and 32 months. Due to variability in study designs and the reporting of results, meta-analysis was not possible. Eight trials evaluated tobramycin and the results of these indicated that lung function (as measured by FEV_1) was higher and exacerbations of lung infection (according to various different measures) were fewer in the group treated with antibiotics. There was a greater increase in resistance to antibiotics in the antibiotic group than the placebo group. No trial subjects were found to have auditory or renal impairment but tinnitus, voice alteration, hemoptysis and cough were more frequent with tobramycin than placebo. One trial, with 115 participants, compared tobramycin with colistin and found that after one month the mean difference in FEV_1 was 6.33 (95% confidence interval −0.04 to 12.70) in favour of tobramycin. The authors concluded that inhaled antibiotic treatment probably reduces the rate of exacerbations and improves lung function but it was not possible to calculate a pooled estimate of the level of benefit. They stated that tobramycin is the agent with the best evidence of effectiveness and that more research is needed to determine whether the benefit of inhaled antibiotics is maintained in the longer term and the significance of the emergence of antibiotic-resistant organisms.

Langton Hewer SC, Smyth AR. 2010. **Antibiotic strategies for eradicating Pseudomonas aeruginosa in people with cystic fibrosis.** Cochrane Database of Systematic Reviews(11).

Most people with CF eventually acquire background respiratory tract infection with *Pseudomonas aeruginosa*. Once chronic infection with this organism becomes established it is almost impossible to eradicate and it is associated with increased morbidity and mortality. This review aimed to determine whether antibiotic treatment of early *P. aeruginosa* infection in children and adults with CF eradicates the organism, improves clinical and microbiological outcomes and is superior to or more cost-effective than other strategies. Four RCTs (95 participants in total) met the review's inclusion criteria and the authors identified another two on-going trials. Evidence from two trials (of low methodological quality) showed that treatment of early *P. aeruginosa* infection with inhaled tobramycin results in microbiological eradication of the organism from respiratory secretions more often than placebo, OR 0.15 (95% CI 0.03 to 0.65) and that this effect may persist for up to 12 months. The authors concluded that nebulised antibiotics, either alone or in combination with oral antibiotics, were better than no treatment for early infection with *P. aeruginosa* and that eradication may be sustained in the short term. They stated that overall, their review found insufficient evidence to indicate which antibiotic strategy should be used for the eradication of early *P. aeruginosa* infection in people with CF.

Jones AP, Wallis C. 2010. **Dornase alfa for cystic fibrosis.** Cochrane Database of Systematic Reviews(3).

Dornase alfa (Pulmozyme®) is a highly purified solution of recombinant human deoxyribonuclease (rhDNase). Inhaled via a nebuliser it reduces viscosity in the lungs, promoting improved clearance of secretions. It is an expensive therapy, costing around £7000 (NZ$13500) per patient per year in the U.K. (in 2009). This review aimed to determine whether the use of dornase alfa in CF is associated with improved and morbidity and mortality compared to placebo or other mucolytics and to identify any adverse events associated with its use. The authors found 15 trials (2469 participants) meeting their inclusion criteria. Twelve studies compared dornase alfa to placebo or no dornase alfa treatment; one compared daily dornase alfa with hypertonic saline and alternate day dornase alfa; and two compared daily dornase alfa to hypertonic saline. Study lengths ranged from six days to three years. There were no significant differences in mortality between treatment groups and the authors noted that this was not surprising given that most trials were short term. Lung function (as measured by FEV_1 and FVC) improved in the treatment groups and there were significant differences between the intervention and control groups in percentage changes from baseline in lung function measures at one month (data from four trials), three months, six months and two years; there was a non-significant difference at three years (data from one trial only for each of these periods). There was considerable heterogeneity between trials. The only adverse effects reported more frequently in the intervention group (in one trial only) were voice alteration and rash. There was insufficient data for the reviewers to analyse differences in antibiotic use, days of inpatient treatment or quality of life. The authors concluded that there is evidence that dornase alfa over a one-month period is associated with improved lung function in people with CF and they noted that one trial lasting six months also found the same effect. They stated that one trial indicated that two years of therapy significantly improved FEV_1 in children and non-significantly reduced the risk of infective exacerbations, and that voice alteration and rash appeared to be the only adverse effects reported with increased frequency in intervention groups in the RCTs.

Wark P, McDonald VM. 2010**. Nebulised hypertonic saline for cystic fibrosis.** Cochrane Database of Systematic Reviews(6).

Nebulised hypertonic saline (HS) is a salt water solution with a salt concentration of 3% or more inhaled as a fine mist through a mask or mouthpiece. This review included controlled trials comparing HS to placebo or other mucolytic therapy, for any duration or dose regimen in people with CF (of any age or disease severity). There were 12 such trials (442 participants aged 6 to 46 years) identified by the authors. Based on the results of these trials the authors concluded that treatment with 7% HS for 48 weeks was associated with a small improvement in FEV_1 at four weeks but that this was not sustained at 48 weeks (based on the primary outcome measure of the only long-term trial). They stated that although HS (unlike RhDNAse) does not improve long term lung function it does improve quality of life and reduce pulmonary exacerbations and it appears to be inexpensive and safe and not to increase risk of infection.

Southern KW, Merelle MM, Dankert-Roelse JE, et al. 2009. **Newborn screening for cystic fibrosis.** Cochrane Database of Systematic Reviews(4).

This review considered whether early detection of Cystic Fibrosis via newborn screening results in improved clinical outcomes (by preventing or reducing irreversible organ damage), and greater quality of life and survival. The authors found two suitable randomised controlled trials and analysed the data from one of them (the 1998 Wisconsin trial). In this trial 650,341 neonates were screened for CF and the results of screening were withheld from half the families and investigators until the children were 4 years old to provide the control group (unless the parents requested the results). There were benefits for the screened group in improved growth and nutrition but the effect of screening on long-term pulmonary function was confounded by other factors. Screening was found to be cheaper than traditional diagnosis.

Cochrane reviews which found that there were some RCTs related to the topic of the review but these did not provide clear guidance for the use of the therapy in question
The following topics relating to the treatment of cystic fibrosis have been the subject of Cochrane reviews which found that, although there were some adequate quality RCTs of the intervention in question, these did not provide conclusive guidance regarding the use of the intervention (topics are followed by the year of the review): oxygen therapy (2013), nebulized and oral thiol derivatives (2013), comparison of long-acting insulins, short-acting insulins and oral hypoglycemic agents for CF-related diabetes (2013), comparison of antibiotic therapy based on conventional antimicrobial susceptibility testing to antibiotic therapy based on combination antimicrobial susceptibility testing in the treatment of acute pulmonary exacerbations in people with CF and chronic infection with *P. aeruginosa* (2013), timing of dornase alfa inhalation (2013), palivizumab for prophylaxis against respiratory syncytial virus infection 2013), antibiotic adjuvant therapy for pulmonary infection (2013), vitamin K supplementation (2013), topical nasal steroids for treating nasal polyposis (2013), inhaled antibiotics for pulmonary exacerbations (2013), active cycle of breathing technique (2012), ursodeoxycholic acid for CF-related liver disease (2013), standard versus biofilm antimicrobial susceptibility testing to guide antibiotic therapy (2012), inhaled corticosteroids (2012), conventional chest physiotherapy compared to other airway clearance techniques (2013), topical cystic fibrosis transmembrane conductance regulator gene replacement for CF-related lung disease (2012), single vs. combination intravenous antibiotic therapy (2012), home vs. hospital intravenous antibiotic therapy (2012), elective vs. symptomatic intravenous antibiotic therapy (2012), vitamin D supplementation (2012), omega-3 fatty acids (2011), inspiratory muscle training (2011), self-management education (2011), vaccines for preventing influenza (2011), oscillating devices for airway clearance (2011), oral anti-pseudomonal antibiotics (2010), psychological interventions for people with CF and their families (2009), positive expiratory pressure physiotherapy for airway clearance (2009), oral protein calorie supplementation for children with chronic disease (2009).
Cochrane reviews which found that there were no RCTs of adequate quality related to the topic of the review
The following topics relating to the treatment of cystic fibrosis have been the subject of Cochrane reviews which found that there was no high quality evidence which could be used to determine the efficacy or otherwise of the intervention (topics are followed by the year of the review): Anti-IgE therapy for allergic bronchopulmonary aspergillosis in people with CF (2013), duration of intravenous antibiotic therapy (2013), interventions for the eradication of methicillin-resistant *Staphylococcus aureus* (MRSA) (2013), enteral tube feeding (2012), chemical pleurodesis versus surgical intervention for persistent and recurrent pneumothoraces (2013), antibiotic treatment for nontuberculous mycobacteria lung infection (2012), antibiotic treatment for *Burkholderia cepacia complex* in people with CF experiencing a pulmonary exacerbation (2012), pneumococcal vaccination in adults or children with CF(2012), vitamin A supplementation (2012), disease modifying anti-rheumatic drugs in people with CF-related arthritis (2012), totally implantable vascular access devices (2012), antifungal therapies for allergic bronchopulmonary aspergillosis (2012), antibiotic treatment for *Stenotrophomonas maltophilia* (2012), timing of hypertonic saline inhalation (2012), anti-inflammatory drugs and analgesics for managing symptoms in people with CF-related arthritis(2012), neuraminidase inhibitors for the treatment of influenza infection in people with CF (2011), singing for children and adults with CF (2010).
Other Reviews
Towns SJ, Bell SC. 2011. **Transition of adolescents with cystic fibrosis from paediatric to adult care**. The clinical respiratory journal, 5(2), 64-75 Improvements in the treatment of CF over recent decades have led to increasing numbers of young people with CF requiring care from the adult health system. This review article by two Australian authors provides a good overview of the issues involved in the transition of adolescents with CF from paediatric to adult care. Important factors in successful transition are: early planning and preparation, facilitating self-management skills, having a coordinated approach including young people with CF, their families and the paediatric and adult teams, detailed communication with provision of a written referral report and documentation of prior CF complications, feedback between the paediatric and adult healthcare teams, and on-going audit of the transition process.

Note: The publications listed were identified using the search methodology outlined in Appendix 1 (Search Methods for Policy Documents and Evidence-Based Reviews)

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