Cystic Fibrosis

Current Awareness Newsletter

January/February 2016
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- Journal of Cystic Fibrosis
- American Journal of Respiratory and Critical Care Medicine
- Thorax
- Chest

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Journal of Cystic Fibrosis
Vol.15, iss.1, January 2016
http://www.cysticfibrosisjournal.com/current

Colonscopic screening shows increased early incidence and progression of adenomas in cystic fibrosis
02 February 2016, David E. Niccum, Joanne L. Billings, Jordan M. Dunitz, Alexander Khoruts

Reversible airway obstruction in cystic fibrosis: Common, but not associated with characteristics of asthma
28 January 2016, Hagit Levine, Malena Cohen-Cymerknoh, Nitai Klein, Moshe Hoshen,

Measurement of fecal elastase improves performance of newborn screening for cystic fibrosis
27 January 2016, Juerg Barben, Corina S. Rueegg, Maja Jurca, Johannes Spalinger, Claudia E. Kuehni, the Swiss Cystic Fibrosis Screening Group

Microbiological yield from induced sputum compared to oropharyngeal swab in young children with cystic fibrosis
26 January 2016, Marco Zampoli, Komala Pillay, Henri Carrara, Heather J. Zar, Brenda Morrow

Host response to cytotoxins in children with cystic fibrosis
25 January 2016, 00:00:00 | Ashley D. Chadha, Isaac P. Thomsen, Natalia Jimenez-Truque,

Advanced glycation end products are elevated in cystic fibrosis-related diabetes and correlate with worse lung function
23 January 2016, William R. Hunt, Beth R. Helfman, Nael A. McCarty, Jason M. Hansen

Ultrasound and magnetic resonance imaging assessment of joint disease in symptomatic patients with cystic fibrosis arthropathy

Serum retinol levels and pulmonary function in children and adolescents with cystic fibrosis
16 January 2016, 00:00:00 | J.W. Woestenenk, R.H.J. Houwen
selective agar can be useful for recovery of from sputum samples of cystic fibrosis patients
14 January 2016, Vladislav Raclavsky, Radko Novotny

Implementation of newborn screening for cystic fibrosis in Norway. Results from the first three years

YKL-40 as marker of severe lung disease in cystic fibrosis patients
08 January 2016, Salvatore Leonardi, Giuseppe Fabio Parisi, Antonino Capizzi, Sara

Gastric emptying and gastro-oesophageal reflux in children with cystic fibrosis
08 January 2016, Bruno Hauser, Jean De Schepper, Anne Malfroot, Elke De Wachter, Iris De Schutter,

Distribution of the species of in a French Cystic Fibrosis Centre and multilocus sequence typing analysis reveal the predominance of and clonal relationships between some clinical and environmental isolates
08 January 2016, Lucie Amoureux, Julien Bador, Fatma Bounoua Zouak, Angélique Chapuis,

CFTR modulators and pregnancy: Our work has only just begun
07 January 2016, Christopher H. Goss, Donald R. VanDevanter

Replies to “Is the home environment an important factor in the occurrence of fungal events in cystic fibrosis?”
06 January 2016, Steffi Rocchi, Bénédicte Richaud-Thiriez, Coralie Barrera, Frédéric Grenouillet, Jean-

Low sodium status in cystic fibrosis—as assessed by calculating fractional Na excretion—is associated with decreased growth parameters
06 January 2016, Christiane Knepper, Helmut Ellemunter, Johannes Eder, Katharina Niedermayr,

The effect of CFTR modulation on the disease progression of cystic fibrosis in the era of precision medicine
04 January 2016, J. Stuart Elborn, Jane Davies, Scott Bell, Nico Derichs

Serum retinol and pulmonary function in young people with cystic fibrosis
04 January 2016, M. Francisco Rivas-Crespo

New insights into disease progression for the CFTR modulator-treated cystic fibrosis patient
30 December 2015, Susanna A. McColley, Jane Davies, Felix Ratjen, Manu Jain

Tracheal diverticula in cystic fibrosis—A potentially important underreported finding on chest CT
30 December 2015, Gabriela Gayer, Ifat Sarouk, Nayrouz Kanaany, Ori Efrati

Advanced curriculum for cystic fibrosis: Integrating genomic-driven data into patient-centered treatment strategies
29 December 2015, J. Stuart Elborn, Isabelle Sermet-Gaudelus, Patrick A. Flume, Susan Madge,

Newborn screening for cystic fibrosis — The parent perspective
29 December 2015, Corina S. Rueegg, Jürg Barben, Gaudenz M. Hafen, Alexander Moeller, Maja Jurca, Ralph Fingerhut, Claudia E. Kuehni, The Swiss Cystic Fibrosis Screening Group

The importance of the mundane—Nebuliser care and hygiene
22 December 2015, John E. Moore
Preliminary comparison of normalized T1 and non-contrast perfusion MRI assessments of regional lung disease in cystic fibrosis patients
21 December 2015, Shannon B. Donnola, Elliott C. Dasenbrook, David Weaver, Lan Lu,

Killing effect of nanoencapsulated colistin sulfate on from cystic fibrosis patients
18 December 2015, E. Sans-Serramitjana, E. Fusté, B. Martínez-Garriga, A. Merlos, M. Pastor,

Newborn bloodspot screening for cystic fibrosis: What do antenatal and postnatal women know about cystic fibrosis?
18 December 2015, C. Fitzgerald, B. Linnane, E. Heery, N. Conneally, S. George, P. Fitzpatrick

Response to Letter to the Editor: HbA1c as a screening tool for cystic fibrosis related diabetes
17 December 2015, Juliana C. Burgess, Nicola Bridges, Banya Winston, Khin M. Gyi,

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Predictors of non-referral of patients with cystic fibrosis for lung transplant evaluation in the United States
16 December 2015, Kathleen J. Ramos, Bradley S. Quon, Kevin J. Psoter, Erika D. Lease,

A successful uncomplicated CF pregnancy while remaining on Ivacaftor
14 December 2015, Rachel Kaminski, Dilip Nazareth

Creation and characterization of an airway epithelial cell line for stable expression of CFTR variants
13 December 2015, Laura B. Gottschalk, Briana Vecchio-Pagan, Neeraj Sharma, Sangwoo T. Han,

An evaluation strategy for potential QTc prolongation with chronic azithromycin therapy in cystic fibrosis
11 December 2015, Patrick John Lenehan, Craig M. Schramm, Melanie Sue Collins

Psychological resilience and intolerance of uncertainty in coping with cystic fibrosis
10 December 2015, Horst Mitmansgruber, Ulrike Smrekar, Bianca Rabanser, Thomas Beck,

Pharmacological rescue of mutant CFTR protein improves the viscoelastic properties of CF mucus
08 December 2015, Ambra Gianotti, Valeria Capurro, Paolo Scudieri, Luis J.V. Galietta, Oscar Moran, Olga Zegarra-Moran
04 December 2015, S. Madge, D. Sands

Epidemic infection in patients with cystic fibrosis is not a risk factor for poor clinical Outcomes following lung transplantation
02 December 2015, Julia Pritchard, Mitesh V. Thakrar, Ranjani Somayaji, Michael G. Surette, Harvey R. Rabin, Doug Helmersen, Dale Lien, Swathi Purighalla, Barbara Waddell, Michael D. Parkins

Bronchial epithelial cell lines and primary nasal epithelial cells from cystic fibrosis respond differently to cigarette smoke exposure
01 December 2015, Mark Thomas Shaw Williams, Francine de Courcey, David Comer,

Interferon response of the cystic fibrosis bronchial epithelium to major and minor group rhinovirus infection
21 November 2015, Aline Schögler, Andrea B. Stokes, Carmen Casaulta, Nicolas Regamey,
Web-based symptom screening in cystic fibrosis patients: A feasibility study
20 November 2015, Julie Balzano, Ashley Fresenius, Patricia Walker, Maria Berdella,

A longitudinal analysis of chronic MRSA and co-infection in cystic fibrosis: A single-center study
20 November 2015, Maret L. Maliniak, Arlene A. Stecenko, Nael A. McCarty

CFTR potentiator therapy ameliorates impaired insulin secretion in CF patients with a gating mutation
04 November 2015, Reuven Tsabari, Hila Iron Elyashar, Malena Cohen Cymerknownh,

Infant lung function tests as endpoints in the ISIS multicenter clinical trial in cystic fibrosis
04 November 2015, Stephanie D. Davis, Felix Ratjen, Lyndia C. Brumback, Robin C. Johnson, Amy G. Filbrun, Gwendolyn S. Kerby, Howard B. Panitch, Scott H. Donaldson, Margaret Rosenfeld, for the ISIS Study Group

Non-allergic asthma as a CFTR-related disorder
30 October 2015, Angela Schulz, Burkhard Tümler

CFTR dysfunction can be involved in CBAVD, pancreatitis or bronchiectasis.
HbA1c: An effective screening tool for cystic fibrosis related diabetes?
30 October 2015, Marie-Angela Schnyder, Christian Benden, Christoph Schmid

Using Hba1c as a screening tool for Cystic Fibrosis Related Diabetes
29 October 2015, John Widger, Shihab Hameed, Chee Y. Ooi, Charles Verge

A small molecule neutrophil elastase inhibitor, KRP-109, inhibits cystic fibrosis mucin degradation
29 October 2015, Shashi Chillappagari, Christian Müller, Poornima Mahavadi, Andreas Guenther,

IV-treated pulmonary exacerbations in the prior year: An important independent risk factor for future pulmonary exacerbation in cystic fibrosis
22 October 2015, Donald R. VanDevanter, Nathan J. Morris, Michael W. Konstan

Single-cell high resolution melting analysis: A novel, generic, pre-implantation genetic diagnosis (PGD) method applied to cystic fibrosis (HRMA CF-PGD)
19 October 2015, A. Destouni, M. Poulou, G. Kakourou, C. Vrettou, M. Tzetis, J. Traeger-Synodinos,

Piperacillin/tazobactam continuous infusion at 12G/1.5G per day in CF patients results in target plasma-concentrations
18 October 2015, Kristina Öbrink-Hansen, Søren Jensen-Fangel, Birgitte Brock,

Cystic fibrosis in young children: A review of disease manifestation, progression, and response to early treatment
07 October 2015, Donald R. VanDevanter, Jennifer S. Kahle, Amy K. O'Sullivan, Slaven Sikirica,

Comparing the harmful effects of nontuberculous mycobacteria and Gram negative bacteria on lung function in patients with cystic fibrosis
05 October 2015, Tavs Qvist, David Taylor-Robinson, Elisabeth Waldmann, Hanne Vebert Olesen,

Bronchopulmonary infection–colonization patterns in Spanish cystic fibrosis patients: Results from a national multicenter study
28 September 2015, Juan de Dios Caballero, Rosa del Campo, Ana Royuela, Amparo Solé, Luis Máiz,
Use of gene sequence clustering to estimate the prevalence of different species among Cystic Fibrosis patients in the UK
24 September 2015, Amy Coward, Dervla T.D. Kenna, Claire Perry, Kate Martin, Michel Doumith,

Renin-associated hypertension after bronchial artery embolization in cystic fibrosis
24 September 2015, Nathalie Coolen, Hervé Gouya, Reem Kanaan, Isabelle Honoré, Jeanne Chapron,

Causes of death in French cystic fibrosis patients: The need for improvement in transplantation referral strategies!
18 September 2015, Clémence Martin, Cécile Hamard, Reem Kanaan, Véronique Boussaud,

Diagnostic accuracy and distress associated with oropharyngeal suction in cystic fibrosis
17 September 2015, Michael Doumit, Yvonne Belessis, Sacha Stelzer-Braid, Kylie-Ann Mallitt,

The impact of a national population carrier screening program on cystic fibrosis birth rate and age at diagnosis: Implications for newborn screening
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The 1-min sit-to-stand test—A simple functional capacity test in cystic fibrosis?
09 September 2015, Thomas Radtke, Milo A. Puhan, Helge Hebestreit, Susi Kriemler

CF healthcare workers feel unprepared in providing suitable end of life care and desire more education: Results of a nationwide survey
08 September 2015, Jessica Goggin, Rubin I. Cohen

Advance care planning in cystic fibrosis: Current practices, challenges, and opportunities
08 September 2015, Elisabeth P. Dellon, Elaine Chen, Jessica Goggin, Karen Homa, Bruce C. Marshall,

Faecal proteomics: A tool to investigate dysbiosis and inflammation in patients with cystic fibrosis
29 August 2015, Griet Debyser, Bart Mesuere, Lieven Clement, Jens Van de Weygaert,

Inhaled alpha-proteinase inhibitor therapy in patients with cystic fibrosis
25 August 2015, Amit Gaggar, Junliang Chen, James F. Chmiel, Henry L. Dorkin, Patrick A. Flume,

Anti-IgY antibodies augment bacterial clearance in a murine pneumonia model
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The pharmacokinetics and toxicity of morning vs. evening tobramycin dosing for pulmonary exacerbations of cystic fibrosis: A randomised comparison

Tigecycline-induced acute pancreatitis in a cystic fibrosis patient: A case report and literature review
14 August 2015, Michael T. Hemphill, Kellie R. Jones

Limited premature termination codon suppression by read-through agents in cystic fibrosis intestinal organoids
05 August 2015, D.D. Zomer-van Ommen, L.A.W. Vijftigtschild, E. Kruisselbrink, A.M. Vonk,

An evaluation of different steam disinfection protocols for cystic fibrosis nebulizers
29 July 2015, K. Hohenwarter, W. Prammer, W. Aichinger, G. Reychler
A randomized controlled trial of vitamin D replacement strategies in pediatric CF patients
23 July 2015, Tregony Simoneau, Gregory S. Sawicki, Carly E. Milliren, Henry A. Feldman,

Optical coherence tomography detects structural abnormalities of the nasal mucosa in patients with cystic fibrosis
23 July 2015, Ute Oltmanns, Karin Palmowski, Mark Wielpütz, Nicolas Kahn, Eva Baroke,

Long-term improvement of lung clearance index in patients with mild cystic fibrosis lung disease: Does hypertonic saline play a role?
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A semi-blinded study comparing 2 methods of measuring nasal potential difference: Subcutaneous needle versus dermal abrasion
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Methionine reduces tobramycin-induced ototoxicity without antimicrobial interference in animal models
09 July 2015, Daniel J. Fox, Morris D. Cooper, Cristian A. Speil, Melissa H. Roberts, Susan C. Yanik,

The impact of Cystic Fibrosis Transmembrane Regulator Disruption on cardiac function and stress response
25 June 2015, Kai Jiang, Sen Jiao, Megan Vitko, Rebecca Darrah, Chris A. Flask, Craig A. Hodges,

Fungal contamination of nebuliser devices used by people with cystic fibrosis
20 June 2015, D. Peckham, K. Williams, S. Wynne, M. Denton, K. Pollard, R. Barton

Molecular epidemiology of complex isolates in Ireland
10 June 2015, C. O’Driscoll, J. Konjek, B. Heym, M.M. Fitzgibbon, B.J. Plant, M. Ní Chróinín,

oropharyngeal colonization in children and adolescents with cystic fibrosis
03 June 2015, Susanna Esposito, Carla Colombo, Antonella Tosco, Enza Montemitro, Sonia Volpi, Luca Ruggiero, Mara Lelii, Arianna Bisogno, Claudio Pelucchi, Nicola Principi, Italian Pneumococcal Study Group on Cystic Fibrosis

Skeletal muscle contractility and fatigability in adults with cystic fibrosis
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A novel culture medium for isolation of rapidly-growing mycobacteria from the sputum of patients with cystic fibrosis
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Lack of evidence of increased risk of bacterial transmission during cystic fibrosis educational programmes
20 May 2015, Winnie Ridderberg, Camilla Andersen, Michael Væth, Vibeke Bregnballe,

Deleterious impact of hyperglycemia on cystic fibrosis airway ion transport and epithelial repair
24 April 2015, Claudia Bilodeau, Olivier Bardou, Émilie Maillé, Yves Berthiaume,

Assessment of epithelial sodium channel variants in nonwhite cystic fibrosis patients with non-diagnostic genotypes
18 April 2015, Marie-Luise Brennan, Lynn M. Pique, Iris Schrijver
Is the raised volume rapid thoracic compression technique ready for use in clinical trials in infants with cystic fibrosis?
15 April 2015, Stefan Matecki, Lisa Kent, Kris de Boeck, Muriel Le Bourgeois, Stefan Zielen, Cesare Braggion, H.G.M. Arets, Judy Bradley, Stephanie Davis, Isabelle Sermet, Philippe Reix, on behalf of the respiratory function group of the European Cystic Fibrosis Society Clinical Trial Network

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Development and evaluation of a palliative care curriculum for cystic fibrosis healthcare providers
25 March 2015, Rachel W. Linnemann, Patricia J. O'Malley, Deborah Friedman, Anna M.

Alterations in blood leukocytes of G551D-bearing cystic fibrosis patients undergoing treatment with ivacaftor
12 March 2015, Preston E. Bratcher, Steven M. Rowe, Ginger Reeves, Tambra Roberts,

Comparative, and analyses of a CFTR splicing mutation: Importance of functional studies to establish disease liability of mutations
28 February 2015, Anabela S. Ramalho, Luka A. Clarke, Marisa Sousa, Verónica Felicio,

Effect of ivacaftor in patients with advanced cystic fibrosis and a mutation: Safety and efficacy in an expanded access program in the United States
11 February 2015, Jennifer Taylor-Cousar, Minoo Niknian, Geoffrey Gilmartin, Joseph M. Pilewski, for the VX11-770-901 investigators

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A randomised trial of hypertonic saline during hospitalisation for exacerbation of cystic fibrosis

Decreased lung function in 7-year-old children with early-life organophosphate exposure
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Urbanisation but not biomass fuel smoke exposure is associated with asthma prevalence in four resource-limited settings

UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening
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Long-term impact of developing a postoperative pulmonary complication after lung surgery
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Response to: 'Lumacaftor/ivacaftor for patients homozygous for Phe508del-CFTR: should we curb our enthusiasm? by Jones and Barry

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Vol.149, iss.1, January 2016
http://journal.publications.chestnet.org/issue.aspx

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Cough Intensity Is Respiratory Muscle Activation Important and Does It Relate to Symptoms?
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Choice of Imaging Studies in Acutely Ill Pregnant Women
01 January 2016, Firoz T, Miller MA, Bourjeily G.

Lung Density in Extremely Large Healthy Lungs

A Man in His 60s With Circulatory Collapse

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Postoperative Complications in Obesity Hypoventilation Syndrome and Hypercapnic OSA CO 2 Levels Matter!
01 January 2016, Cooksey J, Mokhlesi B.

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POINT: Is the Apnea-Hypopnea Index the Best Way to Quantify the Severity of Sleep-Disordered Breathing? Yes
01 January 2016, Rapoport DM

Evaluation of Occupational and Environmental Factors in the Assessment of Chronic Cough in Adults A Systematic Review
01 January 2016, Tarlo SM, Altman KW, French CT, et al.

COUNTERPOINT: Is the Apnea-Hypopnea Index the Best Way to Quantify the Severity of Sleep-Disordered Breathing? No
01 January 2016, Punjabi NM.

Effect of e-Cigarette Use on Cough Reflex Sensitivity

Ultrasound Guidance Facilitates Radial Artery Catheterization A Meta-analysis With Trial Sequential Analysis of Randomized Controlled Trials

Quantitative CT Scanning Analysis of Pure Ground-Glass Opacity Nodules Predicts Further CT Scanning Change

Rebuttal From Dr Rapoport
01 January 2016, Rapoport DM

Risk Stratification of Patients With Acute Symptomatic Pulmonary Embolism Based on Presence or Absence of Lower Extremity DVT Systematic Review and Meta-analysis

Rebuttal From Dr Punjabi
01 January 2016, Punjabi NM.

Clinical Characteristics of Connective Tissue Disease-Associated Interstitial Lung Disease in 1,044 Chinese Patients

Efficacy and Safety of Corticosteroids for Community-Acquired Pneumonia A Systematic Review and Meta-Analysis

Smart Technology in Lung Disease Clinical Trials
01 January 2016, Geller NL, Kim D, Tian X.

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Sleep Bruxism in Respiratory Medicine Practice
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Defining the Asthma-COPD Overlap Syndrome in a COPD Cohort

Various Mechanistic Pathways Representing the Aging Process Are Altered in COPD

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Asthma-COPD Overlap
01 January 2016, Barnes PJ.

Practice Patterns and Outcomes of Treatments for Atrial Fibrillation During Sepsis A Propensity-Matched Cohort Study

Postoperative Complications in Patients With Unrecognized Obesity Hypoventilation Syndrome Undergoing Elective Noncardiac Surgery
01 January 2016, 00:00:00 | Kaw R, Bhatia P, Paz y Mar H, et al.

Slow and Study Support for a Randomized Trial of β-Blockade in Sepsis-Associated Atrial Fibrillation
01 January 2016, Semler MW, Wheeler AP

Heritability of OSA in a Rural Population

Ethnic Variation in Response to IM Triamcinolone in Children With Severe Therapy-Resistant Asthma

Patient With Slow-Growing Mediastinal Mass Presents With Chest Pain and Dyspnea

A 42-Year-Old Woman With Abnormal Chest CT Scan and Chylous Ascites
01 January 2016, Panchabhai TS, Bandyopadhyay D, Yadav R, et al.

A 26-Year-Old Woman With Systemic Lupus Erythematosus Presenting With Orthopnea and Restrictive Lung Impairment
01 January 2016, Panchabhai TS, Bandyopadhyay D, Highland KB, et a
New from the Cochrane Library Systematic Reviews on Cystic Fibrosis

**Bronchoscopy-guided antimicrobial therapy for cystic fibrosis**
Kamini Jain, Claire Wainwright, Alan R Smyth: Online Publication Date: January 2016

**Abstract**
**Background:** Early diagnosis and treatment of lower respiratory tract infections are the mainstay of management of lung disease in cystic fibrosis. When sputum samples are unavailable, treatment relies mainly on cultures from oropharyngeal specimens; however, there are concerns regarding the sensitivity of these to identify lower respiratory organisms.

**Anti-inflammatory drugs and analgesics for managing symptoms in people with cystic fibrosis-related arthritis**
Judith Thornton, Satyapal Rangaraj: Online Publication Date: January 2016

**Abstract**
**Background:** Arthritis remains a relatively infrequent complication of cystic fibrosis, but is a cause of significant morbidity when it does occur. Two distinct types of arthritis are described in cystic fibrosis: cystic fibrosis-related arthropathy (CFA) and hypertrophic pulmonary osteoarthropathy (HPO). Management of arthritis in people with cystic fibrosis is uncertain and complex because of the underlying disease and its intense treatment. This is an update of a previously published review.

**Antibiotic treatment for Burkholderia cepacia complex in people with cystic fibrosis experiencing a pulmonary exacerbation**
Alex Horsley, Andrew M Jones, Robert Lord: Online Publication Date: January 2016

**Abstract**
**Background:** Chronic pulmonary infection is a hallmark of lung disease in cystic fibrosis. Infections dominated by organisms of the Burkholderia cepacia complex, a group of at least 18 closely-related species of gram-negative bacteria, are particularly difficult to treat. These infections may be associated with a fulminant necrotising pneumonia. Burkholderia cepacia complex bacteria are resistant to many common antibiotics and able to acquire resistance against many more.

**Ataluren and similar compounds (specific therapies for premature termination codon class I mutations) for cystic fibrosis**
Aisha Aslam, Ian P Sinha, Kevin W Southern: Online Publication Date: January 2016

**Abstract**
This is the protocol for a review and there is no abstract. The objectives are as follows: To evaluate the benefits and harms of ataluren and similar compounds on clinically important outcomes in people with CF with class I mutations (PTCs).
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Cystic fibrosis: Overview of the treatment of lung disease
Author: Richard H Simon, MD
Literature review current through: Jan 2016. | This topic last updated: Jan 06, 2016.
INTRODUCTION — Cystic fibrosis (CF) is a multisystem disorder caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene, located on chromosome 7. Pulmonary disease remains the leading cause of morbidity and mortality in patients with CF.
The treatment of CF lung disease is experiencing a period of rapid evolution, supported by well-designed clinical trials and improved understanding of the genetics and pathophysiology of the disease. Undoubtedly, these advancements are responsible for a substantial portion of the improvement that has occurred in patient survival.

Cystic fibrosis: Clinical manifestations and diagnosis
Author: Julie P Katkin, MD
Literature review current through: Jan 2016. | This topic last updated: Dec 11, 2015.
INTRODUCTION — Cystic fibrosis (CF) is the most common life-shortening autosomal recessive disease among Caucasian populations, with a frequency of 1 in 2000 to 3000 live births. The median predicted survival for CF patients in the United States was 39.3 years (95% CI, 37.3-41.4) according to the Cystic Fibrosis Foundation 2014 Registry Report. The usual presenting symptoms and signs include persistent pulmonary infection, pancreatic insufficiency, and elevated sweat chloride levels. However, many patients demonstrate mild or atypical symptoms, and clinicians should remain alert to the possibility of CF even when only a few of the usual features are present.
An overview of the clinical manifestations and diagnosis of CF will be presented here. The genetics, pathogenesis, and treatment of CF are reviewed separately.

Cystic fibrosis: Genetics and pathogenesis
Author: Julie P Katkin, MD
Literature review current through: Jan 2016. | This topic last updated: Sep 02, 2014.
INTRODUCTION — Cystic fibrosis (CF) is a multisystem disease affecting the digestive system, sweat glands, and the reproductive tract, but progressive lung disease continues to be the major cause of morbidity and mortality. Patients with CF have abnormal transport of chloride and sodium across the respiratory epithelium, resulting in thickened, viscous airway secretions [1,2]. Over a highly variable time course ranging from months to decades after birth, individuals eventually develop chronic infection of the respiratory tract with a characteristic array of bacterial flora, leading to progressive respiratory insufficiency and eventual respiratory failure [3].
The genetics and pathogenesis of cystic fibrosis are discussed here. Details of the clinical manifestations and effects of the disease process are discussed separately.
New from NICE

Cystic fibrosis (F508del mutation) - lumacaftor (with ivacaftor) [ID786]

Status: In progress
Anticipated publication date: July 2016
Process: STA
Referral date: September 2015

Provisional Schedule
Closing date for invited submissions / evidence submission: 11 November 2015
1st appraisal committee meeting: 24 February 2016

Project Team
Associate Director: Helen Knight
Technical Lead: Martyn Burke
Communications manager: Laura Gibson
Project manager: Kate Moore
Technical Advisor: TBC

Email enquiries: If you have any queries please email tacommd@nice.org.uk


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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
- Psychological
- 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: Lumacaftor and ivacaftor in the management of patients with cystic fibrosis: current evidence and future prospects.

Citation: Therapeutic advances in respiratory disease, Dec 2015, vol. 9, no. 6, p. 313-326

Author(s): Kuk, Kelly, Taylor-Cousar, Jennifer L

Abstract: Cystic fibrosis (CF) is a genetic disorder that causes multiorgan morbidity and premature death, most commonly from pulmonary dysfunction. Mutations in the CF transmembrane conductance regulator (CFTR) gene, of which almost 2000 have been described, result in a dysfunctional CFTR protein. This protein is an adenosine triphosphate binding anion channel, present primarily at the surface of epithelial cells. Loss of function mutations in this anion channel result in decreased or absent chloride/bicarbonate transport. The subsequent abnormal salt and water transport at epithelial cell surfaces leads to thickened secretions, and infection or inflammation in affected organs. In the last 20 years, therapeutics have been developed to treat the signs and symptoms of CF. However, in 2012, the small molecule drug, ivacaftor, became the first approved therapy that addresses the basic defect in CF. Ivacaftor is a potentiator of CFTR channels defective in their chloride/bicarbonate gating/conductance, but present at the epithelial cell surface. It is only approved for 10 mutations carried by approximately 7% of the population of patients with
CF. F508del is the most common CFTR mutation, present in homozygosis in approximately 50% of patients with CF. The F508del mutation results in multiple CFTR channel defects that require both correction (stabilization of misfolded CFTR and trafficking to the epithelial cell membrane) and potentiation. This article reviews the in vitro and clinical trial data for the potential use of the potentiator, ivacaftor, and the corrector, lumacaftor, in patients with CF.

**Title:** Improvements in symptomatic treatment strategies for cystic fibrosis: Delivering CF care in the 21st century

**Citation:** Expert Opinion on Orphan Drugs, January 2016, vol./is. 4/1(5-19), 2167-8707 (02 Jan 2016)

**Author(s):** Addy C., Downey D.G., Elborn J.S.

**Abstract:** Introduction: Cystic Fibrosis (CF) is a life-limiting multisystem disease characterized by viscid secretions in multiple organ systems. Survival has increased significantly with average survival now over 40 years. CF care in the 21st century will face different challenges to the 20th century-balancing modulating the basic genetic defect with caring for a larger adult population living with complex multisystem disease into middle age. Areas covered: We review the latest advances in CF therapeutics and their place within CF care. Precision Medicine and the impact of CFTR modulators on costs of care are highlighted. We discuss the role of the lung microbiome and its impact on management of lung infection. Advances in inhaled antibiotics and the rise of dry powder inhalers are evaluated. Screening and management of complications and comorbidities will form a much larger part of CF care, especially CF-related Diabetes, Renal and Bone disease. Current evidence surrounding managing complications is appraised and future research avenues highlighted. Expert opinion: Therapeutic options across all areas of CF care are increasing. Comparative effectiveness research is needed to establish where new treatments fit into 21st century CF Care. Increasing personalization comes with rising costs of care which must be balanced against cost-effectiveness in overall delivery of care.

**Title:** Tobramycin inhalation powder (TOBI Podhaler<sup></sup>) for the treatment of lung infection in patients with cystic fibrosis

**Citation:** Expert Review of Anti-Infective Therapy, January 2016, vol./is. 14/1(9-17),

**Author(s):** Vazquez-Espinosa E., Marcos C., Alonso T., Giron R.M., Gomez-Punter R.M.,

**Abstract:** Cystic fibrosis (CF) is an autosomal recessive inherited disease secondary to a defect in the CF transmembrane conductance regulator gene (CFTR). Mortality in CF is associated with impairment of lung function in which bacterial infection plays a fundamental role. The
microorganism Pseudomonas aeruginosa (P. aeruginosa) is a marker of poor prognosis. Tobramycin was the first parenteral antibiotic to be used as inhaled medication in CF. Owing to its beneficial effects; it was subsequently used in designed inhaled formulations. The first formulation was the inhalation solution, which improved lung function, lowered hospitalization rates, and reduced the courses of intravenous antibiotic. However, the high associated costs and time necessary to administer the medication negatively affected quality of life. The recent development of tobramycin inhalation powder has optimized treatment. The dry powder inhaler is a simple device that reduces administration time and improves adherence. As there is no risk of bacterial contamination, disinfection is unnecessary.

Title: Adherence pattern to study drugs in clinical trials by patients with cystic fibrosis.

Citation: Pediatric pulmonology, Feb 2016, vol. 51, no. 2, p. 143-146 (February 2016)

Author(s): Pugatsch, Thea, Shoseyov, David, Cohen-Cymberknoh, Malena, Hayut, Batya,

Abstract: Clinical trials are all based on the assumption that patients are adherent to the study protocol. Many reports indicate that general adherence of patients with CF to their daily routine therapies is poor. However, no data exists on adherence to study drug regimens. All clinical trials carried out at the Hadassah CF Center from 2008 to 2013 were reviewed. Actual adherence as determined by counted drugs was analyzed according to drug administration mode, study lengths and number of study visits. A subset of patients answered a two-part questionnaire covering study specific and general treatment specific issues. Eight studies including 118 patients, with patient numbers varying between 4 and 32 per trial were analyzed. For 7/8 studies mean adherence was between 78% to 100%. Comparison with administration mode showed that adherence decreased substantially if the drugs were not provided as "ready to be used" (63%). Study length influenced adherence, the longer the study the poorer the adherence (82% trial beginning, 44% post 36 months [two combined studies with identical drug]). A substantial decrease was noted over Holiday periods and during the summer vacation months. No correlation was found between number of study visits and adherence to study drug. Adherence to study drug is generally higher than that for regular treatment. Study length, mode of administration, and timing according to Holidays and vacations adversely affect adherence.

Title: Magnesium in cystic fibrosis-Systematic review of the literature.

Citation: Pediatric pulmonology, Feb 2016, vol. 51, no. 2, p. 196-202 (February 2016)

Author(s): Santi, Maristella, Milani, Gregorio P, Simonetti, Giacomo D, Fossali, Emilio F, Bianchetti,
Abstract: The metabolism of sodium, potassium, and chloride and the acid-base balance are sometimes altered in cystic fibrosis. Textbooks and reviews only marginally address the homeostasis of magnesium in cystic fibrosis. We performed a search of the Medical Subject Headings terms (cystic fibrosis OR mucoviscidosis) AND (magnesium OR hypomagnes[ae]mia) in the US National Library of Medicine and Excerpta Medica databases. We identified 25 reports dealing with magnesium and cystic fibrosis. The results of the review may be summarized as follows. First, hypomagnesemia affects more than half of the cystic fibrosis patients with advanced disease; second, magnesemia, which is normally age-independent, relevantly decreases with age in cystic fibrosis; third, aminoglycoside antimicrobials frequently induce both acute and chronic renal magnesium-wasting; fourth, sweat magnesium concentration was normal in cystic fibrosis patients; fifth, limited data suggest the existence of an impaired intestinal magnesium balance. Finally, stimulating observations suggest that magnesium supplements might achieve an improvement in respiratory muscle strength and mucolytic activity of both recombinant and endogenous deoxyribonuclease. The first comprehensive review of the literature confirms that, despite being one of the most prevalent minerals in the body, the importance of magnesium in cystic fibrosis is largely overlooked. In these patients, hypomagnesemia should be sought once a year. Furthermore, the potential of supplementation with this cation deserves more attention.

Title: Inspiratory Muscle Strength and Endurance in Children and Adolescents with Cystic Fibrosis.

Citation: Respiratory care, Feb 2016, vol. 61, no. 2, p. 184-191 (February 2016)

Author(s): Vendrusculo, Fernanda M, Heinzmann-Filho, João P, Piva, Taila C, Marostica, Paulo Jc,

Abstract: Pulmonary changes that occur in cystic fibrosis may influence inspiratory muscle strength and endurance. We evaluated inspiratory muscle strength and endurance in children and adolescents with cystic fibrosis in comparison with healthy subjects. This is a cross-sectional observational study with subjects with cystic fibrosis and paired healthy individuals, age 6-18 y. Spirometry, impulse oscillometry, plethysmography, manovacuometry, and a protocol of inspiratory muscle endurance were performed. Subjects with cystic fibrosis (n = 34) had higher maximum percent-of-predicted inspiratory pressure (PImax) than healthy (n = 68) subjects (118.5 ± 25.8% vs 105.8 ± 18.0%) and no significant difference in endurance (60.9 ± 13.3% vs 65.3 ± 12.3%). When restricting the analysis to subjects without Pseudomonas aeruginosa colonization and with FEV1 > 80%, PImax values were significantly higher, and inspiratory muscle endurance was lower, in comparison with the control group. PImax correlated significantly with FVC (r = 0.44, P = .02) and FEV1 (r = 0.41, P = .02), whereas endurance correlated better with total airway resistance (r = 0.35, P = .045) and with central airway resistance (r = 0.48, P = .004). Children and adolescents with cystic
fibrosis with no colonization by P. aeruginosa and normal lung function present increased inspiratory muscle strength and decreased endurance compared with healthy individuals, indicating that changes in the respiratory muscle function seem to be distinctly associated with pulmonary involvement. Strength was related to pulmonary function parameters, whereas endurance was associated with airway resistance.

**Title:** Decline in Forced Expiratory Volume in 1 Second in Cystic Fibrosis—Watch the Pendulum Swing.

**Citation:** The Journal of Pediatrics, Feb 2016, vol. 169, p. 7-9 (February 2016)

**Author(s):** Pittman, Jessica E, Davis, Stephanie

**Title:** Forced Expiratory Volume in 1 Second Variability Helps Identify Patients with Cystic Fibrosis at Risk of Greater Loss of Lung Function.

**Citation:** The Journal of Pediatrics, Feb 2016, vol. 169, p. 116 (February 2016)

**Author(s):** Morgan, Wayne J, VanDevanter, Donald R, Pasta, David J, Foreman, Aimee J, Wagener, Jeffrey S, Konstan, Michael W, Scientific Advisory Group, Investigators and Coordinators of the Epidemiologic Study of Cystic Fibrosis

**Abstract:** To evaluate several alternative measures of forced expiratory volume in 1 second percent predicted (FEV1 %pred) variability as potential predictors of future FEV1 %pred decline in patients with cystic fibrosis. We included 13,827 patients age ≥6 years from the Epidemiologic Study of Cystic Fibrosis 1994-2002 with ≥4 FEV1 %pred measurements spanning ≥366 days in both a 2-year baseline period and a 2-year follow-up period. We predicted change from best baseline FEV1 %pred to best follow-up FEV1 %pred and change from baseline to best in the second follow-up year by using multivariable regression stratified by 4 lung-disease stages. We assessed 5 measures of variability (some as deviations from the best and some as deviations from the trend line) both alone and after controlling for demographic and clinical factors and for the slope and level of FEV1 %pred. All 5 measures of FEV1 %pred variability were predictive, but the strongest predictor was median deviation from the best FEV1 %pred in the baseline period. The contribution to explanatory power (R(2)) was substantial and exceeded the total contribution of all other factors excluding the FEV1 %pred rate of decline. Adding the other variability measures provided minimal additional value. Median deviation from the best FEV1 %pred is a simple metric that markedly improves prediction of FEV1 %pred decline even after the inclusion of demographic and clinical characteristics and the FEV1 %pred rate of decline. The routine calculation of this variability measure could allow clinicians to better identify patients at risk and therefore in need of increased intervention.
Title: Preferences and Stated Adherence for Antibiotic Treatment of Cystic Fibrosis Pseudomonas Infections.

Citation: The patient, Feb 2016, vol. 9, no. 1, p. 59-67 (February 2016)

Author(s): Mohamed, Ateesha Farah, Johnson, F Reed, Balp, Maria-Magdalena, Calado, Frederico

Abstract: Our objective was to quantify preferences and stated adherence for inhaled antibiotic treatments in cystic fibrosis (CF). Adult CF patients and parents of pediatric patients in the US who were members of the Cystic Fibrosis Foundation and who had Pseudomonas aeruginosa at least twice a year completed an online, discrete-choice experiment survey (response rate 4.4 %). Respondents answered five treatment-choice questions evaluating pairs of hypothetical CF treatment profiles. Stated-adherence questions followed two randomly selected treatment-choice questions. Data were analyzed using random-parameters logit (RPL). For a combination of attribute levels, the utility is estimated by summing the relevant attribute-level parameter estimates. For the stated-adherence questions, we tabulated the changes in the percentages of respondents who would be 95 % adherent for various changes in inhaled antibiotic-medication administration features. The final sample was 271 adult patients and 209 parents. Switching from a 30-min nebulizer twice daily to a 10-min dry powder inhaler (DPI) twice daily was 6.3 times more important for patients and 2.0 times more important for parents than an improvement in dry cough side effect from moderate to mild. Stated adherence for respondents was 20-30 % greater for DPIs versus nebulizers. Lower frequency of administration, shorter administration times for a given device, and milder dry cough appear to improve stated adherence to antibiotic treatment of CF lung infections.

Title: Importance of Local Epidemiology in Prevalence and Resistance of Cystic Fibrosis-related Pathogens.

Citation: The Pediatric infectious disease journal, Feb 2016, vol. 35, no. 2, p. 229.

Author(s): Hufnagel, Markus, König, Stefanie, Theilacker, Christian

Title: A randomised trial of hypertonic saline during hospitalisation for exacerbation of cystic fibrosis.

Citation: Thorax, Feb 2016, vol. 71, no. 2, p. 141-147 (February 2016)

Author(s): Dentice, Ruth L, Elkins, Mark R, Middleton, Peter G, Bishop, Jennifer R, Wark, Peter A B,

Abstract: The mucoactive effects of hypertonic saline should promote exacerbation resolution in people with cystic fibrosis (CF). To determine the effects of hypertonic saline inhalation during hospitalisation for exacerbation of CF on length of stay, lung function, symptoms, oxygenation,
exercise tolerance, quality of life, bacterial load and time to next hospitalisation. 132 adults with an exacerbation of CF were randomised to inhale three nebulised doses a day of either 4 mL 7% saline or a taste-masked control of 0.12% saline, throughout the hospital admission. The primary outcome measure was length of hospital stay. All participants tolerated their allocated saline solution. There was no significant difference in length of stay, which was 12 days in the hypertonic saline group and 13 days in controls, with a mean between-group difference (MD) of 1 day (95% CI 0 to 2). The likelihood of regaining pre-exacerbation FEV1 by discharge was significantly higher in the hypertonic saline group (75% vs 57%), and the number needed to treat was 6 (95% CI 3 to 65). On a 0-100 scale, the hypertonic saline group had significantly greater reduction in symptom severity than the control group at discharge in sleep (MD=13, 95% CI 4 to 23), congestion (MD=10, 95% CI 3 to 18) and dyspnoea (MD=8, 95% CI 1 to 16). No significant difference in time to next hospitalisation for a pulmonary exacerbation was detected between groups (HR=0.86 (CI 0.57 to 1.30), p=0.13). Other outcomes did not significantly differ. Addition of hypertonic saline to the management of a CF exacerbation did not reduce the length of hospital stay. Hypertonic saline speeds the resolution of exacerbation symptoms and allows patients to leave hospital with greater symptom resolution.

Title: Translating the genetics of cystic fibrosis to personalized medicine.

Citation: Translational research: the journal of laboratory and clinical medicine, Feb 2016, vol. 168, p. 40-49 (February 2016)

Author(s): Corvol, Harriet, Thompson, Kristin E, Tabary, Olivier, le Rouzic, Philippe, Guillot, Loïc

Abstract: Cystic fibrosis (CF) is the most common life-threatening recessive genetic disease in the Caucasian population. This multiorgan disease is caused by mutations in the gene encoding the CF transmembrane conductance regulator (CFTR) protein, a chloride channel recognized as regulating several apical ion channels. The gene mutations result either in the lack of the protein at the apical surface or in an improperly functioning protein. Morbidity and mortality because of the mutation of CFTR are mainly attributable to lung disease resulting from chronic infection and inflammation. Since its discovery as the causative gene in 1989, much progress has been achieved not only in clinical genetics but also in basic science studies. Recently, combinations of these efforts have been successfully translated into development and availability for patients of new therapies targeting specific CFTR mutations to correct the CFTR at the protein level. Current technologies such as next gene sequencing and novel genomic editing tools may offer new strategies to identify new CFTR variants and modifier genes, and to correct CFTR to pursue personalized medicine, which is already developed in some patient subsets. Personalized medicine or P4 medicine ("personalized," "predictive," "preventive," and "participatory") is currently booming for CF. The various current and
future challenges of personalized medicine as they apply to the issues faced in CF are discussed in this review. Copyright © 2016 Elsevier Inc. All rights reserved.

**Title:** How to Monitor Early Cystic Fibrosis Lung Disease. By Multiple-Breath Washout, Chest Computed Tomography, or Both?

**Citation:** American journal of respiratory and critical care medicine, Jan 2016, vol. 193, no. 1, p. 7-8

**Author(s):** Singer, Florian, Casaulta, Carmen, Latzin, Philipp

**Title:** Lung Clearance Index and Structural Lung Disease on Computed Tomography in Early Cystic Fibrosis.

**Citation:** American journal of respiratory and critical care medicine, Jan 2016, vol. 193, no. 1, p. 60-67 (January 1, 2016)

**Author(s):** Ramsey, Kathryn A, Rosenow, Tim, Turkovic, Lidija, Skoric, Billy, Banton, Georgia,

**Abstract:** The lung clearance index is a measure of ventilation distribution derived from the multiple-breath washout technique. It has been suggested as a surrogate for chest computed tomography to detect structural lung abnormalities in individuals with cystic fibrosis (CF); however, the associations between lung clearance index and early structural lung disease are unclear. We assessed the ability of the lung clearance index to reflect structural lung disease on the basis of chest computed tomography across the entire pediatric age range. Lung clearance index was assessed in 42 infants (ages 0-2 yr), 39 preschool children (ages 3-6 yr), and 38 school-age children (7-16 yr) with CF before chest computed tomography and in 72 healthy control subjects. Scans were evaluated for CF-related structural lung disease using the Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis quantitative outcome measure. In infants with CF, lung clearance index is insensitive to structural disease (κ = -0.03 [95% confidence interval, -0.05 to 0.16]). In preschool children with CF, lung clearance index correlates with total disease extent. In school-age children, lung clearance index correlates with total disease extent. In school-age children, lung clearance index correlates with extent of total disease, bronchiectasis, and air trapping. In preschool and school-age children, lung clearance index has a good positive predictive value (83-86%) but a poor negative predictive value (50-55%) to detect the presence of bronchiectasis. These data suggest that lung clearance index may be a useful surveillance tool to monitor structural lung disease in preschool and school-age children with CF. However, lung clearance index cannot replace chest computed tomography to screen for bronchiectasis in this population.

**Title:** Clinafloxacin for Treatment of Burkholderia cenocepacia Infection in a Cystic Fibrosis Patient.

**Citation:** Antimicrobial agents and chemotherapy, Jan 2016, vol. 60, no. 1, p. 1-5
Author(s): Balwan, Akshu, Nicolau, David P, Wungwattana, Minkey, Zuckerman, Jonathan B,


Title: Hemodynamic predictors of long term survival in end stage cystic fibrosis.

Citation: International journal of cardiology, Jan 2016, vol. 202, p. 221-225

Author(s): Scarsini, Roberto, Prioli, Maria A, Milano, Elena G, Castellani, Carlo, Pesarini, Gabriele,

Abstract: Pulmonary hypertension (PH) is often found in cystic fibrosis (CF) patients affected by end-stage lung disease but its impact on outcome remains unclear. Pulmonary arterial compliance (PAC) is an important determinant of right ventricle (RV) workload and it is a strong predictor of survival in other forms of PH. The aim of this study is to investigate whether PAC is a predictor of long-term prognosis in a population of CF patients affected by advanced lung disease. Between 2000 and 2014, 178 patients with CF have been evaluated for lung transplantation in our CF Center. Right heart catheterization (RHC) and follow up data were retrievable and analyzed in 141 of them. PAC was defined as the ratio between stroke volume (SV) and pulse pressure (PP) at heart catheterization. The association of PAC with survival was tested at 4 years and compared to other hemodynamic parameters. PH prevalence was 56.4%. Most patients had mild elevation of pulmonary artery pressure (PAP). No difference in mortality was observed in patients with PH compared to patients with normal PAP (HR 0.95: 95% CI 0.49-1.89, p=0.89). At receiver operating characteristic curve (ROC) analysis, the optimal prognostic cut-off point of PAC was 1.95ml/mmHg. An impaired PAC (≤1.95ml/mmHg) was a strong independent predictor of long-term mortality (HR 3.44: 95% CI 1.51-7.85: p=0.003). Impaired PAC is associated with poor prognosis in CF patients awaiting lung transplantation. Other traditional hemodynamic parameters add no prognostic information.

Title: Deleterious impact of hyperglycemia on cystic fibrosis airway ion transport and epithelial repair.
Cystic fibrosis (CF)-related diabetes (CFRD) is associated with faster pulmonary function decline. Thus, we evaluated the impact of hyperglycemia on airway epithelial repair and transepithelial ion transport, which are critical in maintaining lung integrity and function. Non-CF and CF airway epithelial cells were exposed to low (LG) or high (HG) glucose before ion current and wound repair rate measurements. CFTR and K(+) currents decreased after HG treatments. HG also reduced the wound healing rates of non-CF and CF cell monolayers. Although CFTR correction with VRT-325 accelerated the healing rates of CF cells monolayers under LG conditions, this improvement was significantly abrogated under HG conditions. Our data highlights a deleterious impact of hyperglycemia on ion transport and epithelial repair functions, which could contribute to the deterioration in lung function in CFRD patients. HG may also interfere with the beneficial effects of CFTR rescue on airway epithelial repair.

Title: Development and evaluation of a palliative care curriculum for cystic fibrosis healthcare providers.

Primary palliative care refers to basic skills that all healthcare providers can employ to improve quality of life for patients at any stage of disease. Training in these core skills is not commonly provided to clinicians caring for cystic fibrosis (CF) patients. The objective of this study was to assess change in comfort with core skills among care team members after participation in CF-specific palliative care training focused on management of burdensome symptoms and difficult conversations. A qualitative needs assessment was performed to inform the development of an 18-hour curriculum tailored to the chronicity and complexity of CF care. A 32-question pre- and post-course survey assessed CF provider comfort with the targeted palliative care skills in 5 domains using a 5-point Likert scale (1=very uncomfortable, 3=neutral, 5=very comfortable). Among course participants (n=16), mean overall comfort score increased by 0.9, from 3 (neutral) to 3.9 (comfortable) (p<0.001). Mean comfort level increased significantly (range 0.8 to 1.4) in each skill domain: use of supportive care resources, pain management, non-pain symptom management, communication, and psychosocial skills. CF-specific palliative care training was well received by
participants and significantly improved self-assessed comfort with core skills.

**Title:** Advance care planning in cystic fibrosis: Current practices, challenges, and opportunities.

**Citation:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. 96-101 (January 2016)

**Author(s):** Dellon, Elisabeth P, Chen, Elaine, Goggin, Jessica, Hom, Karen, Marshall, Bruce C, Sabadosa, Kathryn A, Cohen, Rubin I

**Abstract:** Studies in cystic fibrosis (CF) report late attention to advance care planning (ACP). The purpose of this study was to examine ACP with patients receiving care at US adult CF care programs. Chart abstraction was used to examine ACP with adults with CF dying from respiratory failure between 2011 and 2013. We reviewed 210 deaths among 67 CF care programs. Median age at death was 29 years (range 18-73). Median FEV1 in the year preceding death was 33% predicted (range 13-100%); 68% had severe lung disease with FEV1<40% predicted. ACP was documented for 129 (61%), often during hospitalization (61%). Those with ACP had earlier documentation of treatment preferences, before the last month of life (73% v. 35%; p=<0.01). Advance directives were completed by 93% of those with ACP versus 75% without (p<0.01); DNR orders and health care proxy designation occurred more often for those with ACP. Patients awaiting lung transplant had similar rates of ACP as those who were not (67% v. 61%; p=0.55). The frequency of ACP varied significantly among the 29 programs contributing data from four or more deaths. ACP in CF often occurs late in the disease course. Important decisions default to surrogates when opportunities for ACP are missed. Provision of ACP varies significantly among adult CF care programs. Careful evaluation of opportunities to enhance ACP and implementation of recommended approaches may lead to better practices in this important aspect of CF care.

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**Title:** Effect of ivacaftor in patients with advanced cystic fibrosis and a G551D-CFTR mutation: Safety and efficacy in an expanded access program in the United States.

**Citation:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. 116-122 (January 2016)

**Author(s):** Taylor-Cousar, Jennifer, Niknian, Minoo, Gilmartin, Geoffrey, Pilewski, Joseph M,

**Abstract:** Ivacaftor is the first therapeutic agent approved for the treatment of cystic fibrosis (CF) that targets the underlying molecular defect. Patients with severe lung disease were excluded from the randomized Phase 3 trials. This open-label study was designed to provide ivacaftor to patients in...
critical medical need prior to commercial product availability. CF patients aged ≥6 years with a G551D-CFTR mutation and FEV1 ≤ 40% predicted or listed for lung transplant received ivacaftor 150mg every 12h. The primary endpoint was safety as determined by adverse events. Secondary endpoints included assessment of lung function and weight. The rate of serious adverse events was consistent with disease severity. At 24 weeks of treatment with ivacaftor, there was a mean absolute increase in percent predicted FEV1 of 5.5 percentage points and a 3.3 kg mean absolute increase in weight from baseline. In patients with severe lung disease, ivacaftor was well tolerated and was associated with improved lung function and weight gain.

**Title:** Long-term improvement of lung clearance index in patients with mild cystic fibrosis lung disease: Does hypertonic saline play a role?

**Citation:** Journal of cystic fibrosis: official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. 123-126 (January 2016)

**Author(s):** Ellemunter, Helmut, Eder, Johannes, Fuchs, Susanne, Gappa, Monika, Steinkamp, Gratiana

**Abstract:** To assess whether long-term inhalation with hypertonic saline is able to halt the progression of mild CF lung disease, we analyzed longitudinal data of lung clearance index (LCI) and spirometry. A total of 34 patients with mild lung disease (FEV1 ≥ 70% of predicted) had at least one LCI result before and ≥2 LCI measurements after start of hypertonic saline (HS) therapy. After a mean follow-up of 39.7 (SD 7.4) months after starting HS, LCI improved significantly from 7.89 (SD 1.35) at baseline to 6.96 (SD 1.03), and 19/34 patients had a normal LCI value at the last measurement. No decrease in mean FEV1 was observed. Thus, ventilation inhomogeneity can improve in patients with mild lung disease.

**Title:** Skeletal muscle contractility and fatigability in adults with cystic fibrosis.

**Citation:** Journal of cystic fibrosis: official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. e1. (January 2016)

**Author(s):** Gruet, Mathieu, Decorte, Nicolas, Mely, Laurent, Vallier, Jean-Marc, Camara, Boubou,

**Abstract:** Recent discovery of cystic fibrosis transmembrane conductance regulator expression in human skeletal muscle suggests that CF patients may have intrinsic skeletal muscle abnormalities potentially leading to functional impairments. The aim of the present study was to determine whether CF patients with mild to moderate lung disease have altered skeletal muscle contractility and greater muscle fatigability compared to healthy controls. Thirty adults (15 CF and 15 controls)
performed a quadriceps neuromuscular evaluation using single and paired femoral nerve magnetic stimulations. Electromyographic and mechanical parameters during voluntary and magnetically-evoked contractions were recorded at rest, during and after a fatiguing isometric task. Quadriceps cross-sectional area was determined by magnetic resonance imaging. Some indexes of muscle contractility tended to be reduced at rest in CF compared to controls (e.g., mechanical response to doublets stimulation at 100Hz: 74±30Nm vs 97±28Nm, P=0.06) but all tendencies disappeared when expressed relative to quadriceps cross-sectional area (P>0.5 for all parameters). CF and controls had similar alterations in muscle contractility with fatigue, similar endurance and post exercise recovery. We found similar skeletal muscle endurance and fatigability in CF adults and controls and only trends for reduced muscle strength in CF which disappeared when normalized to muscle cross-sectional area. These results indicate small quantitative (reduced muscle mass) rather than qualitative (intrinsic skeletal muscle abnormalities) muscle alterations in CF with mild to moderate lung disease.

Title: Risk Factors for Hearing Loss in Patients with Cystic Fibrosis.

Citation: Journal of the American Academy of Audiology, Jan 2016, vol. 27, no. 1, p. 6-12

Author(s): Tarshish, Yael, Huang, Lin, Jackson, Frank I, Edwards, Julianne, Fligor, Brian,

Abstract: Patients with cystic fibrosis (CF) are at increased risk for sensorineural hearing loss (SNHL) due, at least in part, to the ototoxic side effects of routine CF therapies. However, the prevalence of SNHL and additional factors contributing to the development of SNHL are unknown. To identify risk factors associated with the development of SNHL in a large cohort of CF patients who had been referred for audiometric testing. A retrospective study of audiometric results and medication information in a cohort of patients with CF. Records of 178 CF patients seen at Boston Children’s Hospital for audiometric testing from 2007 to 2010 were reviewed. Mean age of patients was 18 yr (standard deviation = 10 yr), and 98 (55%) of the patients were female. Audiometric results, medications, and hospitalizations were recorded. Multivariable logistic regression was used to evaluate the association between SNHL and the number of hospitalizations and chronic antibiotic use in the year prior to the patients' audiometry. In this sample, 37/178 (21%) patients had SNHL. Twenty-nine (78%) of the 37 patients had bilateral SNHL and 8 (22%) had unilateral SNHL. Across all age groups, the majority of patients had a bilateral hearing loss (HL). A multivariable model showed that older age and more frequent hospitalizations were associated with SNHL. The number of courses of chronic antibiotics in the year prior to audiometric testing was not correlated with rate of HL. This study suggests that age and frequency of hospitalizations are key predictors of HL development. Increased awareness and regular screening for SNHL should be included in the routine care of CF patients, particularly those at the highest risk. American Academy of Audiology.
**Title:** Peripheral quantitative computed tomography (pQCT) bone measurements in children with cystic fibrosis.

**Citation:** Pediatric pulmonology, Jan 2016, vol. 51, no. 1, p. 28-33 (January 2016)

**Author(s):** Bai, Wei, Binkley, Teresa L, Wallace, James W, Carver, Terrence W, Specker, Bonny L

**Abstract:** Individuals with cystic fibrosis (CF) have low bone density and increased fracture risk. Cross-sectional study investigating whole body bone mineral content (WBBMC), bone geometry and strength in 12 children with CF compared to 23 age- and sex-matched controls with and without adjusting for age, height, and body composition. CF group had lower WBBMC than controls ($P = 0.007$) with larger differences at older ages (age-by-group, $P = 0.08$). CF group had decreased height ($P = 0.006$), a trend of lower lean mass per height ($P = 0.08$), and no difference in relationship between WBBMC and lean mass compared to controls ($P = 0.65$). Periosteal and endosteal circumferences were smaller in CF (each, $P = 0.02$). Positive relationships of cortical area and bone strength with age were attenuated with CF (group-by-age; each, $P < 0.01$). Children with CF have similar WBBMC relative to lean mass as controls. Cortical bone area and bone strength were less in CF group compared to controls, with greater differences in older children.

**Title:** Nationwide mortality trends for adult cystic fibrosis patients requiring endotracheal intubation

**Citation:** Critical Care Medicine, December 2015, vol./is. 43/12 SUPPL. 1(176)

**Author(s):** Siuba M., Attaway A., Bannon S., Jacono F., Dasenbrook E.

**Abstract:** Learning Objectives: Traditionally there has been a restrictive approach to endotracheal intubation (ETI) of CF patients given lack of benefit. However, with the advent of more advanced ICU and CF treatment modalities, ICU survival in CF has increased overall. Debate still remains about the utility of intubation, as outcomes in this population have historically been poor. Current studies have been limited by either data from a single-center or small number of patients. This study was conducted to assess the trends in mortality rate of adult patients with CF in a large nationwide database. Methods: We performed a cohort study using the Nationwide Inpatient Sample's (NIS) Healthcare Utilization Project (HCUP) database between the yr 2002 to 2012. The NIS represents 20% of all hospital data in the US. We queried patients with the diagnostic code of "cystic fibrosis," and then searched for the procedure code "endotracheal intubation and mechanical ventilation." Our data included ages 18 and above, and maternal related discharges or those with diagnostic codes for lung transplant were excluded. Hospital mortality was calculated and trends were analyzed with Chi-square testing. The primary diagnostic code, if different from "cystic fibrosis," was queried...
as well. Results: 932 admissions contained the diagnostic code of cystic fibrosis and the procedure code for ETI from 2002-2012. Overall in-hospital mortality rate was 44.1% (524/932). The mortality rate was 59.8% (21/32) in 2002 as compared with 46.0% (46/100) in 2012 (P=0.0957). The three most common primary diagnostic codes were "Cystic fibrosis," "Respiratory failure; insufficiency; arrest," and "Complication of device; implant or graft." Conclusions: To date, this is the largest study evaluating mortality rates in this population. Over 50% of CF patients who underwent ETI in 2012 survived to hospital discharge. These findings may help intensivists weigh the risks and benefits of endotracheal intubation in this patient population.

**Title:** Glucose intolerance in cystic fibrosis as a determinant of pulmonary function and clinical status.

**Citation:** Diabetes research and clinical practice, Dec 2015, vol. 110, no. 3, p. 276-284

**Author(s):** Lavie, Moran, Fisher, Dor, Vilozni, Daphna, Forschmidt, Rinat, Sarouk, Ifat,

**Abstract:** Cystic fibrosis related diabetes (CFRD) is associated with a decrease in pulmonary function and nutritional status. We investigated the clinical significance of impaired glucose tolerance (IGT) in cystic fibrosis (CF) patients. Fifty-five CF patients (aged 22.8±9.2 years, 29 males, mean FEV1 67.9±22% predicted, mean BMI-SDS -0.23±1.1) underwent a 2-h Oral Glucose Tolerance Test (OGTT) with 30-min interval measurements of glucose and insulin. Additional clinical and laboratory data were obtained from the medical charts. Thirty-eight participants (69%) had normal glucose tolerance (NGT), 13 (23.7%) had IGT, and 4 (7.3%) had newly diagnosed CFRD. Compared to patients with NGT, patients with IGT had significantly lower BMI-SDS (-1.1±0.8 vs. 0.1±1.1, p<0.001), mean FEV1 (57±19 vs. 74±21% predicted, p<0.01), and albumin (3.9±0.3 vs. 4.3±0.2g/dl, p=0.004), and higher fibrinogen (376±56 vs. 327±48g/dl, p=0.02). Patients with IGT had impaired β-cell function, with reduced first phase insulin secretion, a delayed insulin peak, and significantly lower total insulin secretion, HOMA-%B and insulinogenic index. Seven patients had HbA1c in the "diabetic" range (≥6.5%; 47.5mmol/mol), however, HbA1c was not a sensitive or specific marker of glucose tolerance status. IGT in CF patients is associated with increased inflammation and decreased nutritional status and pulmonary function.

**Title:** Variation in lung function is associated with worse clinical outcomes in cystic fibrosis.

**Citation:** Jornal brasileiro de pneumologia : publicação oficial da Sociedade Brasileira de Pneumologia e Tisilogia, Dec 2015, vol. 41, no. 6, p. 509-515 (December 2015)

**Author(s):** Heinzmann-Filho, João Paulo, Pinto, Leonardo Araujo, Marostica, Paulo José
Abstract: To determine whether the variation in lung function over one year is associated with worse clinical outcomes, as well as with a decline in lung function in the following years, in patients with cystic fibrosis (CF). This was a retrospective study involving CF patients (4-19 years of age), evaluated over a three-year period. We evaluated demographic characteristics, chronic Pseudomonas aeruginosa infection, antibiotic use, hospitalization, six-minute walk distance (6MWD), and lung function. The inclusion criterion was having undergone pulmonary function testing at least three times in the first year and at least once in each of the next two years. We evaluated 35 CF patients. The variation in FEV1 in the first year (ΔFEV1) was greater among those who, in the third year, showed reduced FEV1, had a below-average 6MWD, or were hospitalized than among those with normal FEV1, normal 6MWD, or no hospital admissions, in that same year (p < 0.05), although no such difference was found for antibiotic use in the third year. Subjects showing a ΔFEV1 ≥ 10% also showed a greater decline in FEV1 over the two subsequent years (p = 0.04). The ΔFEV1 also showed an inverse correlation with absolute FEV1 in the third year (r = -0.340, p = 0.04) and with the rate of FEV1 decline (r = -0.52, p = 0.001). Linear regression identified ΔFEV1 as a predictor of FEV1 decline (coefficient of determination, 0.27). Significant variation in lung function over one year seems to be associated with a higher subsequent rate of FEV1 decline and worse clinical outcomes in CF patients. Short-term ΔFEV1 might prove useful as a predictor of CF progression in clinical practice.

Title: Cardiorespiratory and sensory responses to exercise in adults with mild cystic fibrosis.

Citation: Journal of applied physiology (Bethesda, Md. : 1985), Dec 2015, vol. 119, no. 11, p. 1289-1296 (December 1, 2015)

Author(s): Quon, Bradley S, Wilkie, Sabrina S, Molgat-Seon, Yannick, Schaeffer, Michele R,

Abstract: The purpose of this study was to evaluate cardiorespiratory fitness and reasons for exercise curtailment in a contemporary adult cystic fibrosis (CF) cohort with mild lung disease. Adults with mild CF (n = 19, forced expiratory volume in 1 s = 95 ± 17% predicted) were age-, sex-, ethnicity-, and body mass index-matched to healthy controls (n = 19) and underwent a detailed cardiopulmonary cycle exercise test. While CF subjects had a reduced peak oxygen uptake compared with controls, the values were normal when expressed as %predicted in 14/19 (74%) of subjects. Both groups demonstrated a normal cardiovascular limitation to exercise and stopped exercise primarily because of leg fatigue. Despite not being exercise-limited by respiratory factors, there was some evidence of ventilatory abnormalities as patients with mild CF had increased end-inspiratory lung volumes and reached an inflection/plateau in tidal volume relative to minute ventilation at lower exercise intensities compared with controls. Subjects with CF were not more likely to
demonstrate expiratory flow limitation compared with controls and did not have evidence of dynamic hyperinflation during exercise. Despite increased end-inspiratory lung volumes and an earlier tidal volume inflection/plateau, CF subjects did not experience higher levels of dyspnea. In an exploratory analysis, a significant inverse correlation was observed between sweat chloride and peak work rate. Adult CF subjects with relatively well preserved spirometry have normal exercise performance relative to reference values and are primarily limited by nonrespiratory factors. However, ventilatory abnormalities were detected even in this mild CF cohort and should be evaluated in future therapeutic trials focused on disease-modifying therapies in mild CF.

**Title:** An exploration of partnership through interactions between young 'expert' patients with cystic fibrosis and healthcare professionals.

**Citation:** Journal of clinical nursing, Dec 2015, vol. 24, no. 23-24, p. 3528-3537 (December 2015)

**Author(s):** MacDonald, Kath, Irvine, Lindesay, Smith, Margaret Coulter

**Abstract:** To explore how young 'expert patients' living with Cystic Fibrosis and the healthcare professionals with whom they interact perceive partnership and negotiate care. Modern healthcare policy encourages partnership, engagement and self-management of long-term conditions. This philosophy is congruent with the model adopted in the care of those with Cystic Fibrosis, where self-management, trust and mutual respect are perceived to be integral to the development of the ongoing patient/professional relationship. Self-management is associated with the term; 'expert patient'; an individual with a long-term condition whose knowledge and skills are valued and used in partnership with healthcare professionals. However, the term 'expert patient' is debated in the literature as are the motivation for its use and the assumptions implicit in the term. A qualitative exploratory design informed by Interpretivism and Symbolic Interactionism was conducted. Thirty-four consultations were observed and 23 semi-structured interviews conducted between 10 patients, 2 carers and 12 healthcare professionals. Data were analysed thematically using the five stages of 'Framework' a matrix-based qualitative data analysis approach and were subject to peer review and respondent validation. The study received full ethical approval. Three main themes emerged; experiences of partnership, attributes of the expert patient and constructions of illness. Sub-themes of the 'ceremonial order of the clinic', negotiation and trust in relationships and perceptions of the expert patient are presented. The model of consultation may be a barrier to person-centred care. Healthcare professionals show leniency in negotiations, but do not always trust patients' accounts. The term 'expert patient' is unpopular and remains contested. Gaining insight into structures and processes that enable or inhibit partnership can lead to a collaborative approach to service redesign and a revision of the consultation model.
Title: Survival in Patients with Advanced Non-cystic Fibrosis Bronchiectasis Versus Cystic Fibrosis on the Waitlist for Lung Transplantation.

Citation: Lung, Dec 2015, vol. 193, no. 6, p. 933-938 (December 2015)

Author(s): Hayes, Don, Kopp, Benjamin T, Tobias, Joseph D, Woodley, Frederick W, Mansour,

Abstract: Survival in non-cystic fibrosis (CF) bronchiectasis is not well studied. The United Network for Organ Sharing database was queried from 1987 to 2013 to compare survival in adult patients with non-CF bronchiectasis to patients with CF listed for lung transplantation (LTx). Each subject was tracked from waitlist entry date until death or censoring to determine survival differences between the two groups. Of 2112 listed lung transplant candidates with bronchiectasis (180 non-CF, 1932 CF), 1617 were used for univariate Cox and Kaplan-Meier survival function analysis, 1173 for multivariate Cox models, and 182 for matched-pairs analysis based on propensity scores. Compared to CF, patients with non-CF bronchiectasis had a significantly lower mortality by univariate Cox analysis (HR 0.565; 95 % CI 0.424, 0.754; p < 0.001). Adjusting for potential confounders, multivariate Cox models identified a significant reduction in risk for death associated with non-CF bronchiectasis who were lung transplant candidates (HR 0.684; 95 % CI 0.475, 0.985; p = 0.041). Results were consistent in multivariate models adjusting for pulmonary hypertension and forced expiratory volume in one second. Non-CF bronchiectasis with advanced lung disease was associated with significantly lower mortality hazard compared to CF bronchiectasis on the waitlist for LTx. Separate referral and listing criteria for LTx in non-CF and CF populations should be considered.

Title: A five-year retrospective analysis of adherence in cystic fibrosis.

Citation: Pediatric pulmonology, Dec 2015, vol. 50, no. 12, p. 1224-1229 (December 2015)

Author(s): Shakkottai, Aarti, Kidwell, Kelley M, Townsend, Monica, Nasr, Samya Z

Abstract: We conducted a retrospective analysis of medication adherence and health outcomes over a 5-year period in children with cystic fibrosis (CF). Adherence was calculated for several commonly prescribed CF medications by comparing the actual number of times a prescription was filled in a 12-month period to the number of times it should have been filled based on the prescribed supply. We used prescription refill histories as documented by three major specialty pharmacies used by our patients. A binomial mixed effects model was used to investigate the longitudinal association between adherence and age group (0-5, 6-12, and 13-21 years) with gender, year in the study, lung function, body mass index (BMI), and annual hospitalization rate included as potential confounders.
The 0-5 years group had the highest overall adherence (P = 0.009). The 6-12 years group had significantly better adherence to inhaled medications as compared to oral medications (P = 0.020). Within each group, for any given year in the study, having a higher BMI was associated with greater odds of adherence (P < 0.0001). There were no associations between adherence and gender, lung function or hospitalization rate (P > 0.05). There are significant age differences in adherence. Younger patients have better overall adherence likely secondary to increased parental supervision. Having better nutritional status is associated with improved adherence.

Title: Lung function comparison between two decades in cystic fibrosis children: A single centre study.

Citation: Pediatric pulmonology, Dec 2015, vol. 50, no. 12, p. 1237-1243 (December 2015)

Author(s): Tridello, Gloria, Volpi, Sonia, Assael, Baroukh M, Meneghelli, Ilaria, Passiu, Marianna,

Abstract: The purpose of this study was to compare two cohorts of cystic fibrosis (CF) patients born and treated in two different decades, diagnosed through a CF neonatal screening program. We compared pulmonary function decline from 10 to 15 years of age in patients with cystic fibrosis born between 1979 and 1984 (Cohort 1) and between 1991 and 1996 (Cohort 2). Forced expiratory volume in 1 sec (FEV1%) and forced expiratory flow from 25% to 75% (FEF 25-75%) were analyzed by a linear mixed model approach. The differences between the two cohorts were estimated and the overall cohort effect was tested. Ninety-two patients (51 males, 41 females) fulfilled the selection criteria. Pancreatic insufficiency and CF related diabetes were present in 91% and 20% of patients, respectively. The mean absolute decrement of FEV1% was 9.2 (standard deviation [SD] 11.2) in Cohort 1 and 0.6 (SD 10.4) in Cohort 2 (P < 0.001). The mean decrement of FEF 25-75% was 16.3 (SD 19.5) in Cohort 1 and 1.3 (SD 16.8) in Cohort 2 (P < 0.001) and the Pseudomonas aeruginosa (Pa) colonization was 28% and 15% respectively (P = 0.1). Our results show that pulmonary function has clearly ameliorated over a decade in young CF patients, in a period during which several significant therapeutic changes have been introduced, such as dornase alfa, tobramycin and hypertonic saline. To our knowledge this is the first study showing a cohort effect in patients diagnosed after neonatal screening.

Title: Airway clearance techniques used by people with cystic fibrosis in the UK.

Citation: Physiotherapy, Dec 2015, vol. 101, no. 4, p. 340-348 (December 2015)

Author(s): Hoo, Z H, Daniels, T, Wildman, M J, Teare, M D, Bradley, J M
Abstract: To describe the current use of airway clearance techniques among people with cystic fibrosis (CF) in the UK, and the baseline characteristics for users of different airway clearance techniques. Analysis of the UK CF Registry 2011 data. All people with CF in the UK aged ≥11 years (n=6372). Of the 6372 people on the UK CF registry in 2011, 89% used airway clearance techniques. The most commonly used primary techniques were forced expiratory techniques (28%) and oscillating positive expiratory pressure (PEP) (23%). Postural drainage and high-frequency chest wall oscillation were used by 4% and 1% of people with CF, respectively. The male:female ratio of individuals who used exercise as their primary airway clearance technique was 2:1, compared with 1:1 for other techniques. Individuals with more severe lung disease tended to use devices such as non-invasive ventilation or high-frequency chest wall oscillation. Forced expiratory techniques and oscillating PEP are the most common airway clearance techniques used by people with CF in the UK, and postural drainage and high-frequency chest wall oscillation are the least common techniques. This is significant in terms of planning airway clearance technique trials, where postural drainage has been used traditionally as the comparator. The use of airway clearance techniques varies between countries, but the reasons for these differences are unknown.

Title: The Short-Term Effect of Breathing Tasks Via an Incentive Spirometer on Lung Function Compared With Autogenic Drainage in Subjects With Cystic Fibrosis.

Citation: Respiratory care, Dec 2015, vol. 60, no. 12, p. 1819-1825 (December 2015)

Author(s): Sokol, Gil, Vilozni, Daphna, Hakimi, Ran, Lavie, Moran, Sarouk, Ifat, Bar, Bat-El, Dagan, Adi,

Abstract: Forced expiration may assist secretion movement by manipulating airway dynamics in patients with cystic fibrosis (CF). Expiratory resistive breathing via a handheld incentive spirometer has the potential to control the expiratory flow via chosen resistances (1-8 mm) and thereby mobilize secretions and improve lung function. Our objective was to explore the short-term effect of using a resistive-breathing incentive spirometer on lung function in subjects with CF compared with the autogenic drainage technique. This was a retrospective study. Subjects with CF performed 30-45 min of either the resistive-breathing incentive spirometer (n = 40) or autogenic drainage (n = 32) technique on separate days. The spirometer encourages the patient to exhale as long as possible while maintaining a low lung volume. The autogenic drainage technique includes repetitive inspiratory and expiratory maneuvers at various tidal breathing magnitudes while exhalation is performed in a sighing manner. Spirometry was performed before and 20-30 min after the therapy. Use of a resistive-breathing incentive spirometer improved FVC and FEV1 by 5-42% in 26 subjects.
The forced expiratory flow during the middle half of the FVC maneuver (FEF25-75%) improved by >20% in 9 (22%) subjects. FVC improved the most in subjects with an FEV1 of 40-60% of predicted. Improvements negatively correlated with baseline percent-of-predicted FVC values provided improvements were above 10% (r(2) = 0.28). Values improved in a single subjects using the autogenic drainage technique. These 2 techniques may allow lower thoracic pressures and assist in the prevention of central airway collapse. The resistive-breathing incentive spirometer is a self-administered simple method that may aid airway clearance and has the potential to improve lung function as measured by FVC, FEV1, and FEF25-75% in patients with CF.

Title: Decline in Forced Expiratory Volume in 1 Second in Cystic Fibrosis—Watch the Pendulum Swing.

Citation: Journal of Pediatrics, 2016, vol./is. 169/(7-9),

Title: Forced Expiratory Volume in 1 Second Variability Helps Identify Patients with Cystic Fibrosis at Risk of Greater Loss of Lung Function.

Citation: Journal of Pediatrics, 2016, vol./is. 169/(116-116)

Abstract: Objective: To evaluate several alternative measures of forced expiratory volume in 1 second percent predicted (FEV1 %pred) variability as potential predictors of future FEV1 %pred decline in patients with cystic fibrosis.

Study Design: We included 13 827 patients age ≥6 years from the Epidemiologic Study of Cystic Fibrosis 1994-2002 with ≥4 FEV1 %pred measurements spanning ≥366 days in both a 2-year baseline period and a 2-year follow-up period. We predicted change from best baseline FEV1 %pred to best follow-up FEV1 %pred and change from baseline to best in the second follow-up year by using multivariable regression stratified by 4 lung-disease stages. We assessed 5 measures of variability (some as deviations from the best and some as deviations from the trend line) both alone and after controlling for demographic and clinical factors and for the slope and level of FEV1 %pred.

Results: All 5 measures of FEV1 %pred variability were predictive, but the strongest predictor was median deviation from the best FEV1 %pred in the baseline period. The contribution to explanatory power (R(2)) was substantial and exceeded the total contribution of all other factors excluding the FEV1 %pred rate of decline. Adding the other variability measures provided minimal additional value.

Conclusions: Median deviation from the best FEV1 %pred is a simple metric that markedly improves prediction of FEV1 %pred decline even after the inclusion of demographic and clinical characteristics and the FEV1 %pred rate of decline. The routine calculation of this variability measure could allow clinicians to better identify patients at risk and therefore in need of increased intervention.
Title: Ciprofloxacin dry powder inhaler in cystic fibrosis

Citation: BMJ Open Respiratory Research, 2016, vol./is. 3/1(no pagination), 2052-4439 (2016)

Author(s): Elborn J.S.

Title: Higher risk of acute cellular rejection in lung transplant recipients with cystic fibrosis

Citation: Annals of Transplantation, December 2015, vol./is. 20/(769-776),

Author(s): Lunardi F., Nannini N., Balestro E., Loy M., Marulli G., Calabrese F., Vuljan S.E., Schia von M., Perissinotto E., Rea F.

Abstract: Background: Acute cellular rejection (ACR) affects up to 40% of recipients within the first year after lung transplant (LTx). The aim of this study was to determine the frequency of ACR and associated major risk factors in cystic fibrosis (CF) recipients. Bronchiolitis obliterans syndrome (BOS) and 1-year/long-term survival were also evaluated. Material/Methods: ACR was reviewed in 643 scheduled biopsies from 44 CF (Group 1) versus 89 other recipients (Group 2). We performed univariate/multivariate analyses of risk factors for ACR and BOS, and survival analysis. Results: Group 1 showed higher ACR frequency, especially for ACR >A2. Multivariable generalized linear models considering both native lung disease and age showed that higher values of ACR index were significantly related to the pretransplant diagnosis of CF. BOS and long-term survival were not influenced by the increased incidence of ACR. Poorer long-term survival was observed in Group 2. Conclusions: CF recipients have a higher ACR risk, which may be due to enhanced immune activation related to a genetic disorder, and younger age.

Title: CFTR Modulator Therapies for Cystic Fibrosis

Citation: Pediatric, Allergy, Immunology, and Pulmonology, December 2015, vol./is. 28/4(230-236)

Author(s): Trimble A.T., Donaldson S.H.

Abstract: The cloning of cystic fibrosis transmembrane conductance regulator (CFTR) set into motion a cascade of discoveries that have helped to reveal the underlying pathophysiologic basis of cystic fibrosis (CF). This discovery and the knowledge that followed have also provided the opportunity to target this basic defect, with the hope of reversing or preventing the serious clinical consequences that result from absent CFTR function. With the recent approval of 2 therapies that directly modulate CFTR function in more than half of the CF population, we are now at the beginning of a pathway to providing increasingly effective therapies that have the potential to provide a fundamental change in the outcome of most patients with CF.
**Title:** Lung Transplantation in Cystic Fibrosis: Trends and Controversies

**Citation:** Pediatric, Allergy, Immunology, and Pulmonology, December 2015, vol./is. 28/4(237-243)

**Author(s):** Blatter J., Sweet S.

**Abstract:** This article is not an overview of all facets of lung transplantation in cystic fibrosis (CF), but rather it is intended as a review of current allocation controversies, as well as of trends in diagnostics and management in lung transplant recipients and in patients with end-stage lung disease. Despite changes in donor and recipient selection, long-term survival in pediatric lung transplant has continued to be limited by chronic lung allograft dysfunction (CLAD). Due to, in part, this short survival benefit, transplant continues to be an appropriate option for only a subset of pediatric patients with CF. The feasibility of transplant as a therapeutic option is also affected by the limited pediatric organ supply, which has moreover contributed to controversy over lung allocation. Debates over the allocation of this scarce resource, however, may also help to drive innovation in the field of lung transplant. Longer pretransplant survival-as aided by new lung bypass technologies, for example-could help to alleviate organ shortages, as well as facilitate the transport of organs to suitable pediatric recipients. Improved diagnosis and treatment for CLAD and for antibody-mediated rejection have the potential to extend survival in pediatric lung transplant. Regardless, the relative rarity of transplant could pose future challenges for pediatric lung transplant programs, which require adequate numbers of patients to maintain proper expertise.

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**Title:** Advances in Imaging Cystic Fibrosis Lung Disease

**Citation:** Pediatric, Allergy, Immunology, and Pulmonology, December 2015, vol./is. 28/4(220-229)

**Author(s):** Walkup L.L., Woods J.C.

**Abstract:** Cystic fibrosis (CF) is a life shortening, multiorgan disease, in which morbidity and mortality are dominated by pulmonary pathologies, including mucous obstruction, chronic lung infections, progressive bronchiectasis, and declining lung function. Promising new therapies, including those that target the cystic fibrosis transmembrane conductance regulator (CFTR) protein, have shown impressive efficacy in treating CF patients with specific genotypes. While spirometry is the clinical gold standard for evaluating CF lung disease, it has known insensitivities to mild lung disease and statistical weaknesses in small cohorts. Imaging has begun to play an important role in evaluating the structural abnormalities associated with CF lung disease progression. X-ray computed tomography (CT) has been established as a modality with validated metrics to evaluate disease severity, even in young patients with mild disease. Magnetic resonance imaging (MRI), as a
nonionizing alternative, has very strong potential for similar metrics and longitudinal use through the lifespan. In this brief review, recent advancements in imaging CF lung disease in pediatrics are discussed, specifically in the contexts of X-ray CT, ultra-short echo time MRI, and hyperpolarized-gas MRI, with an emphasis on how emerging techniques will likely impact the management of CF lung disease in the era of CFTR-modulator therapies, targeted at smaller subpopulations of CF with specific genotypes. In the future, techniques that provide sensitive, quantitative measurements of regional lung structure and function longitudinally will become increasingly important as outcome measures for clinical trials and for monitoring individual CF patients.

Title: Survival in Cystic Fibrosis: Trends, Clinical Factors, and Prediction Models

Citation: Pediatric, Allergy, Immunology, and Pulmonology, December 2015, vol./is. 28/4(244-249)

Author(s): Chin M., Earlam K., Aaron S.D.

Abstract: Cystic fibrosis (CF) is an autosomal recessive genetic disease that results in multiple medical complications, and ultimately decreased survival of affected patients. Due to multiple advances in early diagnosis, nutrition, and aggressive treatment of complications, survival of these patients has improved dramatically in the past 40 years. However, despite improved care, patients still die at a relatively young age, most commonly due to respiratory failure. In order to extend survival, the sickest patients with CF are considered for lung transplant. An accurate understanding of a CF patient's expected survival and health trajectory is critical for appropriate patient selection and timing of transplantation. This review discusses how survival in CF has changed over the past four decades, the clinical factors that are associated with survival, as well as the use of models to predict survival and optimal timing of lung transplant in patients with CF.

Microbiological

Title: Cystic Fibrosis Frequently Asked Questions: Question 4: What is the appropriate duration of therapy for respiratory exacerbations in Cystic Fibrosis patients infected with Pseudomonas aeruginosa?

Citation: Paediatric respiratory reviews, Jan 2016, vol. 17, p. 60-62 (January 2016)

Author(s): Sutton, Kathryn M, Fitzgerald, Dominic A

Title: Burkholderia cepacia complex: Clinical course in cystic fibrosis patients

Citation: BMC Pulmonary Medicine, December 2015, vol./is. 15/1(no pagination),
Author(s): Folescu T.W., da Costa C.H., Cohen R.W.F., Neto O.C.C., Albano R.M.,

Abstract: Background: Pulmonary deterioration after B. cepacia complex (BCC) colonization has a heterogeneous pattern. The aim was to investigate the clinical outcome of BCC colonization in CF patients chronically colonized with P. aeruginosa. Methods: CF patients chronically colonized with P. aeruginosa were divided into three groups: intermittent (I), chronic (II) and no colonization (III) with BCC. Body mass index (BMI) percentile and spirometric parameters were analyzed at three different times in each group. Results: Fifty-six patients chronically colonized with P. aeruginosa were included. Of these, 27 also had evidence of BCC colonization (13 intermittent and 14 chronic). BMI percentile was significantly lower among patients chronically colonized by both P. aeruginosa and BCC. Mean values of FEV<sub>1</sub> and FVC % were also significantly lower in these patients, both at the time of chronic BCC colonization and 24 months forward. Conclusions: Chronic BCC colonization is associated with significant loss of lung function. Lower BMI might be a risk factor for chronic BCC colonization, preceding these events.

Title: Tigecycline-induced acute pancreatitis in a cystic fibrosis patient: A case report and literature review.

Citation: Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. e9. (January 2016)

Author(s): Hemphill, Michael T, Jones, Kellie R

Abstract: The purpose of this case report is to increase awareness of tigecycline-associated pancreatitis, specifically in patients who may be predisposed to develop pancreatitis. A 22-year-old male with cystic fibrosis developed acute bronchitis, with sputum cultures significant for Mycobacterium chelonae. He was started on tigecycline on two separate occasions, in each case developing pancreatitis as evidenced by symptomatology, elevated pancreatic enzymes and, in one case, by CT imaging. On both occasions, symptomatology improved and enzymes normalized after discontinuation of tigecycline. Current literature including two recent review pieces is discussed. The unique aspects of the case are highlighted, including the particular risk of drug-associated pancreatitis in those with cystic fibrosis. The results of this case, in the context of current literature, suggest that clinicians should be aware of the potential for pancreatitis when using tigecycline. Clinicians should be particularly mindful of this complication in patients with comorbidities that might increase the risk of pancreatitis above that of the general population.

Title: Infection control strategies that successfully controlled an outbreak of Mycobacterium abscessus at a cystic fibrosis center.

Citation: American journal of infection control, Feb 2016, vol. 44, no. 2, p. 154-159

Author(s): Kapnadak, Siddhartha G, Hisert, Katherine B, Pottinger, Paul S, Limaye, Ajit P, Aitken, Moira L

Abstract: Mycobacterium abscessus infection in patients with cystic fibrosis (CF) can result in accelerated clinical decline and the potential for direct or indirect transmission between patients has been recently demonstrated. Data on the outcomes of M abscessus outbreaks and the efficacy of specific infection control procedures in patients with CF remain limited. This study provides follow-up from an outbreak of pulmonary M abscessus in our center, highlighting outcomes and strategies that appear to have prevented further spread of the organism. Data from our adult CF center (1989-2015) were analyzed, including chart reviews of all patients with positive mycobacterial sputum
cultures, cultures from environment surfaces, and epidemiologic evaluation of infected patients. Following an M abscessus outbreak in 2009, infection control policies were intensified based on CF guidelines and surveillance data were collected and reviewed. Five cases of M abscessus were involved in the outbreak; 3 patients died during follow-up. An environment search failed to reveal an intermediary source of transmission between patients. After implementation of infection control measures composed of staff/patient education, environment sterilization, and patient isolation, no new cases were detected. Direct or indirect patient-to-patient transmission of M abscessus is a threat in the CF population. A multifaceted infection control strategy based on CF guidelines was effective in halting transmission in our center.

Title: Pseudomonas aeruginosa antibiotic resistance in Australian cystic fibrosis centres.

Citation: Respirology (Carlton, Vic.), Feb 2016, vol. 21, no. 2, p. 329-337 (February 2016)

Author(s): Smith, Daniel J, Ramsay, Kay A, Yerkovich, Stephanie T, Reid, David W, Wainwright,

Abstract: In cystic fibrosis (CF), chronic Pseudomonas aeruginosa infection is associated with increased morbidity, antibiotic treatments and mortality. By linking Australian CF registry data with a national microbiological data set, we examined the association between where treatment was delivered, its intensity and P. aeruginosa antibiotic resistance. Sputa were collected from paediatric and adult CF patients attending 18 Australian CF centres. P. aeruginosa antibiotic susceptibilities determined by local laboratories were correlated with clinical characteristics, treatment intensity and infection with strains commonly shared among Australian CF patients. Between-centre differences in treatment and antibiotic resistance were also compared. Large variations in antibiotic usage, maintenance treatment practices and multi-antibiotic resistant P. aeruginosa (MARPA) prevalence exist between Australian CF centres, although the overall proportions of MARPA isolates were similar in paediatric and adult centres (31% vs 35%, P = 0.29). Among paediatric centres, MARPA correlated with intravenous antibiotic usage and the Australian state where treatment was delivered, while azithromycin, reduced lung function and treating state predicted intravenous antibiotic usage. In adult centres, body mass index (BMI) and treating state were associated with MARPA, while intravenous antibiotic use was predicted by gender, BMI, dornase-alpha, azithromycin, lung function and treating state. In adults, P. aeruginosa strains AUST-01 and AUST-02 independently predicted intravenous antibiotic usage. Increased treatment intensity in paediatric centres and the Australian state where treatment was received are both associated with greater risk of MARPA, but not worse clinical outcomes.

Title: New Inhaled Antimicrobial Formulations for Use in the Cystic Fibrosis Patient Population.

Citation: The Annals of pharmacotherapy, Feb 2016, vol. 50, no. 2, p. 133-140 (February 2016)

Author(s): Campbell, Christopher T, McCaleb, Rachael, Manasco, Kalen B

Abstract: To review the current literature on inhaled antibiotic therapies currently in clinical trials for cystic fibrosis (CF) patients. A literature search was performed using PubMed (1975 to September 2015), International Pharmaceutical Abstracts (1970 to September 2015), and MEDLINE (1946 to September 2015) to identify studies for inclusion. The following search terms were used: cystic fibrosis, inhaled amikacin, inhaled liposomal amikacin, inhaled vancomycin, and/or inhaled levofloxacin. All English-language phase II to III studies evaluating efficacy and/or safety, case reports, and retrospective studies of inhaled amikacin, inhaled vancomycin, and inhaled levofloxacin in CF patients were included. Currently available inhaled antibiotics, tobramycin and aztreonam, have demonstrated improvement in respiratory function of CF patients. Newer agents have shown
potentially similar efficacy, with improvement in ease of use. Limited data suggest that inhaled liposomal amikacin and levofloxacin are both noninferior to tobramycin in terms of improvements in respiratory function. Inhaled levofloxacin has a lower rate of hospitalizations secondary to respiratory exacerbations and a reduction in the Pseudomonas aeruginosa sputum density compared with inhaled tobramycin. Inhaled vancomycin use has been documented in case reports and 2 small retrospective eradication trials, although data are limited to support its use. The horizon of inhaled antibiotic choices for CF patients is promising. The introduction of different drug classes and formulations to treat resistant Gram-negative and Gram-positive organisms increases the number of options for patients for both eradication and treatment of chronic colonization.

**Title:** How and why to monitor Pseudomonas aeruginosa infections in the long term at a cystic fibrosis centre.

**Citation:** The Journal of hospital infection, Jan 2016, vol. 92, no. 1, p. 54-60 (January 2016)

**Author(s):** Kalferstova, L, Vilimovska Dedeckova, K, Antuskova, M, Melter, O, Drevinek, P

**Abstract:** Pseudomonas aeruginosa is a major cystic fibrosis (CF) pathogen causing chronic respiratory infections and posing a risk for cross-infection between patients with CF. To propose an algorithm for long-term surveillance of P. aeruginosa and assess its suitability for monitoring the epidemiological situation at a CF centre with approximately 300 patients. Over a nine-year period, over 300 P. aeruginosa isolates from 131 infected patients were tested by multi-locus sequence typing (MLST) and/or random amplified polymorphic DNA (RAPD) assay. MLST analysis led to the identification of 97 different sequence types which were distributed among 17 RAPD-generated (pseudo)clusters. This indicates that the easy-to-perform RAPD assay is only suitable for intra-individual, not interindividual, strain analyses. No epidemic strains were observed. Longitudinal analysis revealed that 110 of the 131 patients were infected with the same strain over the observation period, whereas 21 patients had a strain replacement or a new infection. Chronic infection was found in 99 of the 131 patients, and the remaining 32 patients met the criteria for intermittent infection (as defined by the Leeds criteria). Eighteen of the 32 patients (56%) with intermittent infection were infected with the same strain for up to nine years. The strain type only changed in 16% of 131 patients with chronic or intermittent infection. As many as 56% of patients considered to have intermittent infection were actually chronically infected with the same strain for many years.

**Title:** Cystic Fibrosis: A Review of Associated Phenotypes, Use of Molecular Diagnostic Approaches, Genetic Characteristics, Progress, and Dilemmas.

**Citation:** The Journal of molecular diagnostics : JMD, Jan 2016, vol. 18, no. 1, p. 3-14 (January 2016)

**Author(s):** Brennan, Marie-Luise, Schrijver, Iris

**Abstract:** Cystic fibrosis (CF) is an autosomal recessive disease with significant associated morbidity and mortality. It is now appreciated that the broad phenotypic CF spectrum is not explained by obvious genotype-phenotype correlations, suggesting that CF transmembrane conductance regulator (CFTR)-related disease may occur because of multiple additive effects. These contributing effects include complex CFTR alleles, modifier genes, mutations in alternative genes that produce CF-like phenotypes, epigenetic factors, and environmental influences. Most patients in the United States are now diagnosed through newborn screening and use of molecular testing methods. We review the molecular testing approaches and laboratory guidelines for carrier screening, prenatal
testing, newborn screening, and clinical diagnostic testing, as well as recent developments in CF treatment, and reasons for the lack of a molecular diagnosis in some patients.

Title: Pancreatic pathophysiology in cystic fibrosis.

Citation: The Journal of pathology, Jan 2016, vol. 238, no. 2, p. 311-320 (January 2016)

Author(s): Gibson-Corley, Katherine N, Meyerholz, David K, Engelhardt, John F

Abstract: The pancreas is one of the earliest, and most commonly affected, organs in patients with cystic fibrosis (CF). Studying the pathogenesis of pancreatic disease is limited in CF patients, due to its early clinical onset, co-morbidities and lack of tissue samples from the early phases of disease. In recent years, several new CF animal models have been developed that have advanced our understanding of both CF exocrine and endocrine pancreatic disease. Additionally, these models have helped us to better define the influence of pancreatic lesions on CF disease progression in other organs, such as the gastrointestinal tract and lung.

Title: US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis.

Citation: Thorax, Jan 2016, vol. 71 Suppl 1, p. i1. (January 2016)


Abstract: Non-tuberculous mycobacteria (NTM) are ubiquitous environmental organisms that can cause chronic pulmonary infection, particularly in individuals with pre-existing inflammatory lung disease such as cystic fibrosis (CF). Pulmonary disease caused by NTM has emerged as a major threat to the health of individuals with CF but remains difficult to diagnose and problematic to treat. In response to this challenge, the US Cystic Fibrosis Foundation (CFF) and the European Cystic Fibrosis Society (ECFS) convened an expert panel of specialists to develop consensus recommendations for the screening, investigation, diagnosis and management of NTM pulmonary disease in individuals with CF. Nineteen experts were invited to participate in the recommendation development process. Population, Intervention, Comparison, Outcome (PICO) methodology and systematic literature reviews were employed to inform draft recommendations. An anonymous voting process was used by the committee to reach consensus. All committee members were asked to rate each statement on a scale of: 0, completely disagree, to 9, completely agree; with 80% or more of scores between 7 and 9 being considered 'good' agreement. Additionally, the committee solicited feedback from the CF communities in the USA and Europe and considered the feedback in the development of the final recommendation statements. Three rounds of voting were conducted to achieve 80% consensus for each recommendation statement. Through this process, we have generated a series of pragmatic, evidence-based recommendations for the screening, investigation, diagnosis and treatment of NTM infection in individuals with CF as an initial step in optimising management for this challenging condition.

Title: Bacterial colonization status of cystic fibrosis children's toothbrushes: A pilot study.
**Title:** Prevalence of Aspergillus sensitization and allergic bronchopulmonary aspergillosis in cystic fibrosis: systematic review and meta-analysis.

**Citation:** Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology, Dec 2015, vol. 45, no. 12, p. 1765-1778 (December 2015)

**Author(s):** Maturu, V N, Agarwal, R

**Abstract:** The prevalence of Aspergillus sensitization (AS) and allergic bronchopulmonary aspergillosis (ABPA) in cystic fibrosis (CF) has been varyingly reported. The aim of this systematic review was to estimate the overall prevalence of AS/ABPA in CF. We searched the PubMed and EmBase databases for studies reporting the prevalence of AS/ABPA in CF. We calculated the proportion with 95% confidence interval (CI) to assess the prevalence of AS and ABPA in the individual studies and then pooled the results using a random effects model. Statistical heterogeneity was assessed using the I(2) test while publication bias was assessed using both graphical and statistical methods. Our search yielded 64 eligible studies. The pooled prevalence of AS was 39.1% (95% CI: 33.3-45.1) and was higher with skin test compared to specific IgE (43.8% vs. 32.8%, P = 0.002); however, the prevalence did not vary with the type of skin test used (intradermal or percutaneous). The prevalence of ABPA was 8.9% (95% CI: 7.4-10.7) and was higher in adults as compared to children (10.1% vs. 8.9%, P < 0.0001). There was a wide variation in the criteria used for diagnosing ABPA. Almost 50% (12/23) of the publications after 2004 used criteria other than the CF foundation criteria for diagnosing ABPA. There was significant statistical heterogeneity and evidence of publication bias. There is a high prevalence of AS and ABPA in patients with CF. Despite six decades of research, there is still a need to adopt uniform methodology and criteria for the diagnosis of AS/ABPA.

**Title:** Serum Iron Level Is Associated with Time to Antibiotics in Cystic Fibrosis.

**Citation:** Clinical and translational science, Dec 2015, vol. 8, no. 6, p. 754-758 (December 2015)

**Author(s):** Gifford, Alex H, Dorman, Dana B, Moulton, Lisa A, Helm, Jennifer E, Griffin,
Abstract: Serum levels of hepcidin-25, a peptide hormone that reduces blood iron content, are elevated when patients with cystic fibrosis (CF) develop pulmonary exacerbation (PEx). Because hepcidin-25 is unavailable as a clinical laboratory test, we questioned whether a one-time serum iron level was associated with the subsequent number of days until PEx, as defined by the need to receive systemic antibiotics (ABX) for health deterioration. Clinical, biochemical, and microbiological parameters were simultaneously checked in 54 adults with CF. Charts were reviewed to determine when they first experienced a PEx after these parameters were assessed. Time to ABX was compared in subgroups with and without specific attributes. Multivariate linear regression was used to identify parameters that significantly explained variation in time to ABX. In univariate analyses, time to ABX was significantly shorter in subjects with Aspergillus-positive sputum cultures and CF-related diabetes. Multivariate linear regression models demonstrated that shorter time to ABX was associated with younger age, lower serum iron level, and Aspergillus sputum culture positivity. Serum iron, age, and Aspergillus sputum culture positivity are factors associated with shorter time to subsequent PEx in CF adults.

Title: Managing Pseudomonas aeruginosa respiratory infections in cystic fibrosis.

Citation: Current opinion in infectious diseases, Dec 2015, vol. 28, no. 6, p. 547-556

Author(s): Langan, Katherine M, Kotsimbos, Tom, Peleg, Anton Y

Abstract: The current guidelines and recent clinical research in the management of Pseudomonas aeruginosa respiratory infections in cystic fibrosis (CF) are reviewed. Areas where further research is required will also be highlighted. P. aeruginosa is a key respiratory pathogen in CF. Inhaled tobramycin or colistin is recommended for early eradication to prevent establishment of chronic infection. Other antibiotic options are currently being investigated. The long-term success of eradication strategies is also now being assessed. The use of inhaled antibiotics in the management of chronic P. aeruginosa infection is an area of active investigation. Acute pulmonary exacerbations are still a major cause of morbidity and mortality. Guidelines continue to recommend combination intravenous therapy but further research is required to clarify the advantage of this approach. Multidrug resistance is common and potentially more effective antipseudomonal antibiotics may soon become available. The management of P. aeruginosa respiratory infection in CF remains a challenging area, especially in the setting of multidrug resistance. The role of inhaled antibiotics continues to be expanded. Further research is required in the key areas of eradication and management of chronic infection and acute pulmonary exacerbations to identify those treatments that optimize long-term, clinical benefits.

Title: The ΔF508 Mutation in the Cystic Fibrosis Transmembrane Conductance Regulator Is Associated With Progressive Insulin Resistance and Decreased Functional β-Cell Mass in Mice.

Citation: Diabetes, Dec 2015, vol. 64, no. 12, p. 4112-4122 (December 2015)

Author(s): Fontés, Ghislaine, Ghislain, Julien, Benterki, Isma, Zarrouki, Bader, Trudel,

Abstract: Cystic fibrosis (CF) is the result of mutations in the cystic fibrosis transmembrane conductance regulator (CFTR). CF-related diabetes affects 50% of adult CF patients. How CFTR deficiency predisposes to diabetes is unknown. Herein, we examined the impact of the most frequent cftr mutation in humans, deletion of phenylalanine at position 508 (ΔF508), on glucose homeostasis in mice. We compared ΔF508 mutant mice with wild-type (WT) littermates. Twelve-week-old male ΔF508 mutants had lower body weight, improved oral glucose tolerance, and a trend toward higher insulin tolerance. Glucose-induced insulin secretion was slightly diminished in ΔF508
mutant islets, due to reduced insulin content, but ΔF508 mutant islets were not more sensitive to proinflammatory cytokines than WT islets. Hyperglycemic clamps confirmed an increase in insulin sensitivity with normal β-cell function in 12- and 18-week-old ΔF508 mutants. In contrast, 24-week-old ΔF508 mutants exhibited insulin resistance and reduced β-cell function. β-Cell mass was unaffected at 11 weeks of age but was significantly lower in ΔF508 mutants versus controls at 24 weeks. This was not associated with gross pancreatic pathology. We conclude that the ΔF508 CFTR mutation does not lead to an intrinsic β-cell secretory defect but is associated with insulin resistance and a β-cell mass deficit in aging mutants.

Title: Management of Pseudomonas aeruginosa infection in cystic fibrosis patients using inhaled antibiotics with a focus on nebulized liposomal amikacin.

Citation: Future microbiology, Dec 2015, vol. 10, p. 1901-1912 (December 2015)

Author(s): Ehsan, Zarmina, Clancy, John P

Abstract: Pseudomonas aeruginosa (PsA) is a highly prevalent bacterial organism recovered from the lungs of cystic fibrosis (CF) patients and chronic PsA infection is linked to progressive pulmonary function decline. The eradication and treatment of this organism from CF airways is particularly challenging to CF care providers. Aerosolized antibiotics that target PsA help to slow down growth, maintain lung function and reduce the frequency of pulmonary exacerbations. In this review, we discuss the currently available inhaled antibiotics for management of PsA lung infections in CF patients, with a focus on liposomal amikacin for inhalation (LAI). LAI is a unique formulation of amikacin under development that enhances drug delivery and retention in CF airways via drug incorporation into neutral liposomes. Factors such as once-daily dosing, mucus and biofilm penetration and potentially prolonged off-drug periods make LAI a potentially attractive option to manage chronic PsA lung infections in CF patients.

Title: Linezolid-Resistant Staphylococcus aureus in Children With Cystic Fibrosis.

Citation: Journal of the Pediatric Infectious Diseases Society, Dec 2015, vol. 4, no. 4, p. e163. (December 2015)

Author(s): Yu, Diana, Stach, Leslie M, Newland, Jason G

Title: Cystic Fibrosis Lung Infections: Polymicrobial, Complex, and Hard to Treat.

Citation: PLoS pathogens, Dec 2015, vol. 11, no. 12, p. e1005258. (December 2015)

Author(s): Filkins, Laura M, O'Toole, George A

Title: Ciprofloxacin during upper respiratory tract infections to reduce Pseudomonas aeruginosa infection in paediatric cystic fibrosis: a pilot study.

Citation: Therapeutic advances in respiratory disease, Dec 2015, vol. 9, no. 6, p. 272-280

Author(s): Connett, Gary J, Pike, Katharine C, Legg, Julian P, Cathie, Katrina, Dewar, Ann, Foote,
onset of such episodes might delay onset of infection with this organism. A total of 41 children with CF aged 2-14 years, without chronic Pseudomonas infection, were randomized to receive ciprofloxacin (n = 28) or placebo (n = 13) at the onset of acute viral respiratory infections on an intention to treat basis, during a study period of up to 32 months. There were no unexpected adverse events believed related to the use of the study medication. The rate of withdrawal from the study was low (approximately 7%) and did not differ between groups. Randomization was effective and acceptable to participants. Primary and secondary outcome measures all favoured active treatment, but there were no significant between group differences. The median rate of Pseudomonas isolates was 0/patient/year (interquartile range 0-0.38) in both the active and placebo groups. Kaplan-Meier survival curves showed no significant difference in time to first Pseudomonas isolate between groups. This study demonstrated the clinical feasibility of using oral ciprofloxacin in CF patients at times of viral infection. Within this sample size, no significant association was found between active treatment and decreased growth of Pseudomonas in follow-up microbiological samples. A definitive study would require at least 320 children to demonstrate significant differences in the rate of pseudomonal isolates. © The Author(s), 2015.

**Nutrition**

**Title:** Zinc Supplementation for One Year Among Children with Cystic Fibrosis Does Not Decrease Pulmonary Infection.

**Citation:** Respiratory care, Jan 2016, vol. 61, no. 1, p. 78-84 (January 2016)

**Author(s):** Sharma, Ganesh, Lodha, Rakesh, Shastri, Shivaram, Saini, Savita, Kapil, Arti, Singla, Mohit, Mukherjee, Aparna, Jat, Kana Ram, Kabra, Madhulika, Kabra, Sushil K

**Abstract:** Children with cystic fibrosis may have a deficiency of micronutrients, including zinc, which may affect their susceptibility to infections. There is a paucity of data on zinc supplementation among children with cystic fibrosis. We hypothesized that a pharmacologic dose of zinc administered daily for 12 months would reduce the need for antibiotics by 50%. This double-blind randomized placebo-controlled trial was conducted among children with cystic fibrosis to assess the effect of zinc supplementation on the need for antibiotics and pulmonary function tests. The children, age 5-15 y, of either sex, received either 30-mg zinc tablets or similar looking placebo tablets daily in addition to standard care. They were followed up every month for a period of 12 months and whenever they had pulmonary exacerbations. Their serum zinc was estimated at baseline and at 12 months of enrollment. During each visit, the children underwent a pulmonary function test and sputum culture. Of a total of 43 children screened, 40 were enrolled, and of them, 37 completed the study. The median (interquartile range) number of days of the administration of antibiotics over 12 months of follow-up among the children receiving zinc was 42 (14-97) d. In the placebo group, it was 38 (15-70) d (P = .79). There were no significant differences in the percent-of-predicted FEV1 or change in FEV1 values at 12 months (P = .44). The number of children in whose respiratory specimens Pseudomonas was isolated was similar for the 2 groups at different time intervals. The adverse events reported were similar in the 2 groups. We did not find any significant difference in the need for antibiotics, pulmonary function tests, hospitalization, colonization with Pseudomonas, or the need for antibiotics for children with cystic fibrosis receiving zinc supplementation of 30 mg/d.

**Title:** Nutritional Status Improved in Cystic Fibrosis Patients with the G551D Mutation After Treatment with Ivacaftor.

**Citation:** Digestive diseases and sciences, Jan 2016, vol. 61, no. 1, p. 198-207
Author(s): Borowitz, Drucy, Lubarsky, Barry, Wilschanski, Michael, Munck, Anne, Gelfond, Daniel, Bodewes, Frank, Schwarzenberg, Sarah Jane

Abstract: The cystic fibrosis (CF) transmembrane conductance regulator (CFTR) gating mutation G551D prevents sufficient ion transport due to reduced channel-open probability. Ivacaftor, an oral CFTR potentiator, increases the channel-open probability. To further analyze improvements in weight and body mass index (BMI) in two studies of ivacaftor in patients aged ≥6 years with CF and the G551D mutation. Patients were randomized 1:1 to ivacaftor 150 mg or placebo every 12 h for 48 weeks. Primary end point (lung function) was reported previously. Other outcomes included weight and height measurements and CF Questionnaire-Revised (CFQ-R). Studies included 213 patients (aged ≤ 20 years, n = 105; aged > 20 years, n = 108). In patients ≤20 years, adjusted mean change from baseline to week 48 in body weight was 4.9 versus 2.2 kg (ivacaftor vs. placebo, p = 0.0008). At week 48, change from baseline in mean weight-for-age z-score was 0.29 versus -0.06 (p < 0.0001); change in mean BMI-for-age z-score was 0.26 versus -0.13 (p < 0.0001). In patients >20 years, adjusted mean change from baseline to week 48 in body weight was 2.7 versus -0.2 kg (p = 0.0003). Mean BMI change at week 48 was 0.9 versus -0.1 kg/m^2 (p = 0.0003). There was no linear correlation evident between changes in body weight and improvements in lung function or sweat chloride. Significant CFQ-R improvements were seen in perception of eating, body image, and sense of ability to gain weight. Nutritional status improved following treatment with ivacaftor for 48 weeks.

Psychological

Title: Coping styles in adults with cystic fibrosis: implications for emotional and social quality of life.

Citation: Psychology, health & medicine, Jan 2016, vol. 21, no. 1, p. 102-112 (January 2016)

Author(s): McHugh, Rachel, McFeeters, Danielle, Boyda, David, O'Neill, Siobhan

Abstract: As life expectancy increases, interest has grown surrounding the factors that may influence quality of life (QOL) for people with cystic fibrosis (CF). The aim of the current study was to examine which specific coping styles were positively or negatively associated with social and emotional QOL in a CF sample. One hundred and twenty-two respondents aged 18 and over were recruited through an online support group. Respondents completed the 'CF Questionnaire-Revised (CFQ-R)' and the 'Brief COPE'. The CFQ-R is a disease-specific instrument designed to measure the impact of CF on nine QOL domains and the Brief COPE is a 28 item questionnaire which assesses 14 coping scales. A multivariate regression model revealed that higher substance abuse and disengagement was associated with lower emotional QOL whereas greater use of religion, instrumental coping and acceptance was positively associated with emotional QOL. Active coping was linked to better social QOL and a negative association was reported between distraction coping with both emotional and social domains. Given the burden of CF, ascertaining which factors enhance or diminish emotion and social well-being is now an integral component of QOL research. The current findings may therefore have value in informing clinical interventions which aim to cater for the psychological needs of individuals with CF.

Title: Pilot trial of light therapy for depression in hospitalized patients with cystic fibrosis.

Citation: Journal of affective disorders, Jan 2016, vol. 189, p. 164-168 (January 1, 2016)
**Author(s):** Kopp, Benjamin T, Hayes, Don, Ghera, Princy, Patel, Alpa, Kirkby, Stephen, Kowatch, Robert A, Splaingard, Mark

**Abstract:** Depression is common in cystic fibrosis (CF) and linked with worse outcomes during hospitalization. Bright-light therapy during hospitalizations augments antidepressant regimens and reduces length of stay (LOS) in depressed non-CF patients, but has not been examined in CF patients. 

**METHODS:** Thirty subjects used a light box emitting 10,000lx for 30min each day for 7 straight days following hospital admission for pulmonary exacerbation. Depressive symptom severity (QIDS-C) and quality of life factors (CFQ-R) were recorded pre/post light therapy. Eighty percent of subjects had at least mild depressive symptoms upon admission. Hospitalized CF patients had a significantly lower mean LOS of 11.0±3.6 days compared to a historical cohort from the year prior (13.3±4.4 days, \( p \) value=0.038). There was a significant decrease in depressive symptoms for all subjects receiving light therapy (\( p \) value<0.0001). There was no relation between depressive symptoms and lung function or vitamin D. Six out of twelve quality of life indicators improved with light therapy including the domains of vitality, emotion, and health perceptions. There were no adverse events reported. As a pilot study, the design was limited by a lack of a control group and possible confounding effects of hospitalization treatment on systemic symptoms. Light therapy was well tolerated by hospitalized CF patients and resulted in improved depressive symptoms and quality of life. Light therapy was associated with a reduced length of stay. Large, randomized trials of light therapy may be indicated for hospitalized CF patients.

**Title:** The psychological burden of cystic fibrosis.

**Citation:** Current opinion in pulmonary medicine, Mar 2016, vol. 22, no. 2, p. 187-191

**Author(s):** Quittner, Alexandra L, Saez-Flores, Estefany, Barton, John D

**Abstract:** Cystic fibrosis (CF) is the most common genetic, life-shortening illness among white populations. Management of the disease requires a complex, time-consuming treatment regimen. The purpose of this review is to highlight current research examining the psychological burden of CF, including psychological distress, social challenges, treatment burden, and adherence to daily treatments. Individuals with CF and their parent caregivers report elevated symptoms of depression and anxiety. Recent international guidelines (Cystic Fibrosis Foundation and European Cystic Fibrosis Society) recommend annual screening of these symptoms using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) scales. Symptoms of depression have been associated with decreased adherence, lower quality of life, and higher healthcare costs. Adherence to pulmonary medications has been found to be 50% or less and decreases with age. Poor adherence has been associated with higher healthcare costs, more frequent hospitalizations, and worse quality of life. Individuals with CF face unique challenges that can lead to psychological burden. Screening for these symptoms and developing effective interventions to improve adherence are the key targets for the next 5 years of research.

**Title:** Psychosocial characteristics and predictors of health-care use in families of young children with cystic fibrosis in Western Australia.

**Citation:** Journal of paediatrics and child health, Jan 2016, vol. 52, no. 1, p. 34-39 (January 2016)

**Author(s):** Douglas, Tonia, Green, Jennifer, Park, Judy, Turkovic, Lidija, Massie, John, Shields, Linda

**Abstract:** Early childhood psychosocial experiences determine future health and health-care use. Identifying psychosocial predictors in cystic fibrosis may inform intervention strategies that can...
reduce health-care utilization. The study was designed as a prospective cohort study. The study was set in the only cystic fibrosis clinic in Western Australia. The patients were children up to 6 years diagnosed with cystic fibrosis in Western Australia between 2005 and 2011. Psychosocial data collected for each year of life were compared with Australian population data and analysed as predictors of annual hospital, emergency and outpatient visits. Compared with the Australian population, cystic fibrosis families demonstrated lower socio-economic status and labour supply ($P < 0.001$), increased residential mobility ($P < 0.001$) and trends towards increased rates of parental separation ($P = 0.066$). Marital discord and maternal and child psychological stress significantly predicted increased hospital admissions, emergency and outpatient visits. Social gradients may exist for families of young children with cystic fibrosis in Western Australia with potential implications for child health. Family psychological and relationship stress predicted increased child cystic fibrosis-related health-care use.

**Title:** Mental health in cystic fibrosis: turning the tide.

**Citation:** Thorax, Jan 2016, vol. 71, no. 1, p. 1-2 (January 2016)

**Author(s):** Havermans, Trudy, Staab, Doris

**Title:** International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety.

**Citation:** Thorax, Jan 2016, vol. 71, no. 1, p. 26-34 (January 2016)

**Author(s):** Quittner, Alexandra L, Abbott, Janice, Georgiopoulos, Anna M, Goldbeck, Lutz, Smith, Beth, Hempstead, Sarah E, Marshall, Bruce, Sabadosa, Kathryn A, Elborn, Stuart, International Committee on Mental Health, EPOS Trial Study Group

**Abstract:** Studies measuring psychological distress in individuals with cystic fibrosis (CF) have found high rates of both depression and anxiety. Psychological symptoms in both individuals with CF and parent caregivers have been associated with decreased lung function, lower body mass index, worse adherence, worse health-related quality of life, more frequent hospitalisations and increased healthcare costs. To identify and treat depression and anxiety in CF, the CF Foundation and the European CF Society invited a panel of experts, including physicians, psychologists, psychiatrists, nurses, social workers, a pharmacist, parents and an individual with CF, to develop consensus recommendations for clinical care. Over 18 months, this 22-member committee was divided into four workgroups: Screening; Psychological Interventions; Pharmacological Treatments and Implementation and Future Research, and used the Population, Intervention, Comparison, Outcome methodology to develop questions for literature search and review. Searches were conducted in PubMed, PsychINFO, ScienceDirect, Google Scholar, Psychiatry online and ABDATA by a methodologist at Dartmouth. The committee reviewed 344 articles, drafted statements and set an 80% acceptance for each recommendation statement as a consensus threshold prior to an anonymous voting process. Fifteen guideline recommendation statements for screening and treatment of depression and anxiety in individuals with CF and parent caregivers were finalised by vote. As these recommendations are implemented in CF centres internationally, the process of dissemination, implementation and resource provision should be closely monitored to assess barriers and concerns, validity and use.
Other

**Title:** The Spectrum of CFTR Variants in Nonwhite Cystic Fibrosis Patients: Implications for Molecular Diagnostic Testing.

**Citation:** The Journal of molecular diagnostics : JMD, Jan 2016, vol. 18, no. 1, p. 39-50 (January 2016)

**Author(s):** Schrijver, Iris, Pique, Lynn, Graham, Steve, Pearl, Michelle, Cherry, Athena,

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**Title:** Cystic fibrosis program directors' attitudes toward sexual and reproductive health in young women with CF.

**Citation:** Pediatric pulmonology, Jan 2016, vol. 51, no. 1, p. 22-27 (January 2016)

**Author(s):** Kazmerski, Traci M, Tuchman, Lisa K, Borrero, Sonya, Weiner, Daniel, Pilewski,

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**Title:** Fungal contamination of nebuliser devices used by people with cystic fibrosis.

**Citation:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. 74-77 (January 2016)

**Author(s):** Peckham, D, Williams, K, Wynne, S, Denton, M, Pollard, K, Barton, R

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**Title:** An evaluation of different steam disinfection protocols for cystic fibrosis nebulizers.

**Citation:** Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. 78-84 (January 2016)

**Author(s):** Hohenwarter, K, Prammer, W, Aichinger, W, Reyichler, G

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**Title:** Parenting stress in mothers with cystic fibrosis.

**Citation:** Disability and rehabilitation, Jan 2016, vol. 38, no. 2, p. 174-179 (January 2016)

**Author(s):** Ullrich, Gerald, Bobis, Ingrid, Bewig, Burkhard discuss it, openly.

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**Title:** Searching for a cure for cystic fibrosis. A 25-year quest in a nutshell.

**Citation:** European journal of pediatrics, Jan 2016, vol. 175, no. 1, p. 1-8 (January 2016)

**Author(s):** Bosch, Barbara, De Boeck, Kris

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**Title:** A standardized approach to estimating survival statistics for population-based cystic fibrosis registry cohorts.

**Citation:** Journal of clinical epidemiology, Feb 2016, vol. 70, p. 206-213 (February 2016)

**Author(s):** Sykes, Jenna, Stanojevic, Sanja, Goss, Christopher H, Quon, Bradley S, Marshall, Bruce C, Petren, Kristofer, Ostrenga, Josh, Fink, Aliza, Elbert, Alexander, Stephenson, Anne L
Title: Mortality from cystic fibrosis in Europe: 1994-2010.

Citation: Pediatric pulmonology, Feb 2016, vol. 51, no. 2, p. 133-142 (February 2016)

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Citation: Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, Jan 2016, vol. 15, no. 1, p. 102-108 (January 2016)

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Title: The role of routine hearing screening in children with cystic fibrosis on aminoglycosides: A systematic review.

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Citation: Journal of Pain & Symptom Management, 2016, vol./is. 51/2(379-379)

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