# CF RD AND SW CONSORTIUM

June Newsletter

**Special thanks to our sponsors:**

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## Updates from CFF:

### Shape the future of CF Research on Sexual and Reproductive Health

**Cystic Fibrosis Reproductive & Sexual Health Collaborative (CFReSHC)** provides women with CF the opportunity to partner with health care providers and researchers to shape the future of CF research on sexual and reproductive health issues. With a growing consortium of 350+ members, CFReSHC holds monthly virtual meetings for women with CF to share their experiences, help identify knowledge gaps, and formulate key research questions to inform patient-centered research projects. For more information, visit the CFReSHC website. This work is supported by a CF Foundation community grant.

### Engaging People with CF in the African American Community

Founded by adult with CF, Terry Wright, and his wife, Dr. Michele Wright, CF Foundation **National Organization of African Americans with Cystic Fibrosis** (NOAACF) works to engage, educate, and raise CF awareness in the African-American community to help bring valuable resources, knowledge, empowerment, and support to CF patients, families, healthcare professionals, and the community. Learn about how to join and support their efforts at NOAACF website.

### Got a Big Idea?

Do you have a big idea or know someone with an idea to support the CF Community? The CF Foundation's Impact Grant program is designed to support community members with great ideas and the motivation to turn them into action. Impact Grants provide up to $10,000 per year to individuals or nonprofit organizations for programs that engage and empower the CF community. For more information on eligibility criteria, the application period and process, or previously funded programs, visit the Impact Grants webpage or email impact@cff.org

## Updates from CFRI

### Register Now for CFRI's 36th National CF Education Conference July 28-30, 2023

CFRI's 2023 Conference will be held virtually and in-person at the Grand Bay Hotel San Francisco. Speakers will present on topics including phage therapy, stem cell research, mRNA therapy, and parenting with CF. **View the list of speakers to date here**. Exhibitor booths, the annual awards dinner and dance party make this a full weekend of community connection. Virtual attendees can view all presentations live on our interactive event platform. **Registration to attend in person is $230 (including all presentations and meals). Registration to attend virtually is free. Find more details and a registration link here.** *Sponsored by Viatris, Vertex Pharmaceuticals, Gilead Sciences, Chiesi USA, AbbVie, Genentech, and the Boomer Esiason Foundation.*

### Support Group For Adults with CF Meets Online third Mondays.

The group, facilitated by Meg Dvorak, LCSW, is open to participants nationwide, and meets from 6:00 pm PST to 7:30 pm (9:00 pm – 10:30 pm EST). **To receive the link to the registration page, please email Sabine Brants (sbrants@cfri.org)**. If you registered before, you don't need to do it again.

### CF Caregivers Support Groups Third Tuesday

**Parents of Children third Tuesday** from 5:00 pm – 6:00 pm PST; **Parents/ Spouses/ Partners of Adults** meet from 6:00 pm – 7:00 pm PST. **To receive the link to the registration page, please email Sabine Brants (sbrants@cfri.org).** If you registered before, you don't need to do it again.

### Monthly Support Group for Teenagers with CF Meets Online third Wed

Addresses the unique issues faced by teenagers (aged 13 – 18) living with CF. This peer-to-peer support group is facilitated by Deborah Menet, LCSW, social worker at the Stanford CF Center. Parents must provide consent for their teenagers to attend. **Register for the teen support group.**

### Parents, Students with CF, and CF Social Workers: Order Free Copies of Updated "CF In the Classroom"

CFRI's recently updated "CF in the Classroom" and "Fibrosis Quística en la CLase" booklets were developed to help teachers, school administrators and other educators to better understand cystic fibrosis, and the CF-related issues they should be aware of. They are useful for educating family and friends as well! Available in English and Spanish, in single copies and in bulk. **To order your free copies, please email cfri@cfri.org**. *Made possible through educational grants from Viatris and Vertex.*

### CFRI's Counseling Program Offers Financial Support for Therapy Sessions:

Children and adults with CF and family members (parents, siblings, spouses/ partners) are eligible to receive financial support for six individual sessions with their licensed provider of choice. CFRI may cover up to $120 per session for six sessions. Participants must live in the United States. **Find more information on CFRI's counseling support program here**,or email Sabine at sbrants@cfri.org for any questions.

### A Wealth of Information on Our YouTube and Podbean Channels!

Get information about scholarships, patient assistance, hemoptysis, CF and mental health, bone health, advocacy, CF and COVID-19, and much more. Our CF Community Voices podcast series covers it all! Many recordings on YouTube are available with Spanish and Hindi captions. **Watch or download CFRI's podcasts on our Podbean channel. Watch CFRI's podcasts on our YouTube channel.**

## CME/CE Resources

### CF and Diet and Nutrition: The Changing Paradigm

*Katie McDonald, PhD, Megan Gabel, MD, Amanda Leonard, MPH, RD, LD, CDE, and Alexandra Wilson, MS, RDN, CDE*

For most of their lives, individuals with CF have struggled to gain weight and achieve BMI norms. Now however, a growing number of people with CF are meeting the current criteria for overweight or obesity. What changed? And without specific evidence-based guidance for managing overweight/obesity in people with CF, how should clinicians respond? Read more

### Creative Fuel: Writing Through Suffering

*Bradley Dell*

Taking a therapeutic writing course helped the author cope with his cystic fibrosis, which also helped him connect more strongly to the CF community. Read more

# RDs!

Certified Advanced CF Dietitian (CACFD) applications opened on June 1st! Applications and information is posted on our web-site:

https://www.cfrdswconsortium.com/s-projects-side-by-side

**Congratulations to the following dietitian(s) who received their Advanced CF RD Credentials! They join the list of RDs from previous newsletters.**

Ashley Kilpatrick

## Abstracts

### General/Nutrition

J Cyst Fibros. 2023 Feb 27;S1569-1993(23)00060-7.

**Early life growth trajectories in cystic fibrosis are associated with lung function at age six**

Kevin J Psoter[1], Kimberly M Dickinson[2], Kristin A Riekert[3], Joseph M Collaco[4]

PMID: 36858852

DOI: 10.1016/j.jcf.2023.02.008

**Background:** Higher growth percentiles are associated with more favorable lung function in cystic fibrosis (CF), prompting the creation of CF Foundation (CFF) nutritional guidelines.

**Objectives:** To describe early childhood growth trajectories within CF, to determine if growth trajectories are associated with differences in lung function at age six, and to identify factors that differ between trajectory groups.

**Methods:** Retrospective cohort study of children diagnosed with CF and born 2000-2011 using the US CFF Patient Registry. Annualized growth parameters prior to age six were included in group-based trajectory modeling to identify unique early life growth trajectories. FEV1 percent predicted (FEV1pp) at age six was compared between trajectory groups using linear regression. Factors associated with group membership were identified using multinomial logistic regression.

**Results:** 6,809 children met inclusion criteria. Six discrete growth trajectories were identified, including three groups that began with growth parameters >50th percentile, termed: "always high", "gradual decliner", "rapid decliner", and three which began with growth parameters <50th percentile, termed: "rapid riser", "gradual riser", "always low". FEV1pp at age six was highest for the Always High trajectory. The Always Low trajectory was nearly 10% lower than the Always High trajectory. Sex, ethnicity, newborn screening and pancreatic function were associated with trajectory class membership.

**Conclusions:** Distinct early life growth trajectories were identified within CF. Trajectories that met CFF nutritional guideline recommendations were associated with higher FEV1pp at age six. CF care teams should continue to partner with families to encourage interventions to support optimal growth to improve lung function in CF.

Can J Diet Pract Res. 2023 Mar 29;1-5.

**What is the Perceived Role of the Dietitian Amongst People with Cystic Fibrosis? Results of an International survey**

Hannah L Anderson[1], Veronica Lynch[2], John E Moore[1 2 3], Beverley C Millar[1 2 3]

PMID: 36988118

DOI: 10.3148/cjdpr-2022-044

Cystic fibrosis (CF) is a chronic condition requiring continued input from the CF dietitian as an integral part of the CF multidisciplinary team. In recent years, the longer life expectancy experienced by people with CF (PwCF) means that nutrition advice and therapy are evolving from a focus on nutrition support to prevention and management of comorbidities. Little has been reported regarding the perceived role of the CF dietitian amongst PwCF. We report the responses to 11 questions that were part of a larger international survey distributed to members of national CF charities in 2018-2019. These questions evaluated PwCFs' perspectives on (*i*) the importance of the CF diet, (*ii*) how often PwCF obtain dietary/nutritional advice from their dietitian, (*iii*) the perceived reliability of information given by the dietitian, (*iv*) other sources of CF information and their perceived reliability, and (*v*) how CF nutrition/diet, as well as CF-related diabetes, ranked as research priorities. There were 295 respondents from 13 countries. Almost half of the respondents (46.8%) contacted their CF dietitian on a frequent/more regular basis, compared to medical/scientific journals/medical/scientific search engines. The CF dietitian was considered a reliable source of information, as 84% of the respondents indicated that the information provided was very/generally reliable. At a time when CF care and expectations are changing rapidly, PwCF are in need of trusted and reliable information to make positive changes in lifestyle and habits. Dietitians working with PwCF should appreciate the pivotal and valued role they perform as purveyors of robust evidence-based information to this chronic disease population.

Nutr Hosp. 2023 Apr 20;40(2):280-285.

**Vitamin D levels and their association with oxidative stress and inflammation markers in patients with cystic fibrosis**

Dayana Joyce Marques Queiroz[1], Alexandre Sérgio Silva[2], Celso Costa da Silva Júnior[3], Darlene Camati Persuhn[4], Alcides da Silva Diniz[5], Rafaela Lira Formiga Cavalcanti de Lima[3], Maria Paula de Paiva[1], Constantino Giovanni Braga Cartaxo[6], Patricia Gomes de Matos Bezerra[7], Mateus Duarte Ribeiro[2], Maria da Conceição Rodrigues Gonçalves[1]

PMID: 36719006
DOI: 10.20960/nh.04253

**Introduction:** cystic fibrosis is a disease that causes inflammation, oxidative stress and metabolic changes that lead to nutrient deficiency, such as vitamin D deficiency. On the other hand, it is suggested that vitamin D has anti-inflammatory and antioxidant actions. **Objective:** to evaluate the prevalence of hypovitaminosis D and the association between serum 25 hydroxyvitamin D levels with markers of oxidative stress and inflammation in patients with cystic fibrosis. **Method:** a cross-sectional study was carried out with 48 patients with cystic fibrosis including children, adolescents and adults in the northeast region of Brazil. Blood collection was performed for analysis of 25-hydroxyvitamin D, calcium, parathyroid hormone, inflammatory process (C-reactive protein (CRP) and alpha-1-acid glycoprotein-A1 (A1GPA)) and oxidative stress (malondialdehyde (MDA) and total antioxidant capacity (CAOT)). The statistical analysis was performed using the "Statistical Package for the Social Sciences", adopting a significance level of $p < 0.05$. **Results:** Vitamin D insufficiency/deficiency was found in 64.6 % of patients. After multiple linear regression analysis, MDA showed an inverse association with blood values of 25-Hydroxyvitamin D ($p < 0.05$) conditioned by the presence of inflammatory process markers. When only oxidative stress was evaluated, this association disappeared. **Conclusion:** in conclusion, there was a high prevalence of hypovitaminosis D, with 25(OH)D levels associated with greater oxidative stress when combined with inflammatory markers. Improved vitamin D levels may be an alternative to reduce the damage caused by excess oxidative stress and inflammation in CF patients.

Pediatr Pulmonol. 2023 May;58(5):1463-1470.

**Improvements in body mass index of children with cystic fibrosis following implementation of a standardized nutritional algorithm: A quality improvement project**

Yasemin Gokdemir[1], Ela Erdem Eralp[1], Almala Pinar Ergenekon[1], Cansu Yilmaz Yegit[1], Muruvvet Yanaz[1], Hakan Mursaloglu[2,3], Burcu Uzunoglu[3], Damla Kocamaz[3], Gamze Tastan[3], Amy Filbrun[4], Catherine Enochs[4], Sandra Bouma[4], Courtney Iwanicki[4], Fazilet Karakoc[1], Samya Z Nasr[4], Bulent Karadag[1]

PMID: 36747482
DOI: 10.1002/ppul.26344

**Background:** A collaboration between the University of Michigan (UM) Cystic Fibrosis Center (CFC) and Marmara University (MU) CFC was initiated in MU through conducting Quality Improvement projects (QIP). The global aim was to improve nutritional status of children with CF (cwCF), with a specific aim to increase the mean BMI percentile (BMIp) for cwCF by 10 percentile points in 12 months.

**Methods:** Body mass index (BMI) percentiles of cwCF were categorized as: nutritionally adequate (BMIp ≥ 50%); at risk (BMIp 25%-49%); urgently at risk (BMIp 10%-25%); critically at risk (BMIp < 10%). Appropriate interventions were made according to BMIp category every three months. Forced expiratory volume in one-second percent predicted (FEV1pp), and health-related quality of life (HRQoL) were evaluated.

**Results:** One hundred and eight-two cwCF with a mean age of 9.1 ± 4.3 years were included in the project. Baseline BMIp increased from 25.6 to 37.2 at the 12th month ($p < 0.001$). In the critically at-risk group BMIp increased from 3.6 to 20.5 ($p < 0.001$), in the urgently at risk group from 15.9 to 30.8 ($p < 0.001$), in the at risk group from 37.0 to 44.2 ($p < 0.079$) and in the nutritionally adequate group the increase was from 66.8 to 69.5 ($p < 0.301$). FEV1pp also improved significantly, from 81.3 ± 20.6 to 85.9 ± 20.8 ($p < 0.001$). Physical functioning, eating problems, and respiratory symptoms domains of the HRQoL evaluation improved ($p < 0.05$).

**Conclusion:** This project has led to significant improvements in BMIp, FEV1pp and HRQoL of cwCF; similar projects could easily be implemented by centers in other developing countries.

PLOS Digit Health. 2023 Feb 27;2(2):e0000201.

**A systematic review to explore how exercise-based physiotherapy via telemedicine can promote health related benefits for people with cystic fibrosis**

Ben Bowhay[1], Jos M Latour[2], Owen W Tomlinson[3]

PMID: 36848358
PMCID: PMC9970050
DOI: 10.1371/journal.pdig.0000201

To conduct a systematic review to evaluate the effects of physiotherapy exercises delivered via telemedicine on lung function and quality-of-life in people with Cystic Fibrosis (CF). The databases AMED, CINAHL and MEDLINE were searched from December 2001 until December 2021. Reference lists of included studies were hand-searched. The PRISMA 2020 statement was used to report the review. Studies of any design reported in the English language, included participants with CF, and within outpatient settings were included. Meta-analysis was not deemed appropriate due to the diversity of interventions and heterogeneity of the included studies. Following screening, eight studies with 180 total participants met the inclusion criteria. Sample sizes ranged from 9 to 41 participants. Research designs included five single cohort intervention studies, two randomised control trials and one feasibility study. Telemedicine-based interventions included Tai-Chi, aerobic, and resistance exercise delivered over a study period of six to twelve weeks. All included studies which measured percentage predicted forced expiratory volume in one second found no significant difference. Five studies measuring the Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain found improvements, however, did not meet statistical significance. For the CFQ-R physical domain, measured by five studies, two studies found an improvement, although not statistically significant. No adverse events were reported across all studies. The included studies indicate that telemedicine-based exercise over 6-12 weeks does not significantly change lung function or quality-of-life in people with CF. Whilst the role of telemedicine in the care of pwCF is acceptable and promising; further research with standardised outcome measures, larger sample sizes and longer follow-up are required before clinical practice recommendations can be developed.

Nutrients. 2023 Jan 17;15(3):479.

**Nutritional Care in Children with Cystic Fibrosis**

Elena Mariotti Zani[1], Roberto Grandinetti[1], Daniela Cunico[1], Lisa Torelli[1], Valentina Fainardi[1], Giovanna Pisi[1], Susanna Esposito[1]

PMID: 36771186
PMCID: PMC9921127
DOI: 10.3390/nu15030479

Patients with cystic fibrosis (CF) are prone to malnutrition and growth failure, mostly due to malabsorption caused by the derangement in the chloride transport across epithelial surfaces. Thus, optimal nutritional care and support should be an integral part of the management of the disease, with the aim of ameliorating clinical outcomes and life expectancy. In this report, we analyzed the nutrition support across the different ages, in patients with CF, with a focus on the relationships with growth, nutritional status, disease outcomes and the use of the CF transmembrane conductance regulator (CFTR) modulators. The nutrition support goal in CF care should begin as early as possible after diagnosis and include the achievement of an optimal nutritional status to support the growth stages and puberty development in children, that will further support the maintenance of an optimal nutritional status in adult life. The cornerstone of nutrition in patients with CF is a high calorie, high-fat diet, in conjunction with a better control of malabsorption due to pancreatic enzyme replacement therapy, and attention to the adequate supplementation of fat-soluble vitamins. When the oral caloric intake is not enough for reaching the anthropometric nutritional goals, supplemental enteral feeding should be initiated to improve growth and the nutritional status. In the last decade, the therapeutic possibilities towards CF have grown in a consistent way. The positive effects of CFTR modulators on nutritional status mainly consist in the improvement in weight gain and BMI, both in children and adults, and in an amelioration in terms of the pulmonary function and reduction of exacerbations. Several challenges need to be overcome with the development of new drugs, to transform CF from a fatal disease to a treatable chronic disease with specialized multidisciplinary care.

BDJ Open. 2023 Mar 11;9(1):11.

**Oral care considerations for people with cystic fibrosis: a cross-sectional qualitative study**

Niamh Coffey[1], Fiona O' Leary[2], Francis Burke[2], Barry Plant[3], Anthony Roberts[2], Martina Hayes[4,5]

PMID: 36906647 PMCID: PMC10008013
DOI: 10.1038/s41405-023-00136-w

**Objectives:** To investigate the attitudes of adults with Cystic Fibrosis (CF) towards dental attendance and any perceived barriers to treatment.
**Methods:** A cross sectional survey in the form of a structured, anonymous questionnaire was used to obtain information regarding adults with CF's feelings towards dentists and dental treatment. The final version of the questionnaire was based on a collaborative effort between researchers at Cork University Dental School and Hospital and Cystic Fibrosis (CF) patient advocates from CF Ireland. Participants were recruited via CF Ireland's mailing list and social media channels. The responses underwent descriptive statistical analysis and inductive thematic analysis.
**Results:** A total of 71 people (33 Male: 38 Female) over the age of 18 living with CF in the Republic of Ireland responded to the survey. 54.9% of respondents were unhappy with their teeth. 63.4% felt that CF had an impact on oral health. 33.8% were anxious about attending their dentist. Respondents believed that CF has impacted on their oral health due to the medications and dietary requirements involved, as well as tiredness and other side effects of CF. Reasons for being anxious about attending the dentist included cross infection concerns, issues with the dentist, with tolerating treatment, and with the teeth themselves. Respondents wanted dentists to be aware of the practicalities of dental treatment for people with CF, especially their discomfort with lying back. They also want the dentist to be aware of the impact that their medication, treatment and diet has on their oral health.
**Conclusions:** Over one third of adults with CF reported anxiety about attending the dentist. Reasons for this included fear, embarrassment, cross infection concerns and problems with treatment, especially being in the supine position. Adults with CF want dentists to be aware of the impact that CF can have upon dental treatment and oral health care.

Rev Paul Pediatr. 2023 Mar 3;41:e2021333.

**Quality of anthropometric data measured in children and adolescents with cystic fibrosis: a scoping review**

Fernanda Martins Dias Escaldelai[1], Luiz Vicente Ribeiro Ferreira da Silva Filho[1], Lenycia de Cassya Lopes Neri[1], Denise Pimentel Bergamaschi[1]

PMID: 36888749 PMCID: PMC9984155
DOI: 10.1590/1984-0462/2023/41/2021333

**Objective:** This study aimed to identify methodological aspects involved in determining anthropometric measurements among studies assessing the nutritional status of individuals with cystic fibrosis (CF).
**Methods:** A search of the literature was performed on MEDLINE via Pubmed, Embase, and Web of Science databases. The population comprised children and adolescents with CF. Observational studies and clinical trials using anthropometric and body composition measures and indices determined by dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance assessment (BIA) were included. Use of a standardized procedure for data collection was defined when details on the instruments and their calibration were given, the measuring procedures were described, and when it was clear measures had been determined by a trained team, or the use of an anthropometric reference manual was cited. Data extracted were expressed as absolute and relative frequencies.
**Results:** A total of 32 articles were included, and a total of 233 measures or indices were observed. The most frequently used measures were body mass index (kg/m2; 35%), weight (kg; 33%), and height (cm; 33%). Among the 28 studies that used anthropometric measures, 21 (75%) provided a complete or partial description of the measurement instruments used, 3 (11%) reported information on equipment calibration, 10 (36%) indicated the measurement procedures employed by assessors, and 2 (7%) stated a trained team had carried out the measurements.
**Conclusions:** The poor description of measuring procedures precluded a meaningful evaluation of data quality. Scientific debate on this theme can help raise awareness of the need to ensure quality in collecting and fully presenting data.

J Cyst Fibros. 2023 Mar 5;S1569-1993(23)00059-0.

**Position paper: Models of post-transplant care for individuals with cystic fibrosis**

Edward McKone[1], Kathleen J Ramos[2], Cecilia Chaparro[3], Joshua Blatter[4], Ramsey Hachem[5], Michael Anstead[6], Fanny Vlahos[7], Abby Thaxton[8], Sarah Hempstead[8], Thomas Daniels[9], Michelle Murray[10], Amparo Sole[11], Robin Vos[12], Erin Tallarico[8], Albert Faro[8], Joseph M Pilewski[13]

PMID: 36882349
DOI: 10.1016/j.jcf.2023.02.011

There is no consensus on the best model of care for individuals with CF to manage the non-pulmonary complications that persist after lung transplant. The CF Foundation virtually convened a group of international experts in CF and lung-transplant care. The committee reviewed literature and shared the post-lung transplant model of care practiced by their programs. The committee then developed a survey that was distributed internationally to both the clinical and individual with CF/family audiences to determine the strengths, weaknesses, and preferences for various models of transplant care. Discussion generated two models to accomplish optimal CF care after transplant. The first model incorporates the CF team into care and proposes delineation of responsibilities for the CF and transplant teams. This model is reliant on outstanding communication between the teams, while leveraging the expertise of the CF team for management of the non-pulmonary manifestations of CF. The transplant team manages all aspects of the transplant, including pulmonary concerns and management of immunosuppression. The second model consolidates care in one center and may be more practical for transplant programs that have expertise managing CF and have access to CF multidisciplinary care team members (e.g., located in the same institution). The best model for each program is influenced by several factors and model selection needs to be decided between the transplant and the CF center and may vary from center to center. In either model, CF lung transplant recipients require a clear delineation of the roles and responsibilities of their providers and mechanisms for effective communication.

An Pediatr (Engl Ed). 2023 Apr;98(4):257-266.

**Safety and efficacy of a new supplementation protocol in patients with cystic fibrosis and vitamin D deficiency**

Carmen Mangas-Sánchez[1], María Garriga-García[2], María Juliana Serrano-Nieto[3], Ruth Garcia-Romero[4], Marina Álvarez Beltrán[5], Elena Crehuá-Gaudiza[6], Saioa Vicente-Santamaría[2], Cecilia Martínez-Costa[6], Juan José Díaz-Martín[7], Carlos Bousoño-García[7], David González-Jiménez[7]

PMID: 36932016
DOI: 10.1016/j.anpede.2023.02.015

**Objectives:** Based on the European and American Cystic Fibrosis (CF) consensus recommendations, an increase in vitamin D (VD) supplementation in patients with CF and insufficient or defficient levels was proposed. The objective of our study was to determine the safety and efficacy of this new protocol.

**Material and methods:** Multicentre nonrandomized uncontrolled experimental study. Patients with insufficient levels (<30 ng/mL) received increasing doses of VD (between 800 and 10 000 IU/day). Patients were followed up for 12 months, during which their vitamin and nutritional status, pulmonary function and calcium and phosphate metabolism were assessed.

**Statistical analysis:** t test for paired data and multivariate logistic regression analysis.

**Results:** Thirty patients aged 1-39 years (median, 9.1) completed the follow-up. Two patients were dropped from the study on account of 25-OH VD levels greater than 100 ng/mL at 3 months without clinical or laboratory signs of hypercalcaemia. At 12 months, we observed an increase of 7.6 ng/mL (95% CI, 4.6-10 ng/mL) in the mean 25-OH VD level and an improvement in vitamin status: 37% achieved levels of 30 ng/mL or greater, 50% levels between 20 and 30 ng/mL and 13% remained with levels of less than 20 ng/mL. We found no association between improved VD levels and pulmonary function.

**Conclusions:** The proposed protocol achieved an increase in serum VD levels and a decrease in the percentage of patients with VD insufficiency, although it was still far from reaching the percentages of sufficiency recommended for this entity.

Glob Pediatr Health. 2023 Mar 6;10:2333794X221150728.

**"Just Move It . . . Move It": A Multidisciplinary Motivational Approach to Improve Physical Activity in Children With Cystic Fibrosis**

Valérie Sputael[1], Véronique Gaspar[1], Valentine Weber[1], Kawtar Soussi[1], Christiane Knoop[2], Laurence Hanssens[1]

PMID: 36911754 PMCID: PMC9996715
DOI: 10.1177/2333794X221150728

Regular physical activity (PA) is essential in cystic fibrosis (CF). This study assessed the impact of a motivational interviewing (MI)-based project titled "Just move it . . . move it," aimed at improving the PA of pediatric CF patients. At baseline and month 6, body mass index, spirometric values, and duration of extracurricular sport activities were collected. Concurrently, the maximum oxygen uptake (VO2max) was estimated. MI was performed during each visit. Overall, 19 CF children were included. Ten patients (52.7%) increased their regular PA (mean 1.9 hours/week) between both visits (PA+ group), while 9 did not (PA- group). No significant differences in functional and nutritional values were observed between the groups, while extracurricular sport time significantly increased in the PA+ group. "Just move it . . . move it" seems to be an efficient approach, as it was able to motivate several CF patients to initiate or increase their PA, yet without improving functional parameters.

J Cyst Fibros. 2023 Mar 11;S1569-1993(23)00064-4.

**Acute pancreatitis in pancreatic-insufficient cystic fibrosis patients treated with CFTR modulators**

Ido Sadras[1], Malena Cohen-Cymberknoh[1], Eitan Kerem[1], Benjamin Z Koplewitz[2], Natalia Simanovsky[2], Michael Wilschanski[1], Liron Birimberg-Schwartz[3], Oded Breuer[4]

PMID: 36914434
DOI: 10.1016/j.jcf.2023.02.013

Cystic fibrosis transmembrane conductance regulator modulator therapy is associated with substantial clinical benefit and improved quality of life in patients with cystic fibrosis (CF). While their effect on lung function has been clearly reported, we are still in the process of unraveling the full impact they have on the pancreas. We present two cases of pancreatic-insufficient CF patients who presented with acute pancreatitis shortly after commencing elexacaftor/tezacaftor/ivacaftor modulator therapy. Both patients were treated with ivacaftor for 5 years prior to elexacaftor/tezacaftor/ivacaftor initiation, but had no previous episodes of acute pancreatitis. We suggest that highly effective modulator combination therapy may restore additional pancreatic acinar activity, resulting in the development of acute pancreatitis in the interim until ductal flow is improved. This report adds to the growing evidence for possible restoration of pancreatic function in patients receiving modulator therapy, and highlights that treatment with elexacaftor/tezacaftor/ivacaftor may be associated with acute pancreatitis until ductal flow is restored, even in pancreatic-insufficient CF patients.

Clin Nutr ESPEN. 2023 Apr;54:349-373.

**Systematic review and meta-analysis: Associations of vitamin D with pulmonary function in children and young people with cystic fibrosis**

Raquel Revuelta Iniesta[1], Seren Cook[2], Gemma Oversby[3], Pelagia Koufaki[3], Marietta L Van der Linden[3], Dimitris Vlachopoulos[2], Craig A Williams[2], Don S Urquhart[4]

PMID: 36963882
DOI: 10.1016/j.clnesp.2023.02.006

**Background:** Increasing evidence suggests that vitamin D is associated with pulmonary health, which may benefit children and young people diagnosed with Cystic Fibrosis (cypCF). Therefore, the aim of this systematic review was to evaluate primary research to establish associations between 25OHD and pulmonary health in cypCF.

**Methods:** Electronic databases were searched with keywords related to CF, vitamin D, children/young people and pulmonary function. Included studies were cypCF (aged ≤21 years) treated in a paediatric setting. The primary outcome was lung function [forced expiratory volume in 1 s ($FEV_1$% predicted)] and secondary outcomes were rate of pulmonary exacerbations, 25OHD status and growth. Evidence was appraised for risk of bias using the CASP tool, and quality using the EPHPP tool. A Meta-analysis was performed.

**Results:** Twenty-one studies were included with mixed quality ratings and heterogeneity of reported outcomes. The Meta-analysis including 5 studies showed a significantly higher $FEV_1$% predicted in the 25OHD sufficiency compared to the deficiency group [$FEV_1$% predicted mean difference (95% CI) was 7.71 (1.69-13.74) %; p = 0.01]. The mean ± SD $FEV_1$% predicted for the sufficient (≥75 nmol/L) vs. deficient (<50 nmol/L) group was 94.7 ± 31.9% vs. 86.9 ± 13.2%; $I^2$ = 0%; $\chi^2$ = 0.5; df = 4). Five studies (5/21) found significantly higher rate of pulmonary exacerbations in those who were 25OHD deficient when compared to the sufficient group and negative associations between 25OHD and FEV% predicted. The effects of vitamin D supplementation dosages on 25OHD status (10/21) varied across studies and no study (12/21) showed associations between 25OHD concentration and growth.

**Conclusion:** This systematic review suggests that 25OHD concentration is positively associated with lung function and a concentration of >75 nmol/L is associated with reduced frequency of pulmonary exacerbations, which may slow lung function decline in cypCF. Future randomised clinical trials and mechanistic studies are warranted.

J Cyst Fibros. 2023 Mar 23;S1569-1993(23)00075-9.

**A paradigm shift in cystic fibrosis nutritional care: Clinicians' views on the management of patients with overweight and obesity**

Joanna E Snowball[1], William G Flight[2], Laura Heath[3], Dimitrios A Koutoukidis[4]

PMID: 36966039
DOI: 10.1016/j.jcf.2023.03.011

**Background:** Overweight and obesity among people with cystic fibrosis (pwCF) has become more prevalent since the widespread adoption of CF transmembrane conductance regulator (CFTR) modulator therapies and presents a new challenge for nutritional care. We aimed to explore how clinicians working in CF care approach the management of adults with overweight and obesity.

**Methods:** We conducted semi-structured interviews with n = 20 clinicians (n = 6 physiotherapists, n = 6 doctors and n = 8 dietitians) working in 15 adult CF centres in the United Kingdom. The interviews explored their perspectives and current practices caring for people with CF and overweight/obesity. Data were analysed using reflexive thematic analysis.

**Results:** Four main themes were identified: 1) challenges of raising the topic of overweight and obesity in the CF clinic (e.g., clinician-patient rapport and concerns around weight stigma); 2) the changing landscape of assessment due to CF-specific causes of weight gain: (e.g., impact of CFTR modulators and CF legacy diet) 3) presence of clinical equipoise for weight management due to the lack of CF-specific evidence on the consequences of obesity and intentional weight loss (e.g., unclear consequences on respiratory outcomes and risk of weight related co-morbidities) and 4) opportunities for a safe, effective, and acceptable weight management treatment for people with CF (e.g., working collaboratively with current multidisciplinary CF care).

**Conclusions:** Approaching weight management in the CF setting is complex. Trials are needed to assess the equipoise of weight management interventions in this group and CF-specific issues should be considered when developing such interventions.

Orphanet J Rare Dis. 2023 Mar 20;18(1):62.

**Increasing incidence rate of breast cancer in cystic fibrosis - relationship between pathogenesis, oncogenesis and prediction of the treatment effect in the context of worse clinical outcome and prognosis of cystic fibrosis due to estrogens**

Nela Stastna[1,2], Kristian Brat[3,4], Lukas Homola[4,5], Audun Os[6], Dagmar Brancikova[4,7]

PMID: 36941680 PMCID: PMC10029289

DOI: 10.1186/s13023-023-02671-z

Cystic fibrosis (CF) is the most common genetic disease in the Caucasion population. Thanks to the CFTR modulators therapy, life expectancy will significantly improve. New therapeutic challenges can be expected, including diseases associated with ageing and higher incidence of cancer, as evidenced by recent epidemiological studies. The increasing incidence of tumors includes also breast cancer. The risk of breast cancer is higher in CF patients compared to the general population. Sex hormones, especially estrogens, also affect on the pathophysiology and immunology of the CF. Previous research, has demonstrated unequivocal survival rates for female CF patients compared to their male counterparts. Is demonstrated, that chemotherapy used for breast cancer affects the CFTR channel and CFTR modulator therapy has frequent side effects on breast tissue. In this review, we focus on the effects of female sex hormones on CF disease, pathophysiological relationships between CF and breast cancer, and the impact of antitumor treatment on both, malignant disease and CF. The potential for further investigation is also discussed.

## Psychosocial

J Cyst Fibros.2023 Jan 27;S1569-1993(23)00003-6.

**Cost burden among the CF population in the United States: A focus on debt, food insecurity, housing and health services**

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PMID: 36710098

DOI: 10.1016/j.jcf.2023.01.002

**Background:** Advancements in the cystic fibrosis (CF) field have resulted in longer lifespans for individuals with CF. This has led to more responsibility for complex care regimens, frequent health care, and prescription medication utilization that are costly and may not be fully covered by health insurance. There are outstanding questions about unmet medical needs among the U.S. population with CF and how the financial burden of CF is associated with debt, housing instability, and food insecurity.

**Methods:** Researchers developed the CF Health Insurance Survey (CF HIS) to survey a convenience sample of people living with CF in the U.S. The sample was weighted to reflect the parameters of the 2019 Cystic Fibrosis Foundation Patient Registry Annual Data Report, and chi-square tests and multiple logistic regression models were conducted.

**Results:** A total of 1,856 CF patients in the U.S. were included in the study. Of these, 64% faced a financial burden: 55% of respondents faced debt issues, 26% housing issues, and 33% food insecurity issues. A third reported at least one unmet medical need: 24% faced unmet prescription needs, 12% delayed or shortened a hospitalization, and 10% delayed or skipped a care center visit as a result of the cost of care.

**Conclusions:** People with CF in the U.S. experience high financial burden, which is associated with unmet medical needs. Income is the biggest risk factor for financial burden for people with CF, with people dually covered by Medicare and Medicaid particularly at risk.

Pulm Med. 2023 Jan 23;2023:5082499.

**Patient Perspectives on the Use of Digital Technology to Help Manage Cystic Fibrosis**

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PMID: 36727045

PMCID: PMC9886457

DOI: 10.1155/2023/5082499

**Background:** Digital health technologies (DHTs) have shown potential to improve health outcomes through improved medication adherence in different disease states. Cystic fibrosis (CF) requires care coordination across pharmacies, patients, and providers. DHTs can potentially support patients, providers, and pharmacists in diseases like CF, where high medication burden can negatively impact patient quality of life and outcomes.

**Methods:** In this prospective cohort study, a CF-specific mobile application (Phlo) was distributed to adults with CF who received care at the University of Utah Cystic Fibrosis Center, used an iPhone, and filled prescriptions through the University of Utah Specialty Pharmacy services. Participants were asked to use Phlo for 90 days with an optional 90-day extension period. Participants completed four surveys at baseline and after 90 days. Changes in patient-reported outcomes, adherence, clinical outcomes, and healthcare resource utilization from baseline to 90 days were tracked.

**Results:** Phlo allowed users to track daily regimen activities, contact their care team, receive medication delivery reminders, and share progress with their healthcare team. A web-based dashboard allowed the care team to review reported performance scores from the app. Most patients (67%) said the app improved confidence in and motivation for continuing their regimen. The most important reported benefit of Phlo was having a single location to manage their whole routine.

**Conclusions:** Phlo is a mobile health technology designed to help patients with CF manage their treatment regimen and improve patient-provider communication

# How many billions is enough? Prioritizing profits over patients with cystic fibrosis

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To the Editor,

Cystic fibrosis transmembrane conductance regulator (CFTR) modulators have drastically improved outcomes for many people with cystic fibrosis (CF), including improved lung function and increased life expectancy by targeting the defective CFTR protein.[1, 2] As a result, many more people with CF are now fulfilling key life milestones, including pursuing education, careers, and parenthood.[3] We applaud the research and development efforts of Vertex Pharmaceuticals, the sole manufacturer of CFTR modulators. Vertex has been heralded as a shining star of pharmaceutical companies for personalized medicine and rare disease, and has a stated commitment to the CF community. However, we are appalled at how Vertex is achieving financial success on the backs of vulnerable populations.

Only a small percentage of people with CF worldwide have access to these disease-altering CFTR modulators due to Vertex not allowing the development of generic forms or lowering pricing for lower-income or middle-income countries (LMICs), as done by other pharmaceutical companies for HIV, Hepatitis C, and Covid-19 medications.[4] Due to Vertex's refusal to assist LMICs and Vertex holding the patent for elexacaftor/tezacaftor/ivacaftor until 2037, LMICs will not have generic ETI available for 14 more years. An entire generation of people with CF in LMICs may therefore miss out on the profound benefit of ETI. In many of their corporate actions, Vertex's sole focus is greed and profit without regard for how their policies impact the lives of people with CF.

In the United States, recent decisions by Vertex are also endangering access to CFTR modulators among people who already have been receiving treatment. In October 2022, Vertex announced a plan to drastically decrease its copay assistance coupon program for CFTR modulators. Copay assistance allows many people to afford CFTR modulators, particularly those with high-deductible health insurance, a growing segment of our population. Until now, Vertex's program has provided families $8950 per fill, up to 17 fills annually, which allows Vertex to make about $14,000 per fill in profit from billing the medical insurance company for CFTR modulators patients could not otherwise afford (Table **1**). Vertex is reducing the copay assistance program to only a maximum of $20,000 per year with only $3,500 per fill, far below what many pharmacy plans charge as copayment. For families with health insurance plans that have adopted copay accumulators, $20,000 would only allow for about five medication refills per year, shifting the remaining exorbitant copays to the patient. Health insurance plans with copay accumulators take the maximum value of manufacturer copay assistance as quickly as possible without applying that amount to the deductible or out-of-pocket maximum. The patient is then responsible for paying the entire deductible and the remaining cost of the fills.

CFTR modulators are some of the most expensive drugs in the market, priced by Vertex at over $300,000 a year or over $25,000 a month. This has resulted in Vertex reporting $8,900,000,000 in profit in the past year.[5] This cost is unjustifiably high. CFTR modulators are overpriced compared with quality life years gained[6] and the estimated cost of producing is 90% less than the list price.[7] The fact that Vertex is drastically decreasing its copay assistance program while earning these jaw-dropping profits truly exposes its corporate greed.

As CF clinicians, we are watching as the livelihood of people with CF is increasingly caught in a battle for record-breaking profits between Vertex and many health insurance companies. Vertex claims that their policy changes are a direct result of actions by insurance providers. Many insurance companies have implemented copayment accumulator programs. Such health plans will not allow manufacturer copay assistance coupons to apply to annual deductibles or out-of-pocket maximum. This benefits insurers by increasing profits while offsetting costs to patients. Copayment accumulators were meant to incentivize lower-cost generic medications. However, no generic forms of CFTR modulators are available due to Vertex policies.

People cannot pay thousands of dollars monthly, even for life-altering medications; the choice is paying for medication or paying for food and housing. People with CF already have high out-of-pocket expenses annually (median $8244), which is about a quarter of the median per capita income in the United States.[8] There is no guaranteed coverage if people cannot afford this astronomical out-of-pocket cost. Changing the copay assistance program is akin to denying access to CFTR modulators and will lead to the deterioration of health in people with CF.

We, as healthcare providers for people with CF, will not stand by as corporate greed puts people with CF at risk of losing access to CFTR modulators. We call on Vertex to increase the copay assistance amount to ensure patients' access to CFTR medications for an entire year ($3500/fill, 13 fills yearly). We call on insurance companies to end copay accumulator programs. We call on Congress to pass The Help Ensure Lower Patient Copays Act (HR 5801) to ban copay accumulators. We call on Vertex to reduce the price of CFTR modulators to reflect the value given in the 2020 Institute for Clinical and Economic Review report.

Vertex does not have to drastically decrease copayment assistance, yet they choose to. Insurance companies do not have to include copayment accumulators, yet they choose to. Vertex does not have to charge over $300,000 annually for its drugs, yet they choose to. Vertex and insurance companies choose to put their record-breaking billions of dollars in profits over the lives of people with CF, and they must be held to account for policies that threaten to bankrupt the very people they claim to want to help live longer lives with CF.

**Table 1.** Copayment assistance programs' cost and profits.

| | Copay assistance programs | Maximum annual assistance | Vertex profit minimum per patient annually (list price ~$300,000) |
|---|---|---|---|
| Vertex's former copay assistance program | $8950 × 17 fills | $152,150 | ~ $147,850 |
| Vertex's new copay assistance program | $3500/fill × 5 fills<br>$20,000 maximum | $20,000 | ~ $280,000 if 12 fills/year<br>~ $105,000 if 5 fills/year |
| Our suggested copay assistance program | $3500/fill × 13 fills | $45,500 | ~ $254,500 |

*Note*: The list price for elexacaftor/texacaftor/ivacaftor (ETI) is over $300,000 annually in the United States. The estimated profit for both Vertex's new program assumes patients can afford to pay all out-of-pocket expenses, which is not realistic for many patients. If patients only can afford the five fills per year before discontinuing ETI with Vertex's new copay assistance program, Vertex's profit would decrease to only $105,000 per patient annually.

## 1 CONCLUSION

CFTR modulators have transformed CF but are some of the most expensive medications in the market and are overpriced compared with the value given. The high price of CFTR modulators leaves people with CF dependent on Vertex's copay assistance programs. Despite record-breaking profits, Vertex is drastically decreasing its copayment assistance programs, so people with CF will have to pay thousands of dollars monthly for CFTR modulators or discontinue therapy. Vertex continues to put profits above the lives of people with CF.

Pediatr Pulmonol. 2023 May;58(5):1444-1453.

**Electronic screening for unmet social needs in a pediatric pulmonary clinic: Acceptability and associations with health outcomes**

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PMID: 36721912
DOI: 10.1002/ppul.26339

**Background:** Children with unmet basic needs experience worse health than more advantaged counterparts. There has been limited research on screening for unmet basic needs in pediatric subspecialty care.

**Methods:** Caregivers of established patients in pediatric asthma and cystic fibrosis (CF) clinics were screened for unmet basic needs with an electronic survey, which asked about concerns and stress level (5-point Likert scale) related to food, housing, transportation, health insurance, and childcare, among others. Medical record review provided patient demographic characteristics and clinical data. A follow-up survey with the clinical providers assessed the acceptability of electronic screening for unmet needs.

**Results:** The sample included 214 pediatric patients (N = 105 asthma, N = 109 CF) and their caregivers. Most patients with asthma (76%) were Black, 30% in households with <$20,000 annual income. In contrast, most patients with CF (93%) were white, 12% in households with <$20,000 annual income. Reported needs included food insecurity (29% asthma and 17% CF), healthy food (75% asthma and 87% CF), financial insecurity (45% asthma and 32% CF), health insurance (15% asthma and 28% CF), smoke exposure (24% asthma and 28% CF), child's exercise (21% asthma and 28% CF), living conditions (18% asthma and 17% CF), childcare (11% asthma and 15% CF), transportation (16% asthma and 9% CF), and housing insecurity (10% asthma and 8% CF). Concerns were rated moderately to very stressful. Food insecurity, financial insecurity, and smoke exposure were significantly associated with uncontrolled asthma. In people with CF, concerns about health insurance and child exercise were significantly associated with lower lung function and increased odds of hospitalizations. Clinicians believed that screening was important and should be administered by a designated person on the clinical team.

**Conclusions:** Unmet basic needs and associated stress levels are linked to adverse pediatric pulmonary outcomes. Electronic screening, without face-to-face interaction or paper trail, facilitates high response rates and is easily integrated into clinic flow. Such screenings can identify vulnerable patients for targeted interventions and referral to available community resources.

J Cyst Fibros. 2023 Feb 7;S1569-1993(23)00023-1.

**Suicide attempts in adolescents with cystic fibrosis on Elexacaftor/Tezacaftor/Ivacaftor therapy**

Meliksah Arslan[1], Sarah Chalmers[2], Kelly Rentfrow[3], Janelle M Olson[4], Vicki Dean[4], Mark E Wylam[5], Nadir Demirel[4]

PMID: 36759252
DOI: 10.1016/j.jcf.2023.01.015

Elexacaftor/Tezacaftor/Ivacaftor (ETI) is a recently approved cystic fibrosis (CF) transmembrane conductance regulator modulator therapy that has shown promising clinical and laboratory improvements on multiple organ systems in people with CF (pwCF). While original clinical trials found little to no effect on depression and anxiety, many post-marketing reports have suggested that ETI may be associated with adverse mental health effects. Here we report on two pwCF with adverse mental health effects shortly after starting ETI. Although many factors such as the burden of living with a chronic disease or widespread effects of the Covid-19 pandemic may have contributed to these events, similar reports have led to mounting concern that ETI may be the cause of such events. Regular mental health screening before the initiation of ETI and monitoring for signs and symptoms of mental diseases afterward should be a routine part of care, given the gravity of possible outcomes.

NIHR Open Res 2022 May 9;2:36.

**Exploring the nature of perceived treatment burden: a study to compare treatment burden measures in adults with cystic**

Rana Altabee[1,2], Siobhan B Carr[3,4], Janice Abbott[5], Rory Cameron[1,6], Daniel Office[7], Jessie Matthews[7], Nicholas Simmonds[4,7], Rebecca Cosgriff[8], David Turner[1], Jennifer Whitty[1,6]

PMID: 36855412 PMCID: PMC7614250
DOI: 10.3310/nihropenres.13260.1

**Background:** Despite the importance of reducing treatment burden for people with cystic fibrosis (CF), it has not been fully understood as a concept. This study aims to quantify the treatment burden perceived by CF adults and explore the association between different validated treatment burden measures.

**Methods:** This is a cross-sectional observational study of CF adults attending a single large UK adult center. Participants completed an online survey that contained three different treatment burden scales; CF Questionnaire-Revised (CFQ-R) subscale, CF Quality of Life (CFQoL) subscale, and the generic multimorbidity treatment burden questionnaire (MTBQ).

**Results:** Among 101 participants, the median reported treatment burden by the CFQ-R subscale was 55.5 (IQR 33.3 - 66.6), the CFQoL subscale was 66.6 (IQR 46.6 - 86.6), and the MTBQ reversed global score was 84.6 (IQR 73.1 - 92.3). No correlation was found between respondents' demographic or clinical variables and treatment burden measured via any of the three measures. All treatment burden measures showed correlations against each other. More treatments were associated with high treatment burden as measured by the CFQ-R, CFQoL subscales, and the MTBQ. However, longer treatment time and more complex treatment plans were correlated with high treatment burden as measured by the CFQ-R and CFQoL subscales, but not with the MTBQ.

**Conclusions:** Treatment burden is a substantial issue in CF. Currently, the only available way to evaluate it is with the CF-specific quality of life measure treatment burden subscales (CFQ-R and CFQoL); both indicated that treatment burden increases with more treatments, longer treatment time, and more complex treatments.

Pediatr Pulmonol 2023 Jun;58(6):1798-1801.

**High deductible insurance plans impart economic burden for people with cystic fibrosis**

Ryan C Perkins[1,2], Gregory S Sawicki[1]

PMID: 36858451
DOI: 10.1002/ppul.26382

*No abstract available*

J Cyst Fibros. 2023 Mar;22(2):207-216.

**Sharing decisions on reproductive goals: A mixed-methods study of the views of women who have cystic fibrosis**

Denitza Williams[1], Oluwaseun B Esan[2], Daniela K Schlüter[3], David Taylor-Robinson[2], Shantini Paranjothy[3], Jamie Duckers[4], Natalie Goodchild[5], Rhiannon Phillips[6]

PMID: 36863947
DOI: 10.1016/j.jcf.2023.02.007

**Background:** There are complex medical, psychological, social and economic aspects to becoming a parent with Cystic Fibrosis (CF). A shared decision-making (SDM) approach could help women with CF make informed decisions about their reproductive goals that are sensitive to their individual values and preferences. This study investigated capability, opportunity, and motivation to participate in SDM from the perspective of women with CF.
**Methods:** Mixed-methods design. An international online survey was completed by 182 women with CF, to investigate participation in SDM in relation to reproductive goals, and measures of capability (information needs), opportunity (social environment) and motivation (SDM attitudes and self-efficacy) to engage in SDM. Twenty-one women were interviewed using a visual timelines method to explore their SDM experiences and preferences. Qualitative data were analysed thematically.
**Results:** Women with higher decision self-efficacy reported better experiences of SDM relating to their reproductive goals. Decision self-efficacy was positively associated with social support, age, and level of education, highlighting inequalities. Interviews indicated that women were highly motivated to engage in SDM, but their capability was compromised by lack of information, perception of insufficient opportunities for focused discussions about SDM.
**Conclusions:** Women with CF are keen to engage in SDM about reproductive health, but currently lack sufficient information and support to do so. Interventions at patient, clinician and system levels are needed to support capability, opportunity and motivation to engage equitably in SDM in relation to their reproductive goals.

J Cyst Fibros. 2023 Mar 14;S1569-1993(22)01427-8.

**Medical traumatic stress in cystic fibrosis: A qualitative analysis**

Addison A Cuneo[1], Simon Outram[2], Meghan L Marsac[3], Siena Vendlinski[4], Melvin B Heyman[4], Ngoc Ly[4], Emily von Scheven[4], Emily R Perito[4]

PMID: 36925385
DOI: 10.1016/j.jcf.2022.12.008

**Background:** People living with cystic fibrosis (PwCF) face a lifetime of potentially traumatic illness-related experiences that can lead to posttraumatic stress symptoms. Existing criteria for this type of posttraumatic stress, called medical traumatic stress (MTS), may not fully capture the CF experience. In this study we aimed to explore: 1) illness-related experiences perceived as traumatic in the setting of CF, 2) perceived MTS symptoms in PwCF, and 3) perceived health-related functional impairments from MTS.
**Methods:** Informed by our aims, we developed and piloted guides for semi-structured interviews and focus groups with PwCF, family members of PwCF, and CF medical providers. We then conducted a series of interviews and focus groups. The qualitative analytical process followed Deterding and Waters' three stages of flexible coding for in-depth interviews, generating key themes and sub-themes in each domain of study inquiry.
**Results:** We recruited 51 participants, including 24 PwCF, 7 family members of PwCF, and 20 CF care team members. Illness-related experiences perceived as traumatic were often characterized by themes of loss of agency, threats of bodily harm, and shifts in identity. Prominent MTS symptoms included shame, survivor guilt, burden guilt, germaphobia, and symptom panic. Health-related themes of functional impairments perceived to result from MTS included poor adherence and strained relationships between providers and patients/families.
**Conclusions:** This is the first study to explore the specific experiences of MTS in PwCF. It highlights the need for screening that includes these specific exposure types and symptoms, which may be mitigatable with medical trauma-focused interventions.

Cochrane Database Syst Rev. 2023 Mar 29;3(3):CD013766.

**Psychological interventions for improving adherence to inhaled therapies in people with cystic fibrosis**

Sophie Dawson[1,2], Carla-Jane Girling[3], Lisa Cowap[2], David Clark-Carter[2]

PMID: 36989170 PMCID: PMC10054300 (available on 2024-03-29)
DOI: 10.1002/14651858.CD013766.pub2

**Background:** Adherence to treatment, including inhaled therapies, is low in people with cystic fibrosis (CF). Although psychological interventions for improving adherence to inhaled therapies in people with CF have been developed, no previous published systematic review has evaluated the evidence for efficacy of these interventions.
**Objectives:** The primary objective of the review was to assess the efficacy of psychological interventions for improving adherence to inhaled therapies in people with cystic fibrosis (CF). The secondary objective was to establish the most effective components, or behaviour change techniques (BCTs), used in these interventions.
**Authors' conclusions:** Due to the limited quantity of trials included in this review, as well as the clinical and methodological heterogeneity, it was not possible to identify an overall intervention effect using meta-analysis. Some moderate-certainty evidence suggests that psychological interventions (compared with usual care) probably improve adherence to inhaled therapies in people with CF, without increasing treatment-related adverse events, anxiety and depression (low-certainty evidence). In future review updates (with ongoing trial results included), we hope to be able to establish the most effective BCTs (or 'active ingredients') of interventions for improving adherence to inhaled therapies in people with CF. Wherever possible, investigators should make use of the most objective measures of adherence available (e.g. data-logging nebulisers) to accurately determine intervention effects. Outcome reporting needs to be improved to enable combining or separation of measures as appropriate. Likewise, trial reporting needs to include details of intervention content (e.g. BCTs used); duration; intensity; and fidelity. Large trials with a longer follow-up period (e.g. 12 months) are needed in children with CF. Additionally, more research is needed to determine how to support adherence in 'under-served' CF populations.

## GI

J Cyst Fibros.2023 Jan 28;S1569-1993(23)00019-X.

**The gut microbiome, short chain fatty acids, and related metabolites in cystic fibrosis patients with and without colonic adenomas**

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PMID: 36717332
DOI: 10.1016/j.jcf.2023.01.013

**Background:** Adults with cystic fibrosis (CF) are at increased risk for colon cancer. CF patients have reductions in intestinal bacteria that produce short chain fatty acids (SCFAs), although it is unclear whether this corresponds with intestinal SCFA levels and the presence of colonic neoplasia. The aim of this study was to compare gut microbiome and SCFA composition in patients with and without CF, and to assess associations with colonic adenomas.
**Methods:** Colonic aspirates were obtained from adults with and without CF undergoing colon cancer screening or surveillance colonoscopy. Microbiome characterization was performed by 16S rRNA V3-V4 sequencing. Targeted profiling of SCFAs and related metabolites was performed by LC-MS.
**Results:** 42 patients (21 CF, 21 control) were enrolled. CF patients had significantly reduced alpha diversity and decreased relative abundance of many SCFA-producing taxa. There were no significant differences in SCFA levels in CF patients, although there were reduced levels of branched chain fatty acids (BCFAs) and related metabolites. CF patients with adenomas, but not controls with adenomas, had significantly increased relative abundance of Bacteroides fragilis. CF microbiome composition was significantly associated with isovalerate concentration and the presence of adenomas.
**Conclusions:** CF patients have marked disturbances in the gut microbiome, and CF patients with adenomas had notably increased relative abundance of B. fragilis, a pathogen known to promote colon cancer. Reductions in BCFAs but not SCFAs were found in CF. Further studies are warranted to evaluate the role of B. fragilis as well the biological significance of reductions in BCFAs in CF.

Liver Int. 2023 Apr;43(4):878-887.

**Increase of liver stiffness and altered bile acid metabolism after triple CFTR modulator initiation in children and young adults with cystic fibrosis**

Alexander Schnell[1], Jörg Jüngert[1], Daniel Klett[2], Hannah Hober[1], Natalie Kaiser[1], Renate Ruppel[1], Annika Geppert[2], Christina Tremel[1], Julia Sobel[1], Erika Plattner[1], Sabina Schmitt-Grohé[1], Sabine Zirlik[2], Deike Strobel[2], Markus F Neurath[2], Ferdinand Knieling[1,3], Manfred Rauh[1], Joachim Woelfle[1], André Hoerning[1], Adrian P Regensburger[1,3]

PMID: 36797990
DOI: 10.1111/liv.15544

**Background:** Novel cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies (elexacaftor/tezacaftor/ivacaftor-ETI) promise clinically significant and sustained improvements for patients with cystic fibrosis (CF). In this study, we investigated the impact of ETI therapy on liver stiffness and bile acid metabolism in a cohort of children and young adults with CF.
**Methods:** A prospective observational study (NCT05576324) was conducted from September 2020 to November 2021 enrolling CF patients naive to ETI. Standard laboratory chemistry, sweat test, lung function, share wave velocity (SWV) derived by acoustic radiation force impulse imaging (ARFI) and serum bile acid profiles were assessed before and 6 months after induction of ETI therapy.
**Results:** A total of 20 patients (10 aged <20 years) completed the study. While lung function and BMI improved after ETI therapy, ARFI SWV increased in CF patients <20 years of age (from 1.27 to 1.43 m/s, p = 0.023). Bile acid (BA) profiles revealed a decrease in unconjugated (5.75 vs 1.46, p = 0.007) and increase in glycine-conjugated derivatives (GCDCA) (4.79 vs 6.64 p = 0.016). There was a positive correlation between ARFI SWV values and GCDCA (r = 0.80, p < 0.0001). Glycine-conjugated BA provided high diagnostic accuracy to predict increased ARFI measurements (AUC 0.90) and clinical (Colombo) CFLD grading (AUC 0.97).
**Conclusions:** ARFI SWV and bile acid profiles provide evidence for early increase in liver stiffness and altered bile acid metabolism in young CF patients after initiation of ETI and may serve as synergistic measures for detection of hepatic complications during ETI therapy.

Arch Argent Pediatr. 2023 Mar 9;e202202905.

**Cystic fibrosis liver disease in children - A review of our current understanding**

Guillermo Costaguta[1], Natalie Patey[2], Fernando Álvarez[1,3]

PMID: 36856762
DOI: 10.5546/aap.2022-02905.eng

Cystic fibrosis is the second most common genetic disease in infancy. It is the result of a mutated channel protein, the CFTR, which secretes chloride ions, fluidifying secretions. Recent improvements in the treatment have increased life expectancy in these patients. Nevertheless, liver involvement remains the third cause of death. Unfortunately, our understating of the physiopathology is still deficient. Biliary obstruction secondary to the presence of thick secretions is considered to lead to cirrhosis. However, treatment with ursodeoxycolic acid has not changed the natural history. Furthermore, the presence of portal hypertension in the absence of cirrhosis cannot be explained. Recently, the role of CFTR as modulator of immune tolerance has been proposed, which could explain the presence of a persistent portal inflammation leading to fibrosis, and the gut-liver axis would also have a role in disease presentation and progression.

J Am Pharm Assoc (2003). 2023 May-Jun;63(3):920-924.
**Incidence of transaminitis in adults with cystic fibrosis taking elexacaftor/tezacaftor/ivacaftor**
Marci Wood, Faith Babowicz, Amanda G Kennedy, Martine Antell, Elizabeth Gilhooly, Bradley J Tompkins, Sheela S Reddy
PMID: 36872183
DOI: 10.1016/j.japh.2023.02.015
**Background:** Cystic fibrosis (CF) transmembrane conductance regulator modulators are a cornerstone of CF treatment. However, many patients develop CF liver disease (CFLD) over time, and previous data indicate a risk for transaminase elevation with modulator use. Elexacaftor/tezacaftor/ivacaftor is a commonly prescribed modulator with broad efficacy among CF genomic profiles. Theoretically, elexacaftor/tezacaftor/ivacaftor drug-induced liver injury could exacerbate and further worsen CFLD, but holding modulators can cause a decline in clinical status.
**Objectives:** This study was designed to determine the real-world incidence of transaminase elevations in adult patients with CF taking elexacaftor/tezacaftor/ivacaftor.
**Methods:** This exploratory, retrospective descriptive study included all adults with CF-prescribed elexacaftor/tezacaftor/ivacaftor at our institution's outpatient CF clinic. We explored transaminase elevations in 2 separate outcomes: incidence of transaminase elevations of more than 3 times the upper limit of normal (ULN), and transaminase elevations of 25% or more above baseline.
**Results:** 83 patients were prescribed elexacaftor/tezacaftor/ivacaftor. Nine patients (11%) experienced an elevation of more than 3 times ULN and 62 (75%) experienced an elevation of 25% or more above baseline. The median days to transaminase elevation were 108 and 135 days, respectively. Therapy was not discontinued due to transaminase elevations in any of the patients.
**Conclusion:** Transaminase elevations among adults taking elexacaftor/tezacaftor/ivacaftor were common but did not result in discontinuation of therapy. Pharmacists should be reassured of the liver safety profile of this important medication for patients with CF.

J Surg Case Rep. 2023 Mar 17;2023(3):rjad117.
**Intussusception of the appendix in a young adult: an important differential diagnosis of abdominal pain in cystic fibrosis patients?**
Meena Venkatasami [1], Ellen Cobby [1]
PMID: 36937795 PMCID: PMC10023239
DOI: 10.1093/jscr/rjad117
Cystic fibrosis (CF) is commonly associated with gastrointestinal manifestations from infancy to adulthood. Distal intestinal obstruction syndrome (DIOS) affects 20% of CF patients, where intussusception can be a rare complication. A 20-year-old CF male was diagnosed with a 3-day history of right iliac fossa pain and diarrhoea. Clinical examination revealed a tender palpable mass in the right iliac fossa and raised serum inflammatory markers. Contrast computerized-tomography of the abdomen-pelvis suggested intussusception of the appendix and further confirmed on histological analyses. The patient underwent an open appendicectomy where the intussusception had self-resolved. The literature review indicated a scarcity of data with 10 cases reported of intussusception in adult CF patients. Our case was in line with previous research of transient intussusception. This rare case highlights an importance to carry a higher index of suspicion for gastrointestinal manifestations in CF patients where differential diagnoses of DIOS and intussusception should be considered in the acute presentation.

Med Clin (Barc). 2023 Mar 18;S0025-7753(23)00067-2.
doi: 10.1016/j.medcli.2023.01.021.
**Acute cholecystitis in cystic fibrosis patients after initiation of treatment with elexacaftor/tezacaftor/ivacaftor**
Marta Solís García [1], Claudia Madrid Carbajal [2], Rosa María Girón Moreno [3]
PMID: 36941162
DOI: 10.1016/j.medcli.2023.01.021
*No abstract available*

Diagn Interv Radiol. 2023 Mar 20.
**Pre-emptive transjugular intrahepatic portosystemic shunt in pediatric cystic fibrosis-related liver disease and portal hypertension: prospective long-term results**
Laurens Hermie [#1], Stephanie Van Biervliet [2], Anne Hoorens [3], Lien Van Cauwenberghe [1], Eddy Robberecht [2], Luc Defreyne [1]
PMID: 36994654
DOI: 10.4274/dir.2022.221818
**Purpose:** Portal hypertension (PHT) and its sequelae are the most clinically important manifestations in cystic fibrosis-related liver disease (CFLD). This paper aimed to evaluate the safety and efficacy of a pre-emptive transjugular intrahepatic portosystemic shunt (TIPS) to prevent PHT-related complications in pediatric patients with CFLD.
**Methods:** This was a prospective single-arm study on pediatric patients with CFLD, signs of PHT, and preserved liver function who underwent a pre-emptive TIPS in a single tertiary CF center between 2007 and 2012. The long-term safety and clinical efficacy were assessed.
**Results:** A pre-emptive TIPS was performed on seven patients with a mean age of 9.2 years (± standard deviation: 2.2). The procedure was technically successful in all patients, with an estimated median primary patency of 10.7 years [interquartile range (IQR) 0.5-10.7)]. No variceal bleeding was observed during the median follow-up of 9 years (IQR 8.1-12.9). In two patients with advanced PHT and rapidly progressive liver disease, severe thrombocytopenia could not be stopped. Subsequent liver transplantation revealed biliary cirrhosis in both patients. In the remaining patients with early PHT and milder porto-sinusoidal vascular disease, symptomatic hypersplenism did not occur, and liver function remained stable until the end of the follow-up. Inclusion for pre-emptive TIPS was discontinued in 2013 following an episode of severe hepatic encephalopathy.
**Conclusion:** TIPS is a feasible treatment with encouraging long-term primary patency to avoid variceal bleeding in selected patients with CF and PHT. However, as the progression of liver fibrosis, thrombocytopenia, and splenomegaly is inevitable, the clinical benefits due to pre-emptive placement appear to be minor.

## Endocrine

Menopause. 2023 Apr 1;30(4):401-405.

**Menopause in people with cystic fibrosis**

Katherine Prochownik[1], Raksha Jain, Jennifer L Taylor-Cousar, Daniel R Lavage[1], Olivia M Stransky[2], Holly N Thomas, Traci M Kazmerski

PMID: 36720079
DOI: 10.1097/GME.0000000000002155

This study aimed to describe the menopause experience of people with cystic fibrosis (CF). We conducted a computer-based cross-sectional survey of women with CF 25 years or older at 10 US CF centers exploring a range of sexual and reproductive health concerns, including menopause. We used descriptive statistics to analyze results. Of 460 participants, 5 (3%) were perimenopausal and 34 (7%) were postmenopausal. Of participants perimenopausal or menopausal (n = 39), 97% reported the following menopausal symptoms occurring at least once a week: most commonly early wake-up (83%); stiffness/soreness in joints, neck, or shoulders (65%); and night sweats (65%). Among menopausal participants, the median self-reported age at menopause was 48.5 years (interquartile range, 5.5 y). Thirty percent experienced worsened CF symptoms during menopause, and 42% experienced worsening CF symptoms after menopause. Twenty-four percent of menopausal participants were on estrogen therapy and 15% on estrogen and progesterone therapy. Three-fourths of participants using hormone therapy reported no change in their CF symptoms. One percent of the 460 survey participants reported discussing menopause with their CF provider, despite 19% wanting to discuss this topic with their CF team. This is the first study to describe menopause symptoms of people with CF. People with CF experience a variety of menopausal symptoms and often report a worsening of their CF symptoms after menopause, suggesting an interplay between female sex hormones and CF. Larger studies are needed comparing the sexual and reproductive health experiences and care needs of people with CF in the menopause transition to the general population.

J Cyst Fibros. 2023 Mar;22(2):275-281.
doi: 10.1016/j.jcf.2023.01.010. Epub 2023 Jan 27.

**Diabetes is associated with increased burden of gastrointestinal symptoms in adults with cystic fibrosis**

L R Caley[1], C Zagoya[2], F Duckstein[2], H White[3], D Shimmin[4], A M Jones[5], J Barrett[6], J L Whitehouse[6], R A Floto[7], J G Mainz[8], D G Peckham[9]

PMID: 36710099
DOI: 10.1016/j.jcf.2023.01.010

**Background:** Individuals with diabetes mellitus (DM) are known to frequently experience gastrointestinal (GI) symptoms. In contrast, the impact of cystic fibrosis-related diabetes (CFRD) on accentuating GI symptoms in people with cystic fibrosis (pwCF) is unknown. We sought to examine this.
**Methods:** Abdominal symptoms were measured using the validated CF-specific GI symptom questionnaire - CFAbd-Score© - as part of a multicentre cohort study in pancreatic insufficient adults with CF, not on cystic fibrosis transmembrane conductance regulator (CFTR) modulators. The CFAbd-Score total score (0-100pts), its 5 domains, alongside nine specific GI symptoms associated with DM, were compared between the CFRD and non-CFRD groups.
**Results:** 27 (31%) and 61 (69%) participants with CF were recruited in the CFRD and non-CFRD groups respectively. Total CFAbd-Score and the two domains: gastroesophageal reflux disease and disorders of appetite were significantly higher in the CFRD group compared to the non-CFRD group ($p<0.05$), with the mean total CFAbd-Score being 25.4 ± 2.5 and 18.4 ± 1.5 in the CFRD and non-CFRD groups respectively. Among the nine GI symptoms commonly reported as elevated in DM, bloating and nausea were significantly more common in individuals with CFRD compared to those without ($p<0.05$).
**Conclusions:** Individuals with CFRD overall, have a higher GI symptom burden, according to CFAbd-Scores. Specifically, they experience significantly more bloating and nausea. Close monitoring and further research is needed to better understand and manage GI symptoms in this group.

Ann Endocrinol (Paris). 2023 Feb 9;S0003-4266(23)00031-8.

**Acute soluble fibre supplementation has no impact on reducing post-prandial glucose excursions in adults with cystic fibrosis and glucose intolerance**

Catherine Lehoux Dubois[1], Valérie Boudreau[1], Kathryn J Potter[2], Johann Colomba[1], Annick Lavoie[3], Marjolaine Mailhot[3], Katherine Desjardins[1], Rémi Rabasa-Lhoret[4]

PMID: 36764386
DOI: 10.1016/j.ando.2023.02.001

**Background:** Cystic fibrosis (CF)-related diabetes (CFRD) is a common comorbidity in CF. In CFRD, fasting blood glucose level is often normal, but post-prandial glycaemia (PPG) is problematic. Elevated PPG has been associated to a higher risk of developing CFRD, a worst clinical state and a lower pulmonary function. Interventional studies in type 2 diabetes have demonstrated a beneficial impact of fibre supplement on PPG.
**Methods:** Our objective is to evaluate the efficiency of 2 doses of a soluble fibre supplement to lower PPG in CF patients with glucose intolerance (pre-diabetic or CFRD patients). This is a double-blinded crossover interventional study with three interventions: placebo or psyllium fibre (5.1g or 7.7g) of soluble fibre consumed before breakfast. A second meal (lunch) is also eaten four hours later to evaluate a second meal effect. Blood glucose and insulin were measured during the interventions.
**Results:** In 14 adult CF patients with impaired glucose tolerance (IGT; n=10) or CFRD (n=4), we observed no beneficial effect of fibre supplementation on PPG for both meals. However, all blood glucose levels were lower after the lunch compared to breakfast in spite of the higher carbohydrate content.
**Conclusion:** An acute treatment with fibre supplementation had no effect on blood glucose control in patients with CF-IGT or CFRD.

Can J Diabetes. 2023 Apr;47(3):263-271.e1.

**Canadian Cystic Fibrosis-related Diabetes Clinical Practice Survey: Analysis of Current Practices and Gaps in Clinical Care**

Kathryn J Potter[1], Adèle Coriati[2], Patrick Hicks[3], Larry C Lands[4], Martha L McKinney[3], Valérie Boudreau[1], Anne Bonhoure[1], Paola Luca[5], Josephine Ho[5], Sémah Tagougui[6], Amanda Jober[3], Meghan Pohl[3], Elizabeth T Rosolowsky[7], Julie Gilmour[8], Grace Y Lam[9], Anne L Stephenson[10], Peter A Senior[11], Rémi Rabasa-Lhoret[12], Tamizan Kherani[3]

PMID: 36872137
DOI: 10.1016/j.jcjd.2023.02.002

**Objectives:** Our aim in this study was to identify challenges and gaps in Canadian practices in screening, diagnosis, and treatment of cystic fibrosis-related diabetes (CFRD), with the goal of informing a Canadian-specific guideline for CFRD.
**Methods:** We conducted an online survey of health-care professionals (97 physicians and 44 allied health professionals) who care for people living with CF (pwCF) and/or CFRD (pwCFRD).
**Results:** Most pediatric centres followed <10 pwCFRD and adult centres followed >10 pwCFRD. Children with CFRD are usually followed at a separate diabetes clinic, whereas adults with CFRD may be followed by respirologists, nurse practitioners, or endocrinologists in a CF clinic or in a separate diabetes clinic. Less than 25% of pwCF had access to an endocrinologist with a special interest or expertise in CFRD. Many centres perform screening oral glucose tolerance testing with fasting and 2-hour time points. Respondents, especially those working with adults, also indicate use of additional tests for screening not currently recommended in CFRD guidelines. Pediatric practitioners tend to only use insulin to manage CFRD, whereas adult practitioners are more likely to use repaglinide as an alternative to insulin.
**Conclusions:** Access to specialized CFRD care may be a challenge for pwCFRD in Canada. There appears to be wide heterogeneity of CFRD care organization, screening, and treatment among health-care providers caring for pwCF and/or pwCFRD across Canada. Practitioners working with adult pwCF are less likely to adhere to current clinical practice guidelines than practitioners working with children.

Biomolecules. 2023 Feb 24;13(3):425.

**Cystic Fibrosis Bone Disease: The Interplay between CFTR Dysfunction and Chronic Inflammation**

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PMID: 36979360 PMCID: PMC10046889
DOI: 10.3390/biom13030425

Cystic fibrosis is a monogenic disease with a multisystemic phenotype, ranging from predisposition to chronic lung infection and inflammation to reduced bone mass. The exact mechanisms unbalancing the maintenance of an optimal bone mass in cystic fibrosis patients remain unknown. Multiple factors may contribute to severe bone mass reduction that, in turn, have devastating consequences in the patients' quality of life and longevity. Here, we will review the existing evidence linking the CFTR dysfunction and cell-intrinsic bone defects. Additionally, we will also address how the proinflammatory environment due to CFTR dysfunction in immune cells and chronic infection impairs the maintenance of an adequate bone mass in CF patients.

J Pers Med. 2023 Mar 3;13(3):469..

**Distribution of OGTT-Related Variables in Patients with Cystic Fibrosis from Puberty to Adulthood: An Italian Multicenter Study**

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PMID: 36983651 PMCID: PMC10056682
DOI: 10.3390/jpm13030469

**Background:** Insulin secretion and glucose tolerance is annually assessed in patients with cystic fibrosis (PwCF) through oral glucose tolerance tests (OGTTs) as a screening measure for cystic fibrosis-related diabetes. We aimed to describe the distribution and provide reference quartiles of OGTT-related variables in the Italian cystic fibrosis population.
**Methods:** Cross-sectional study of PwCF receiving care in three Italian cystic fibrosis centers of excellence, from 2016 to 2020. We performed a modified 2-h OGTT protocol (1.75 g/kg, maximum 75 g), sampling at baseline and at 30-min intervals, analyzing plasma glucose, serum insulin, and C-peptide. The modified OGTT allowed for the modeling of β cell function. For all variables, multivariable quantile regression was performed to estimate the median, the 25th, and 75th percentiles, with age, sex, and pancreatic insufficiency as predictors.
**Results:** We have quantified the deterioration of glucose tolerance and insulin secretion with age according to sex and pancreatic insufficiency, highlighting a deviation from linearity both for patients <10 years and >35 years of age.
**Conclusions:** References of OGTT variables for PwCF provide a necessary tool to not only identify patients at risk for CFRD or other cystic fibrosis-related complications, but also to evaluate the effects of promising pharmacological therapies.