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REPORT FROM

ERS International Congress 2022

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Dear friends!

We would like to take the opportunity to give you a summary from ERS-2022 with focus on CF written by 2 CF-doctors: Dr. Daniel Faurholt-Jepsen and Dr. Tavs Qvist both working at CF-centre in Rigshospitalet, Copenhagen. They have covered the scientific part of ERS and in this newsletter you can take part of the selected sessions that they've covered during ERS in Barcelona in the beginning of September 2022.

But first a little update on this year's ERS congress, approximately 19 000 delegates attended the congress, 400 sessions both live and pre-recorded, about 3500 abstracts was shared during these three busy and intense days.

One of the best things with ERS 2022 is that we finally can meet in person and attend a scientific conference just like the "good old days" and to get inspired by the latest research presented by the top experts from all over the world is, as you can imagine, priceless. After 3 intense days my head was full of thoughts like how will the treatment of CF evolve in the future now that patients are getting older and with all the new treatments available? Has the paradigm shifted? CF landscape has changed and the importance of preserving CF lung function and structure from early ages is important more than ever. Do we need to look beyond the spirometry and what about imaging – could that be a tool that will be used even more in the future when it comes to CF? With "new" CF-patients comes also new challenges such as diabetes, pregnancies & obesity and so on and what will this mean to the CF-healthcare – are the healthcare ready for the new CF-patient? Nobody has all the answers right now but what we do have is the ambition and the passion to make the life of CF-patients in the Nordics better and make them live their life to the fullest every single day.

Please enjoy your reading.

Best
Laila Massamiri, MSc
Medical Advisor, Nordic
Chiesi Pharma

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Highlights from ERS 2022 with focus on Cystic Fibrosis

PRESENTED BY DANIEL FAURHOLT-JEPSEN, MD PHD, CONSULTANT IN INFECTIOUS DISEASES

As an infectious disease physician treating patients with complicated pulmonary infections, such as cystic fibrosis, I have attended most of the conferences within cystic fibrosis during the last decade. I've been part of exciting new game-changing treatments covering infection control as well as mucociliary clearance, and in the last years CFTR modulators have been introduced and added to a list of effective treatments changing the life for my patients.

As we are in the middle of a transition in the disease and its management, we are as physicians obliged to seek new knowledge to be able to sustain our expertise in providing world-leading cystic fibrosis care by integrating knowledge from other disciplines as well as look back on our successes in cystic fibrosis. In addition to keep on track on numerous new scientific publications, the conferences provide us with the opportunity again to meet in person to discuss a common way forward and be inspired from experience in related disciplines. The conferences allow easy interaction with peers, basic researchers and industry needed to evolve the field together. An important and often neglected part of cystic fibrosis management is also thinking of mental health in chronic diseases, asthma management, nutrition initiatives, immune-modulation, bone health, endocrinology etc. and how experience from other pulmonary diseases could be translated into our daily work.

So why should a cystic fibrosis physician spend days away from the clinic to attend ERS International when we have other more disease-targeted options? This was the question to myself, before I decided to attend this year's conference. But it did not take many sessions on ERS, before it was obvious why this was the right decision. ERS hosts several sessions on management of pulmonary disease with cross-cutting relevance to cystic fibrosis.

The key session on cystic fibrosis was held the 5th of September on *Advances in cystic fibrosis research* hosted by Drs Madge and Ringhausen covering many aspects of cystic fibrosis. This included new insights in basic science on *Pseudomonas aeruginosa* activity by Agustina Llanos and how we can model the behavior of the mucus layer in the small airways by James Shemilt. Both presentations are relevant to me in the understanding of the direct consequences of a defect CFTR channel, and why we still need to figure out how to target the chronic and often resistant infections that is an ever-important complication, even in the CFTR modulator era. The session also covered real-world data on CFTR modulators that seemingly improve the pancreatic function, but also has

impact on mental health, which is an often-covered theme in our daily talk with the patient. The session made it clear that we have not cured cystic fibrosis, but we are seeing into a future of patients with severe multi-organ damage with an expectedly much longer life than we had ever expected. A multi-disciplinary approach to management is still needed, while the population will steadily grow in numbers. After the session I discussed management with peers, and we all agree that we must remind patients to adhere to their medicines, so we do not loose health control in euphoric times.

We often look for research in cystic fibrosis and its management when treating chronic infections such as *Pseudomonas aeruginosa* and non-tuberculous mycobacteria, but these pathogens are also seen in many other pulmonary diseases such as non-cystic fibrosis bronchiectasis, primary ciliary dyskinesia, and chronic obstructive pulmonary disease (COPD). Although the diseases have much different underlying pathogenesis, they definitely share management. The session *Management of non-tuberculous Mycobacterium avium complex pulmonary disease (MAC-PD) – what the future holds* hosted by Drs Polverino and Rohde reminded us on how difficult it is to predict the trajectories of such difficult-to-treat infection, how difficult it is to eradicate the infection, but also that combination of existing and newer drugs is likely to improve the management, and hopefully the prognosis. We already combine antibiotics and seek new uses of existing drugs likely to have effect on many pathogens, and inhalation therapy is an important way of overcoming intermediate to low susceptibility with high local concentration and little systemic load. This is not only done in my center, but all over the world. In the session *Respiratory infections* and the following case series in *Lungs on fire: Respiratory infections?* the panel discussed the impact of immunology, and whether we should target both the pathogens as well as the immune cells to improve treatment outcomes. This was mainly relevant for chronic Gram-negative infections as well as non-tuberculous mycobacteria. The initiatives treating non-cystic fibrosis bronchiectasis with DPP-1 inhibitors targeting neutrophil granulocytes could be an area of interest targeting the inflammation to reduce lung damage.

Management of mucus plugging with mucociliary clearance and bronchodilation was mainly covered in asthma and COPD sessions, and the experience gained in much larger patient groups are easily translated into my clinical work and thus highly relevant. Also, the management of IgE-related disorders covered in asthma sessions were useful, as we seek new steroid-sparing intervention to treat our cystic fibrosis patients with allergic bronchopulmonary aspergillosis.

As we see into an aging population with cystic fibrosis, we must attend these cross-discipline conferences dealing with multi-morbidity. Management of end-stage COPD is not that different from what we see in cystic fibrosis, and a geriatric sight on cystic fibrosis is already becoming relevant. ERS 2023 will be expanded by additional days and thus many more sessions, and we will definitely attend and bring our own research covering multiple aspects of cystic fibrosis.

Daniel Faurholt-Jepsen
MD PhD, Rigshospitalet, Denmark

How early does lung damage in cystic fibrosis start?

PRESENTED BY TAVS QVIST, MD PHD

A group of scientists from the University of Bern Switzerland led by Doctor Pinelopi Anagnostopoulou and Johannes Schittny presented their latest results at the ERS demonstrating how neonatal mice with CF-like disease display lung damage already at birth. The hypothesized that CF might affect prenatal and postnatal lung development on the level of branching morphogenesis and alveolarization. In their study they used mice with a CF-like defect and compared them to healthy neonatal mice by applying x-ray tomographic high-resolution imaging followed by structural analysis. They showed that CF mice had airspace dilation in both alveoli and in the conduction airways. The research is important because clinical evidence supports early damage in infants with CF meaning that inflammation starts, not at birth, but rather during development in the mother's womb. This raises the question of whether even earlier interventions could be appropriate in CF, such as CF modulation of a diagnosed, but still unborn child.

Can respiratory symptom scores be used to capture acute respiratory events in children with cystic fibrosis?

Physicians from Toronto led by Doctor Felix Ratjen presented a study describing the accuracy of the Cystic Fibrosis Questionnaire-Revised Respiratory score (CFQ-RResp) and the Chronic Respiratory Infection Symptom Score (CRISS) in children with CF. The study is important because these scores are used to measure exacerbations in children with CF and have implications for how clinical trials are evaluated. In the study, scores were evaluated for accuracy using lung clearance index (LCI) and FEV1 as references. Ninety-eight children were included and the scientists showed that the CFQ-RResp was more sensitive (75.6%) than the self-reported scores (32.8%), but that the overall most accurate measure was combining the symptom scores with LCI and FEV1. Thus, combining patient-reported and physiologic outcome measures is the most informative strategy.

Can a novel newborn screening program for cystic fibrosis improve performance?

The Dutch newborn screening (NBS) program for CF started in May 2011 and was evaluated at this year's ERS by a group of Dutch scientists led by Dr. Karin De Winter - De Groot from Utrecht in the Netherlands. The Dutch group showed how periodic screening from 2011-2015 was suboptimal. They evaluated the performance of an adjusted NBS protocol between 2016 and 2020. The Dutch approach to screening contained four steps: immunoreactive trypsinogen as general first step and subsequently pancreatitis-associated protein, Innolipa lineblot and extended gene analysis in a selection of cases and results were compared with the performance of the previous NBS protocol. In 599,137 newborns they found a total of 128 children

had a positive screening for CF, eleven of them were referred based on the new protocol of which five were diagnosed with classic CF. The adjusted Dutch NBS program for CF thus showed a better performance with higher sensitivity and is the kind of real-world data that will be needed to adjust screening protocols across Europe.

Can home spirometry be used for children with cystic fibrosis?

Dr Maya Desai and her research group in Birmingham in the United Kingdom introduced home spirometry during the COVID pandemic and evaluated the results at this years ERS. Their study compared the technology for home spirometry using an apparatus called Nuvoair with that used for standard spirometry in their hospital and they included data from 81 children with CF over a period of 9 months. All patients had paired spirometer measurements taken on the same day and time in clinic. Of 81 children, 54 provided interpretable measurements, 27 were excluded due to poor quality results. All the survey respondents found home spirometer easy to use. 81% of the respondents preferred a combination of home and hospital testing. The study was important because it shows that home spirometry performs well, even in children, although supervision is required.

How else was Cystic Fibrosis Research recognized at this year's ERS?

The ERS mid-career Gold Medal 2022 went to Professor Pierre-Régis Burgel from Cochin Hospital in Paris. He is the national coordinator of the French Cystic Fibrosis Centre Network which contains 47 CF centers and the vice president of the French CF Society.

Tavs Qvist
MD, PhD, Copenhagen Cystic Fibrosis Centre, Rigshospitalet, Denmark

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