Cystic Fibrosis

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You will need a UH Bristol account to access our local subscription resources. You can either update the settings of your existing account by logging in and selecting ‘change organisation’, or you can set up a new UH Bristol account by clicking [here](#) (you will need to register using a Trust PC and a UH Bristol email address).

My Athens account has expired. What should I do?
You can register for a new account [here](#).

I have forgotten my Athens Username / Password. How can I reset it?
**Password:** If you are on a Trust PC, follow the link to [https://register.athensams.net/nhs/forgotten_password.php](https://register.athensams.net/nhs/forgotten_password.php).

**Username and password:** You should email [athens.sdhct@nhs.net](mailto:athens.sdhct@nhs.net) with your full name, full work address, work telephone number and the email address you used to register for the account. In the email subject line put 'Forgotten username and password'. It may take up to five working days to receive your username and a reset password.
New from NICE

17 June 2016

Cost of cystic fibrosis treatment too high for benefit offered, says NICE

NICE - the National Institute for Health and Care Excellence – has said it will not be able to recommend Orkambi (lumacaftor-ivacaftor, Vertex Pharmaceuticals) for treating cystic fibrosis.

In March, NICE publicly consulted on draft guidance which concluded that compared to the current standard of care, the benefit Orkambi offered did not justify its considerable cost. Although Orkambi was shown to reduce instances where people with cystic fibrosis are admitted to hospital, the benefits to lung function – one of the tests used to see how people are improving overall – appeared modest in the short term whilst the long-term benefits were uncertain.

June 2016

Moderate to severe acute post-operative pain: fentanyl transdermal system

NICE advice [ESNM77] Published date:

Summary

The fentanyl transdermal system, Ionsys, is a patient controlled analgesia (PCA) system that delivers fentanyl in a non invasive way across the skin using iontophoresis. It is licensed for the management of acute moderate to severe post operative pain in adults.

The fentanyl transdermal system has comparable efficacy to IV morphine PCA. Its adverse event profile is as expected for an opioid used in post operative pain, and is similar to that of IV morphine PCA. In randomised controlled trials, the fentanyl transdermal system had better user satisfaction than IV morphine PCA, mainly because of improved mobilisation, and more favourable ease of care scores reported by nurses and physiotherapists. However, the clinical significance of these differences is unclear.

Regulatory status: Ionsys was launched in February 2016 for the management of acute moderate to severe post operative pain in adults. It is for hospital use only.
New from the Cochrane Library Systematic Reviews on Cystic Fibrosis

**Topical cystic fibrosis transmembrane conductance regulator gene replacement for cystic fibrosis-related lung disease**

Authors: Tim WR Lee, Kevin W Southern, Luke A Perry, Jahan C Penny-Dimri, Aisha A Aslam

First published: 17 June 2016

Assessed as up-to-date: 16 June 2016

Editorial Group: Cochrane Cystic Fibrosis and Genetic Disorders Group

Abstract

Background

Cystic fibrosis is caused by a defective gene encoding a protein called the cystic fibrosis transmembrane conductance regulator (CFTR), and is characterised by chronic lung infection resulting in inflammation and progressive lung damage that results in a reduced life expectancy.

Objectives

To determine whether topical CFTR gene replacement therapy to the lungs in people with cystic fibrosis is associated with improvements in clinical outcomes, and to assess any adverse effects.
# Training Calendar 2016

*All sessions are 1 hour*

## Literature Searching

An in-depth guide to formulating an effective search strategy and getting the most out of searching key healthcare databases.

## Critical Appraisal

How to assess the strengths and weaknesses of research methods.
Examining different research designs, bias and validity, and frameworks for systematically appraising a medical paper.

## Medical Statistics

A basic introduction to the key statistics in medical articles.
Giving an overview of statistics that compare risk, test confidence, analyse clinical investigations, and test difference.

## Information Resources

A comprehensive overview of Library subscription resources, freely available online resources and 'grey literature'.

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- Wed 13th: Statistics
- Thurs 21st: Information resources
- Fri 29th: Literature Searching

**August** (12pm)
- Tue 2nd: Critical Appraisal
- Wed 10th: Statistics
- Thurs 18th: Information resources
- Fri 26th: Literature Searching

**September** (1pm)
- Fri 2nd: Critical Appraisal
- Mon 5th: Statistics
- Tue 18th: Information resources
- Wed 21st: Literature Searching
- Thurs 29th: Critical Appraisal
Current Awareness Database Articles on Cystic Fibrosis

Below is a selection of articles on cystic fibrosis recently added to the healthcare databases, grouped in the following categories:

- Medical
- Microbiological
- Nutritional
- Other

If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: library@uhbristol.nhs.uk

Medical

Title: Hypoglycaemia in cystic fibrosis in the absence of diabetes: A systematic review.

Citation: Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, May 2016, vol. 15, no. 3, p. 274-284,

Author(s): Armaghanian, N, Brand-Miller, J C, Markovic, T P, Steinbeck, K S

Abstract: Hypoglycaemia in CF in the absence of diabetes or glucose lowering therapies is a phenomenon that is receiving growing attention in the literature. These episodes are sometimes symptomatic and likely have variable aetiologies. Our first aim was to conduct a systematic review of the literature to determine what is known about hypoglycaemia in CF. Our second aim was to assess evidence based guidelines for management strategies. A comprehensive search of databases and guideline compiler entities was performed. Inclusion criteria were primary research articles and evidence based guidelines that referred to hypoglycaemia in CF in the absence of insulin treatment or other glucose lowering therapies. A total of 11 studies (four manuscripts and seven abstracts) and five evidence-based guidelines met the inclusion criteria. Prevalence rates of hypoglycaemia unrelated to diabetes varied between studies (7-69%). Hypoglycaemia was diagnosed during oral glucose tolerance testing or continuous glucose monitoring (CGM). Associations between hypoglycaemia and clinical parameters of BMI, lung function, liver disease and pancreatic insufficiency were measured in some studies. There was no unifying definition of hypoglycaemia in the absence of diabetes. Only two evidence based guidelines reported possible management strategies. The systematic review found limited data on this clinical problem and supports the need for high quality methodological studies that are able to describe the experience and the aetiology(ies) of hypoglycaemia in CF.

Title: Acute Scedosporium apiospermum Endobronchial Infection in Cystic Fibrosis.
**Citation:** The Pediatric infectious disease journal, Jun 2016, vol. 35, no. 6, p. 701-702

**Author(s):** Padoan, Rita, Poli, Piercarlo, Colombrita, Domenico, Borghi, Elisa

**Abstract:** Fungi are known pathogens in cystic fibrosis patients. A boy with cystic fibrosis presented with acute respiratory distress. Bronchoscopy showed airways obstruction by mucus plugs and bronchial casts. Scedosporium apiospermum was identified as the only pathogen. Bronchoalveolar lavage successfully resolved the acute obstruction. Plastic bronchitis is a new clinical picture of acute Scedosporium endobronchial colonization in cystic fibrosis patients.

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**Title:** Relationship between lung function and Modified Shuttle Test performance in adult patients with cystic fibrosis: a cross-sectional, retrospective study.

**Citation:** Physiotherapy, Jun 2016, vol. 102, no. 2, p. 184-188, 1873-1465 (June 2016)

**Author(s):** Doeleman, W R, Takken, T, Bronsveld, I, Hulzebos, E H J

**Abstract:** To investigate the relationship between lung function and exercise capacity in adults with cystic fibrosis (CF), and to develop a CF-specific equation to predict Modified Shuttle Test (MST) performance from baseline data. Cross-sectional, retrospective study. Adult CF centre. One hundred and twenty-seven patients with CF [61 male; mean age 25 years (range 17 to 52 years), mean forced expiratory volume in 1 second (FEV1) 56% predicted (range 15 to 124%)]. MST and FEV1. Overall, a moderate-to-good relationship was found between lung function and MST performance (walking distance vs FEV1% predicted: \(r=0.64, P=0.01\)). This relationship between FEV1 and MST shows an obvious threshold at an FEV1 of 67% predicted. Above this threshold, no significant association was observed between FEV1 and MST performance. However, a strong relationship (MST vs FEV1% predicted: \(r\geq0.74, P<0.01\) for men and \(r=0.79, P<0.01\) for women) was found below an FEV1 of 67% predicted. This study suggests that a strong association exists between lung function (FEV1% predicted) and MST (walking distance) in adult patients with moderate-to-severe CF (FEV1<67% predicted). A reference equation for MST performance was developed for those patients with FEV1 ≤67% predicted, providing a tool to make an a-priori prediction of MST walking distance.

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**Title:** Gastroparesis Concurrent with Adult Cystic Fibrosis; Are They Related?

**Citation:** The American journal of medicine, May 2016, vol. 129, no. 5, p. e21., 1555-7162 (May 2016)

**Author(s):** Mandaliya, Rohan, Hadjiliadis, Denis, Cohen, Sidney

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**Title:** Correction to: Infection in cystic fibrosis: impact of the environment and climate.

**Citation:** Expert review of respiratory medicine, Jun 2016, vol. 10, no. 6, p. 713.,
**Title:** New drug developments in the management of cystic fibrosis lung disease.

**Citation:** Expert opinion on pharmacotherapy, Jun 2016, vol. 17, no. 8, p. 1103-1112

**Author(s):** Turnbull, Andrew R, Davies, Jane C

**Abstract:** Therapies for cystic fibrosis (CF) pulmonary disease have, until recently, all targeted downstream manifestations rather than the root cause of the disease. A step-change in our approach has been achieved in the last few years, with novel small-molecule CFTR modulating drugs entering the clinic. In this article, we will discuss the field of drug development for CF lung disease. The case will be made for the potential benefits of basic defect-targeted strategies, which will be described in detail. Novel therapies directed at the downstream pulmonary manifestations of CF - infection, inflammation, and mucus impaction - will be reviewed. Finally, we will speculate on future directions and challenges. CF drug development is in an exciting phase, catalysed by the impressive results seen in patients with ivacaftor-responsive CFTR mutations. The research field is active with trials of novel therapies targeting the basic defect, alongside drugs targeting downstream effects. In order to detect potentially small improvements due to novel therapies, especially in the context of treating young patients with early disease, sensitive outcome measures and the coordinated efforts of collaborative research networks are crucial.

**Title:** Disease-specific clinical trials networks: the example of cystic fibrosis.

**Citation:** European journal of pediatrics, Jun 2016, vol. 175, no. 6, p. 817-824

**Author(s):** De Boeck, Kris, Bulteel, Veerle, Fajac, Isabelle

**Abstract:** This article describes the steps of the development and the structure of a disease-specific clinical trials network for cystic fibrosis in Europe. Activities such as reviewing study protocols, feasibility assessments, training and standardizing of procedures, and outcome measurements help to bring high-quality clinical trials to the patients. Cooperation with the pharmaceutical industry, other research networks, patient organizations, and regulatory agencies is very important throughout all activities. The European Cystic Fibrosis Society-Clinical Trials Network facilitates the development of new treatments for a rare disease and could be a prototype for other diseases. • Clinical research has led to the first approved treatments targeting the basic Cystic Fibrosis defect. • For a rare disease like Cystic Fibrosis, multicenter international collaboration is needed to obtain solid evidence when testing possible new treatments. What is New: • The Clinical Trials Network established by the European Cystic Fibrosis Society has grown to a fully operational network with well-defined structures, procedures and partnerships. • Standardization of outcome parameters, protocol review, feasibility assessment and other activities help to develop high quality, efficient, relevant and feasible clinical trials, with the aim to bring new treatments to the patients.
Title: Staphylococcus aureus and Pseudomonas aeruginosa co-infection is associated with cystic fibrosis-related diabetes and poor clinical outcomes.

Citation: European journal of clinical microbiology & infectious diseases: official publication of the European Society of Clinical Microbiology, Jun 2016, vol. 35, no. 6, p. 947-953.

Author(s): Limoli, D H, Yang, J, Khansaheb, M K, Helfman, B, Peng, L, Stecenko, A A,

Abstract: Cystic fibrosis-related diabetes (CFRD) patients suffer from accelerated rates of pulmonary decline compared to cystic fibrosis (CF) patients with normal glucose tolerance (NGT). However, the mechanisms underlying this difference are unknown. While CFRD is associated with increased respiratory infections, a link between infection and enhanced pulmonary dysfunction remains unclear. The development of glucose intolerance is spectral, resulting in impaired glucose tolerance (IGT) prior to the diagnosis of CFRD. Inclusion of IGT patients within the NGT group may diminish the ability to identify correlations with CFRD. With this in mind, this study aimed to determine if the association between CFRD and respiratory infections is correlated with pulmonary decline. Respiratory cultures from 234 CF patients with confirmed diagnosis of NGT or CFRD were analyzed to measure rates of infection, focusing on the two most prevalent bacteria in CF, Staphylococcus aureus and Pseudomonas aeruginosa. Infection status was correlated with pulmonary function and confounding clinical variables including age, gender, blood glucose levels, and CF transmembrane conductance regulator (CFTR) phenotype were considered in multivariate analyses. CFRD patients, particularly those with extremely high blood glucose levels, were more likely than NGT patients to be co-infected with S. aureus and P. aeruginosa, compared to infection with only one pathogen. Co-infection was associated with decreased lung function and increased frequency of pulmonary exacerbations, even after adjustment for confounding variables. Alterations in the microbial community composition, as opposed to the presence of a single pathogen, may account for greater pulmonary decline in CFRD patients.

Title: The 1-h oral glucose tolerance test glucose and insulin values are associated with markers of clinical deterioration in cystic fibrosis.


Author(s): Coriati, Adèle, Ziai, Sophie, Lavioie, Annick, Berthiaume, Yves,

Abstract: Cystic fibrosis (CF) is associated with the emergence of CF-related diabetes (CFRD). CFRD is associated with increased risk of accelerated weight and/or lung function loss (clinical degradation). Data in the CF pediatric population reported an association between higher 60-min oral glucose tolerance test (OGTT) plasma glucose values and reduced lung function. Our objective was to evaluate the relationship between the 60-min OGTT insulin and glucose values and markers of clinical degradation in adult patients with CF. This study was based on an ongoing observational cohort of CF adult patients (≥18 years). All patients underwent a 2-h OGTT with 30-min interval sample measurements. Plasma insulin and
glucose levels were measured. Adult patients (N = 240) were categorized based on the 60-min OGTT median values of glucose (G60, 11.0 mmol/L) and/or insulin (I60, 43.4 μU/mL). A negative association was observed between the 60-min OGTT glucose value and pulmonary function (FEV1; P = 0.001), whereas 60-min OGTT insulin values were positively associated with BMI (P = 0.004). Patients with high G60 values displayed lower FEV1 than patients with low G60 values (P = 0.025). Patients with higher I60 values demonstrated higher values of both FEV1 (P = 0.022) and BMI (P = 0.003) than patients with low I60 values. More importantly, when adjusting for BMI, the difference in FEV1 between both groups no longer existed (P = 0.166). Both insulin and glucose values at 60-min OGTT are associated with indicators of clinical degradation in adult patients with CF. Future prospective analyses are essential in establishing the clinical utility of these indicators.

Title: Lumacaftor-ivacaftor (Orkambi) for cystic fibrosis: behind the 'breakthrough'.

Citation: Evidence Based Medicine, 2016, vol./is. 21/3(83-86)

Author(s): Mayer, Martin

Title: Supplementation of ursodeoxycholic acid improves fat digestion and absorption in cystic fibrosis patients with mild liver involvement.

Citation: European Journal of Gastroenterology & Hepatology, 2016, vol./is. 28/6

Author(s): Drzymała-Czyż, Sławomira, Jończyk-Potoczna, Katarzyna, Lisowska,

Abstract: Background: Ursodeoxycholic acid (UDCA) supplementation is recommended for cystic fibrosis (CF) patients with associated liver disease. However, its effect on fat digestion and absorption is not known. Materials and Methods: In 23 patients with mild liver involvement, a C-mixed triglyceride breath test was performed on UDCA supplementation (with and without pancreatic enzymes - standard and increased dose) and after 1 month of UDCA withdrawal. Cumulative percentage dose recovery [CPDR; median (interquartile range)] has been considered to reflect lipid digestion and absorption. Results: The enzyme supplementation resulted in a significant CPDR improvement [0% (0-0) vs. 4.6% (0.4-6.0); P<0.00046]. With the increased dose of enzymes in 16 patients with abnormal C-mixed triglyceride breath test results and lipase dose less than 3000 U/g of fat, higher CPDR values [8.6% (5.6-12.7); P<0.000027] were observed. However, a 1-month UDCA withdrawal resulted in a significant reduction in (P<0.000031) fat digestion and absorption [2.9% (0.7-5.8)]. Conclusion: UDCA supplementation seems to enhance lipid digestion and absorption in pancreatic insufficient CF patients with mild liver involvement. This finding points toward the potential impact of UDCA supplementation on nutritional status in CF patients with liver disease and underscores the often overlooked role of factors other than pancreatic enzymes on digestion and absorption of fats in CF.

Title: Cystic fibrosis: a model system for precision medicine.
**Citation:** Current Opinion in Pediatrics, 2016, vol./is. 28/3(312-317), 10408703

**Author(s):** Martiniano, Stacey L., Sagel, Scott D., Zemanick, Edith T.

**Abstract:** Purpose Of Review: Development of cystic fibrosis transmembrane conductance regulator (CFTR) modulators, small molecule therapies that target the basic defect in cystic fibrosis (CF), represents a new era in CF treatment. This review highlights recent progress in CF therapeutics as an example of precision medicine and personalized approaches to test CFTR modulators using preclinical model systems.

**Recent Findings:** CFTR modulators are now clinically available for approximately 50% of the United States CF population. The CFTR potentiator, ivacaftor, is approved for people with CF ages 2 years and older with at least one gating mutation (G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R) or the R117H conductance mutation. The recent Food and Drug Administration approval of the corrector/potentiator combination, lumacaftor/ivacaftor, expands modulator therapy to people with CF homozygous for the F508del mutation, ages 12 years and older. Ivacaftor and lumacaftor, however, do not fully restore CFTR activity. Thus, next-generation correctors and potentiators are in development. Read-through agents targeting nonsense mutations and genotype agnostic treatments (gene-editing and gene therapy) are also in various phases of clinical development.

**Summary:** CFTR modulators promise to transform the therapeutic landscape in CF in a precision based fashion. Areas of ongoing research include developing drugs for all mutation classes so that all persons with CF can benefit from these therapies, and refining preclinical assays that allow the selection of the most effective treatments on an individual basis.

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**Title:** New and emerging targeted therapies for cystic fibrosis

**Citation:** BMJ (Clinical Research Edition), Apr 2016, vol. 353, no. 8052, p. i859.

**Author(s):** Quon, Bradley S, Rowe, Steven M

**Abstract:** Cystic fibrosis (CF) is a monogenic autosomal recessive disorder that affects about 70?000 people worldwide. The clinical manifestations of the disease are caused by defects in the cystic fibrosis transmembrane conductance regulator (CFTR) protein. The discovery of the CFTR gene in 1989 has led to a sophisticated understanding of how thousands of mutations in the CFTR gene affect the structure and function of the CFTR protein. Much progress has been made over the past decade with the development of orally bioavailable small molecule drugs that target defective CFTR proteins caused by specific mutations. Furthermore, there is considerable optimism about the prospect of gene replacement or editing therapies to correct all mutations in cystic fibrosis. The recent approvals of ivacaftor and lumacaftor represent the genesis of a new era of precision medicine in the treatment of this condition. These drugs are having a positive impact on the lives of people with cystic fibrosis and are potentially disease modifying. This review provides an update on advances in our understanding of the structure and function of the CFTR, with a focus on state of the art targeted drugs that are in development.

**Title:** Lung transplantation for cystic fibrosis: differential characteristics and outcomes between children and adults.
Citation: European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery, May 2016, vol. 49, no. 5, p. 1334-1343, 1873-734X (May 2016)

Author(s): Moreno, Paula, Alvarez, Antonio, Carrasco, Guadalupe, Redel, Javier, Guaman, Hugo Dario, Baamonde, Carlos, Algar, Francisco Javier, Cerezo, Francisco, Salvatierra, Angel

Abstract: The survival benefit of lung transplantation (LTx) for cystic fibrosis (CF) patients is well demonstrated. We aim to compare children and adult CF recipients to assess whether there are differences in survival and clinical outcomes, and to identify risk factors for mortality. A retrospective analysis of 442 consecutive LTx performed at our institution in a 20-year period was conducted. CF patients were distributed into two groups: children (age <18 years) and adults (age ≥18 years). Donor and recipient general demographic data, perioperative and postoperative factors including 30-day mortality, survival, primary graft dysfunction (PGD), complications, acute rejection (AR) and chronic lung allograft dysfunction (CLAD) were analysed and compared between groups. Univariable, Kaplan-Meier and Cox regression analyses were performed. The study group included 120 consecutive CF patients: 50 children (13 ± 3 years) and 70 adults (25 ± 6 years) undergoing 111 bilateral, 4 lobar, 4 combined and 1 unilateral LTx. Comparative analysis (children versus adults): survival (overall; 5, 10 and 15 years) 57, 45, 35% vs 77, 59, 43% (P = 0.32); survival (1-year survivors; 5, 10 and 15 years): 75, 64, 46% vs 90, 75, 59% (P = 0.09); 30-day mortality: 14 vs 16% (P = 0.27); urgent LTx: 32 vs 17% (P = 0.04); use of cardiopulmonary bypass (CPB): 56 vs 28% (P = 0.002); intensive care unit stay: 20 ± 19 vs 10 ± 9 days (P = 0.006); AR episodes (n): 1.4 ± 0.7 vs 1.2 ± 0.8 (P = 0.004). Incidence of PGD and freedom from CLAD did not differ between groups. Predictors of mortality were: use of CPB (HR 3.12; 95% CI 1.33-7.35; P < 0.01), post-transplant diabetes mellitus (HR 2.49; 95% CI 1.13-5.43; P = 0.02) and pneumonia episodes within the first month post-transplant (HR 2.82; 95% CI 1.27-6.29; P = 0.01). Paediatric CF patients usually present with poorer pre-transplant status, require CPB more frequently and have a higher incidence of post-LTx diabetes and infections. This might explain the trend towards a better long-term survival observed in adult CF patients.

Title: A safety evaluation of ivacaftor for the treatment of cystic fibrosis.

Citation: Expert opinion on drug safety, May 2016, vol. 15, no. 5, p. 709-715

Author(s): McColley, Susanna A

Abstract: Ivacaftor is indicated for treatment of cystic fibrosis (CF) mediated by 10 mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene that causes gating or partial function abnormalities. In placebo-controlled and open-label studies, ivacaftor-treated subjects showed improved pulmonary function, nutrition and quality of life measures. This article reviews ivacaftor safety. Safety findings in ivacaftor clinical trials, and reported subsequently, were accessed by a PubMed search using key words "VX-770" or "ivacaftor". Additional information was accessed via Google Search. Transaminitis was noted in ivacaftor and combination lumacaftor-ivacaftor trials. Ivacaftor was associated with cataracts in juvenile rat pups in pre-clinical studies; non-congenital
Cataracts have been found in children taking ivacaftor. Ivacaftor is a CYP3A substrate; CYP3A inhibitors and inducers should be avoided during its administration. Ivacaftor and its M1 metabolite may inhibit CYP3A and P-gp; therefore, ivacaftor may increase systemic exposure to drugs which are substrates of CYP3A and/or P-gp, increasing the potential for adverse events. Ivacaftor therapy may be associated with ocular and hepatic side effects; specific recommendations for monitoring are available. Potential drug interactions should be evaluated in patients taking ivacaftor. High clinical efficacy suggests that the risk benefit ratio of ivacaftor favors therapy.

**Title:** Infection in cystic fibrosis: impact of the environment and climate.

**Citation:** Expert review of respiratory medicine, May 2016, vol. 10, no. 5, p. 505-519

**Author(s):** Ramsay, K A, Stockwell, R E, Bell, S C, Kidd, T J

**Abstract:** In many countries numbers of adults with cystic fibrosis (CF) exceed that of children, with median survival predicted to surpass 50 years. Increasing longevity is, in part, due to intensive therapies including eradication of early infection and suppressive therapies and pulmonary exacerbations. Initial infections with common CF pathogens are thought to arise from the natural environment. We review the impact of climate and environment on infection in CF. Specifically, several studies indicate that higher ambient temperatures, proximity to the equator and the summer season may be linked to the increased prevalence of Pseudomonas aeruginosa in people with CF. The environment may also play an important role in the acquisition of Gram negative organisms other than P. aeruginosa. There is emerging data suggesting that climatic and environmental factors are likely to impact on the risk of infection with NTM and fungi in people which are found extensively throughout the natural environment.

**Title:** IV-treated pulmonary exacerbations in the prior year: An important independent risk factor for future pulmonary exacerbation in cystic fibrosis.

**Citation:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, May 2016, vol. 15, no. 3, p. 372-379, 1873-5010 (May 2016)

**Author(s):** VanDevanter, Donald R, Morris, Nathan J, Konstan, Michael W

**Abstract:** Single-center analyses have suggested that the number of CF pulmonary exacerbations (PEx) treated with intravenous antibiotics an individual has experienced in the prior year is significantly associated with their future PEx hazard. We studied Prior-year PEx association with future PEx hazard by Cox proportional hazards regression among CF Foundation Patient Registry patients who experienced PEx after Jan 1, 2010. Among 13,579 patients, those with 1, 2, 3, or ≥4 Prior-year PEx treated with intravenous antibiotics were at 1.8, 2.9, 4.8, and 8.7 higher PEx hazard vs those without (P<.0001). Adjustment with significant demographic and clinical covariates (univariate Ps.<.0001) reduced Prior-year PEx hazard ratios to 1.6, 2.4, 3.6, and 6.0 (P<.0001). No other covariates had adjusted hazard ratios of >1.7. Prior-year PEx strongly associate with future PEx hazard and should be
accounted for in prospective trials where treatment-associated change in PEx hazard is an efficacy outcome.

**Microbiological**

**Title:** Advancing clinical development pathways for new CFTR modulators in cystic fibrosis.

**Citation:** Thorax, May 2016, vol. 71, no. 5, p. 454-461, 1468-3296 (May 2016)

**Author(s):** Mayer-Hamblett, Nicole, Boyle, Michael, VanDevanter, Donald

**Abstract:** Cystic fibrosis (CF) is a life-shortening genetic disease affecting approximately 70,000 individuals worldwide. Until recently, drug development efforts have emphasised therapies treating downstream signs and symptoms resulting from the underlying CF biological defect: reduced function of the CF transmembrane conductance regulator (CFTR) protein. The current CF drug development landscape has expanded to include therapies that enhance CFTR function by either restoring wild-type CFTR protein expression or increasing (modulating) the function of mutant CFTR proteins in cells. To date, two systemic small-molecule CFTR modulators have been evaluated in pivotal clinical trials in individuals with CF and specific mutant CFTR genotypes that have led to regulatory review and/or approval. Advances in the discovery of CFTR modulators as a promising new class of therapies have been impressive, yet work remains to develop highly effective, disease-modifying modulators for individuals of all CF genotypes. The objectives of this review are to outline the challenges and opportunities in drug development created by systemic genotype-specific CFTR modulators, highlight the advantages of sweat chloride as an established biomarker of CFTR activity to streamline early-phase development and summarise options for later phase clinical trial designs that respond to the adoption of approved genotype-specific modulators into standard of care. An optimal development framework will be needed to move the most promising therapies efficiently through the drug development pipeline and ultimately deliver efficacious and safe therapies to all individuals with CF.

**Title:** Should all adult cystic fibrosis patients with repeated nontuberculous mycobacteria cultures receive specific treatment? A 10-year case-control study.

**Citation:** The European respiratory journal, May 2016, vol. 47, no. 5, p. 1575-1577, 1399-3003 (May 2016)

**Author(s):** Albrecht, Christiane, Ringshausen, Felix, Ott, Sebastian, Wagner, Dirk, Rademacher, Jessica, Schneider, Michael, Welte, Tobias, Pletz, Mathias W

**Title:** Comparing the harmful effects of nontuberculous mycobacteria and Gram negative bacteria on lung function in patients with cystic fibrosis.

**Citation:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, May 2016, vol. 15, no. 3, p. 380-385, 1873-5010 (May 2016)
Author(s): Qvist, Tavs, Taylor-Robinson, David, Waldmann, Elisabeth, Olesen, Hanne Vebert, Waldmann, Elisabeth, Olesen, Hanne Vebert,

Abstract: To better understand the relative effects of infection with nontuberculous mycobacteria and Gram negative bacteria on lung function decline in cystic fibrosis, we assessed the impact of each infection in a Danish setting. Longitudinal registry study of 432 patients with cystic fibrosis contributing 53,771 lung function measures between 1974 and 2014. We used a mixed effects model with longitudinally structured correlation, while adjusting for clinically important covariates. Infections with a significant impact on rate of decline in %FEV1 were Mycobacterium abscessus complex with -2.22% points per year (95% CI -3.21 to -1.23), Burkholderia cepacia complex -1.95% (95% CI -2.51 to -1.39), Achromobacterxylosoxidans -1.55% (95% CI -2.21 to -0.90), and Pseudomonas aeruginosa -0.95% (95% CI -1.24 to -0.66). Clearing M. abscessus complex was associated with a change to a slower decline, similar in magnitude to the pre-infection slope. In a national population we have demonstrated the impact on lung function of each chronic CF pathogen. M. abscessus complex was associated with the worst impact on lung function. Eradication of M. abscessus complex may significantly improve lung function.

Title: Microbial colonization and lung function in adolescents with cystic fibrosis.

Citation: Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, May 2016, vol. 15, no. 3, p. 340-349, 1873-5010 (May 2016)

Author(s): Hector, Andreas, Kirn, Tobias, Ralhan, Anjali, Graepler-Mainka, Ute

Abstract: With intensified antibiotic therapy and longer survival, patients with cystic fibrosis (CF) are colonized with a more complex pattern of bacteria and fungi. However, the clinical relevance of these emerging pathogens for lung function remains poorly defined. The aim of this study was to assess the association of bacterial and fungal colonization patterns with lung function in adolescent patients with CF. Microbial colonization patterns and lung function parameters were assessed in 770 adolescent European (German/Austrian) CF patients in a retrospective study (median follow-up time: 10years). Colonization with Pseudomonas aeruginosa and MRSA were most strongly associated with loss of lung function, while mainly colonization with Haemophilus influenzae was associated with preserved lung function. Aspergillus fumigatus was the only species that was associated with an increased risk for infection with P. aeruginosa. Microbial interaction analysis revealed three distinct microbial clusters within the longitudinal course of CF lung disease. Collectively, this study identified potentially protective and harmful microbial colonization patterns in adolescent CF patients. Further studies in different patient cohorts are required to evaluate these microbial patterns and to assess their clinical relevance. Copyright © 2016 European Cystic Fibrosis Society. Published by Elsevier B.V. All rights reserved.
Psychology

**Title:** OC37 - Adolescents with cystic fibrosis: their perspective.

**Citation:** Nursing children and young people, May 2016, vol. 28, no. 4, p. 80,

**Author(s):** Reisinho, Maria Conceição, Gomes, Bárbara

**Abstract:** Theme: Complex health care and chronic disease management. The adolescent with cystic fibrosis suffers from organic distresses and requires support to deal with the physical symptoms and the psychosocial adaptation. Realize the experience of growing up with cystic fibrosis from the adolescent point of view. Data grounded theory as investigation method and interpretation by Meleis Theory. Study group with 16 adolescents and data collected by interview. From the content analysis of the interviews, we established that the adolescents were living development and health-illness type transitions. We identified the dimension 'developing trust and coping' as adjustment strategy to new contexts. The adolescents' speeches reflected behaviors of involvement in the transition process, being a positive result to the psychosocial development and positive life experience at this stage. The follow up from healthcare professionals may transform a stressful situation into a state of trust. It can also reveal and pinpoint resource strategies to enable adaptation to new circumstances.

**Title:** Depression and anxiety symptoms in Spanish adult patients with cystic fibrosis: associations with health-related quality of life.

**Citation:** General hospital psychiatry, May 2016, vol. 40, p. 39-46, 1873-7714 (2016 May-Jun)

**Author(s):** Olveira, C, Sole, A, Girón, R M, Quintana-Gallego, E, Mondejar, P, Baranda, F,

**Abstract:** Cystic fibrosis (CF) is a chronic disease with an impact on the quality of life. Self-reported symptoms of depression and anxiety were assessed in the Spanish cohort of the International Epidemiological Study on Depression and Anxiety in patients with CF (International Depression-Anxiety Epidemiological Study) and their relationship with health status and health-related quality of life (HRQoL) was evaluated. This cross-sectional study recruited adult patients with CF at 10 Spanish centers. Patients completed the Hospital Anxiety and Depression Scale (HADS) and the Revised Cystic Fibrosis Questionnaire. Demographic and health data were recorded from medical charts. Logistic regression was used to determine the predictors of elevated symptoms of depression and anxiety (HADS≥8). Of the 336 participants recruited (mean age, 28.1 years; 48.2% women), 41 (12.2%) had elevated depression-related scores, and 100 (29.7%) had elevated anxiety-related scores (HADS≥8). After adjusting for confounders, only less education, intravenous antibiotics, psychiatric medications and psychotherapy were significantly associated with elevated psychological symptoms. Specifically, regardless of lung function, patients who were depressed or anxious reported worse HRQoL. The prevalence of elevated symptoms of
depression and anxiety was high in Spanish adult patients with CF, and these symptoms were associated with a decreased HRQoL. Copyright © 2016 Elsevier Inc. All rights reserved.

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**Nutrition**

**Title:** Vitamin A intake and serum retinol levels in children and adolescents with cystic fibrosis.

**Citation:** Clinical Nutrition, 2016, vol./is. 35/3(654-659)

**Author(s):** Woestenenk, Janna W., Broos, Nancy, Stellato, Rebecca K., Arets, Hubertus G.M.,

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**Title:** The clinical benefits of long-term supplementation with omega-3 fatty acids in cystic fibrosis patients - A pilot study.

**Citation:** Prostaglandins, leukotrienes, and essential fatty acids, May 2016, vol. 108, p. 45-50, 1532-2823 (May 2016)

**Author(s):** Hanssens, L, Thiébaut, I, Lefèvre, N, Malfroot, A, Knoop, C, Duchateau, J,

**Abstract:** Effectiveness of omega-3 supplementation in cystic fibrosis (CF) remains controversial. This study sought to evaluate clinical status, exercise tolerance, inflammatory parameters, and erythrocyte fatty acid profile after 1 year of oral omega-3 supplementation in CF patients. Fifteen ΔF508-homozygous patients undergoing chronic azithromycin were randomized to receive omega-3 fish oil supplementation at a dose of 60mg/Kg/day or placebo. In comparison with the previous year, in the supplemented group, the number of pulmonary exacerbations decreased at 12 months (1.7 vs. 3.0, p<0.01), as did the duration of antibiotic therapy (26.5 days vs. 60.0 days, p<0.025). Supplementation significantly increased the levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) as early as <3 months of administration, with concomitant decreases in arachidonic acid (AA) levels. This pilot study suggests that long-term omega-3 supplementation offers several clinical benefits as to the number of exacerbations and duration of antibiotic therapy in CF patients.

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**Other**

**Title:** Physiotherapy for cystic fibrosis in Australia and New Zealand: A clinical practice guideline.

**Citation:** Respirology (Carlton, Vic.), May 2016, vol. 21, no. 4, p. 656-667,

**Author(s):** Button, Brenda M, Wilson, Christine, Dentice, Ruth, Cox, Narelle S,
Abstract: Physiotherapy management is a key element of care for people with cystic fibrosis (CF) throughout the lifespan. Although considerable evidence exists to support physiotherapy management of CF, there is documented variation in practice. The aim of this guideline is to optimize the physiotherapy management of people with CF in Australia and New Zealand. A systematic review of the literature in key areas of physiotherapy practice for CF was undertaken. Recommendations were formulated based on National Health and Medical Research Council (Australia) guidelines and considered the quality, quantity and level of the evidence; the consistency of the body of evidence; the likely clinical impact; and applicability to physiotherapy practice in Australia and New Zealand. A total of 30 recommendations were made for airway clearance therapy, inhalation therapy, exercise assessment and training, musculoskeletal management, management of urinary incontinence, managing the newly diagnosed patient with CF, delivery of non-invasive ventilation, and physiotherapy management before and after lung transplantation. These recommendations can be used to underpin the provision of evidence-based physiotherapy care to people with CF in Australia and New Zealand. © 2016 The Authors Respirology published by John Wiley & Sons Australia, Ltd on behalf of Asian Pacific Society of Respirology.

Title: An exploration of how young people and parents use online support in the context of living with cystic fibrosis

Citation: Health Expectations, Apr 2016, vol. 19, no. 2, p. 309-321, 1369-6513 (April 2016)

Author(s): Kirk, Susan, Milnes, Linda

Abstract: Background: There is increasing recognition of the Internet's potential role in providing information and support for people living with long-term conditions. However, how young people and parents use online forms of self-care support in the context of living with childhood chronic illness has been under-researched. Objective: To explore how online peer support is used by young people and parents to support self-care in relation to cystic fibrosis (CF). Setting and participants: Online forum for young people and parents to support self-care in relation to cystic fibrosis (CF). Setting and participants: Online forum for young people and parents based on a CF charity website. A total of 279 individuals participated in the forum during the study. Design: An online ethnographical approach, involving observing, downloading and analysing discussion group postings. All postings made over a random 4-month period were included (151 discussion threads). Results: The online setting enabled a physically disconnected group to connect and create a safe space to collectively share experiences and receive support to manage and live with cystic fibrosis. Participants exchanged experientially derived advice and views on how to manage treatments, emotions, relationships, identity and support from services. While parents sought information and support on managing specific therapies/services and ways of maintaining their child's health, the information and support young people desired appeared to be more directed at how to 'fit' CF into their everyday lives. Discussion and conclusions: Online support groups appear to supplement professional support in relation to self-management. They enable young people and parents to share experiences, feelings and strategies for living with long-term conditions with peers and develop the expertise to empower them in interactions with health-care professionals. References
Title: The relationship between cardiac hemodynamics and exercise tolerance in cystic fibrosis.

Citation: Heart & lung : the journal of critical care, May 2016, vol. 45, no. 3, p. 283-290,

Author(s): Van Iterson, Erik H, Wheatley, Courtney M, Baker, Sarah E, Morgan, Wayne J,

Abstract: Individuals with cystic fibrosis (CF) have reduced pulmonary function and exercise tolerance. Additionally, these individuals may develop abnormal cardiac function. The implications of abnormal cardiac function on exercise tolerance are unclear in CF. Study relationships between exercise cardiac hemodynamics and exercise tolerance in CF. 17 CF and 25 controls participated in cardiopulmonary exercise testing to measure exercise duration and peak workload (PW). Cardiac index (QI) was measured using acetylene rebreathe and oxygen uptake (VO2) breath-by-breath. Forced expiratory volume in 1-second (FEV1) was performed at rest. Peak QI was 6.7 ± 0.5 vs. 9.1 ± 0.3 mL/min/m(2), CF vs. controls, respectively (P < 0.05). Linear regressions between QI (R(2) = 0.63 and 0.51) and exercise duration or PW were stronger than VO2 (R(2) = 0.35 and 0.37) or FEV1 (R(2) = 0.34 and 0.36) in CF, respectively (P < 0.05). These data are clinically relevant suggesting attenuated cardiac function in addition to low airway function relate to exercise tolerance in CF.
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