

REPORT FROM

ERS Satellite symposium 2024

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ERS, European Respiratory Society is the largest scientific and clinical organisation in respiratory medicine in Europe. We're keeping an eye on interesting events in the respiratory area and are happy to share some highlights in bite size. In this report you will find a summary of very interesting presentations from the online ERS satellite symposium in March. Happy reading!

Best regards from the Nordic Medical team

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Digitalisation in health care

Summary: While the pandemic taught us that there are alternatives to the traditional appointment at a doctor's office, the body of evidence to support telehealth in COPD is still small. This article summarises promising results and highlights areas of relevance for telehealth, as well as the need for more data.

Where are we with telehealth in COPD?

Potential of telehealth

From the talk by Rebecca Disler, Australia, it became clear that telehealth has the potential to add new aspects to care. It can replace or supplement usual care and add the opportunity of longitudinal monitoring of e.g. symptoms. Obviously, an opportunity for telehealth is easier access where distance to health care is a problem¹.



Promising examples exist

Even though data is limited comparing telehealth to usual care, there are promising examples that fuel our interest: In a study by Al Rajeh et al., telehealth was used to collect continuous data rather than single measurements of heartrate and oxygen saturation for early detection of exacerbations². Another example given was the use of telehealth for patient education to prepare for an upcoming conversation about palliative care³.

Is telehealth a good fit for the patient, too?

Professor Disler underlines that more research needs to be performed to draw conclusions if telehealth is superior to usual care, however, from current data, telehealth does not seem to put the caretaker at risk, neither. She also speculates that future research will meet a generation of people 60+ years of age with more natural digital habits and thereby, less anxiety towards use of technology. While there is research published on "Ux", i.e. usability and user satisfaction of digital solutions, the probably most important question is understudied:

What is the patient's perspective on telehealth?

Recommended reading:

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Digital biomarkers in asthma management

Summary: Despite rapid digitalization of the world the use of digital biomarkers in asthma management is underutilized. Wearables such as fitness bands and smartwatches provide the possibility to obtain individualized high-quality data, but the question is – are digital biomarkers ready to revolutionize asthma management?

Adherence and health behaviours, can wearables help?

Continuous monitoring like never before

The growing connectivity in the world provides a substantial potential of digital innovations for management of various diseases – including asthma¹. However, this global digitalization is not reflected in routine care, because of multiple barriers, resulting in underutilization of digital technologies in health care². Today, a large proportion of the world's population own a smartwatch or fitness bands, which provides the potential for continuous monitoring of digital biomarkers and providing valuable insights that may enhance clinical decision-making.

What are digital biomarkers?

Behavioral and physiological data, for example heart rate, physical activity and step counts.

Predicting exacerbation - possible clues

Various applications of digital biomarkers in asthma management have been investigated, including monitoring treatment efficacy, patient stratification, and shared decision-making³. In asthma, prediction of exacerbations would be crucial for patient outcomes and digital interventions can make a significant impact by providing early warning signs



and improving patient awareness. For example, have changes in activity levels⁴, heart rate⁵, nocturnal cough⁶, and sleep quality⁶ been shown to be predictors of future exacerbations. However, clinical trials and realworld evidence of the potential of digital biomarkers is needed to leverage digital technologies transformation in asthma care on a strong scientific foundation.

Making best use of digital biomarkers

In conclusion, integrating digital health technologies into asthma management to enhance patient monitoring, predict exacerbations, and improve outcomes have great potential. But stronger evidence of efficacy and effectiveness is needed to facilitate a broader discussion on how digital innovations can shape the future of asthma care.



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Understanding risk factors of COPD

Summary: Understanding of the risk factors associated to COPD has advanced over the last 2-3 decades. Can COPD be considered anymore merely as a smoking disease? Or are there other fires to fight? Summary of the advances was given by Dr Sundeep Santosh Salvi (Pune, India).

Risk factors for COPD: Not all the same

In addition to respiratory symptoms and postbronchodilator FEV1/FVC <0.7, the presence of risk factors is essential to reach diagnosis of COPD. Understanding of risk factors has grown over time.

Historical retrospective

The term emphysema was used for the first time in 1821 for hyperinflated lung and thought to be related to air pollution. At the same time, occupational exposure was suspected, e.g. in the glass blowing. In 1950's, tobacco smoking was shown to be associated with development of lung cancer and heart disease. Chronic bronchitis was linked to air pollution and occupational exposure^{1,2}. A decade later, more evidence was published to show occupational exposures being related to chronic bronchitis and emphysema, later called as COPD³.



Lung function trajectory of smokers

A major advance in understanding the risk factors of COPD came in 1977, when it was shown that smokers had a very rapid and sharp decline in lung function measured by spirometry. The association between tobacco smoking and COPD was established by this study (figure 1.)⁴



Figure 1. "Fletcher curve". Adapted from Fletcher & Peto (1977): The natural history of chronic airflow obstruction

At risk: farmers

In 1987, COPD was concluded to be a work-related disease among farmers, based on data from a 6-year long study with >12 000 farmers from South-Western Finland. Comparing prevalence of COPD in non-smokers, the non-smoking farmers had a higher prevalence (2.7%) compared to the non-farmers (0.7%). Looking at incidence of chronic bronchitis, the regional difference between the agriculturally dense South-West and the North-



West was considerable: The South-West region had double the incidence of the North-West (1686/yr. vs <800/yr.)⁵.

Non-smoking COPD not so rare

Looking at data from almost 13 thousand nonsmokers over two decades included in the American NHANES study (National Health and Nutrition Evaluation Study, published 1995), about 4% of the men and 5% of women had been diagnosed with COPD, where old age, low income and race could be identified as risk factors⁶. When Ezzati and colleagues published research of estimates of global, smoking-assiciated mortality in 2003, they found that more than half of the deaths were attributed to other risk factors⁷. In the Global Burden of Disease (2018), air pollution (both particulate matter and household) and occupational exposure were identified as major contributors to COPD. In particular in regions with low sociodemographic index, air pollution contributes to a very high degree of non-smoking COPD⁸.

Polluted air and open fire cooking

Dr Salvi and his group have conducted studies of respiratory symptoms in the slum population, finding a higher degree of respiratory symtoms compared to the general population⁹. Looking at prevalence of COPD (confirmed with spirometry) in rural Indian areas, proximity to main road fell out as a risk factor along with increasing age, male gender and using biomass fuel for cooking or heating¹⁰. However, the risk of COPD may also depend on what the open fire kitchen looks like. A comparison between Indian and Thai women showed that the prevalence of COPD was 5.5 times higher for women in India¹¹. The main contributor for this difference was thought to be the existence of an additional window for ventilation in the Thai kitchen.

Malnutrition

Nutrition plays an important role in developing COPD, according to pooled data from the NHANES

study, where a link was made between diet low in antioxidants (Vitamin A, E and selenium) and risk of developing COPD¹². Poor nutrition has also been associated with dysanapsis¹³, which occur early in life and causes a mismatch between airways and lung size (fewer small airways in the lung). Reoccurring respiratory infections may also cause dysanapsis.

COPD, a disease with many etiotypes

The GOLD (2023 and 2024) guidelines¹⁴ mention seven etiotypes of COPD, to bring attention to a diversity of risk factors: in addition to COPD -C (C as in cigarettes), we also have the COPD -G for genetics, -D for development (early life events), -P for pollution, -I for infections, -A for (undertreated/ childhood) asthma and -U for the unknown etiology of disease. A lot of progress in understanding causes of COPD has been made in the past decades to understand different causes of COPD.

Fight social inequities to improve lung health

Socioeconomic status is a risk factor of COPD. From the global point of view, 55% of COPD is associated with non-smoking risk factors. The risk factors associated with non-smoking COPD include air pollution, asthma, occupational exposure, infections, low lung growth, poor socioeconomic status, dietary factors and genetic factors¹⁵. In the high socio-demographic index countries tobacco smoking contributes to 70% of total population attributable risk of COPD, making smoking the most important risk to fight.

Countries with low to middle sociodemographic index also have a higher burden of risks: more air pollution, using biomass fuels for heating and cooking, insufficient protection against occupational exposure, availability of asthma medication, dietary factors in addition to socio economic factors. Working to address and reduce the risk factors of COPD, will continue to be important for lung health globally.



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Biologics in COPD – are we there?

Summary: Despite the implementation of optimized triple therapy, data reveals that COPD patients continue to undergo exacerbations. This underscores the necessity for additional and innovative treatment approaches. The following is a concise overview of recent evidence emerging in the realm of biologics development for COPD.

Current status of biologics in COPD

In Professor Alberto Papi's comprehensive lecture on the evolving landscape of biological treatment in COPD, he emphasized the proven efficacy of triple therapy in reducing the annual exacerbation rate. Despite these advancements, challenges persist as some patients continue to experience exacerbations even with optimized triple therapy. This underscores the urgency for novel and individualized treatment approaches.

Navigating potential molecular targets in COPD

The complex task of navigating potential molecular targets poses a considerable challenge in this field. While exploring the non-type 2 inflammatory response, known for its involvement in exacerbations, studies on non-type 2 mediators like TNF and IL-17A have yielded inconclusive results^{1,2}. Contrary to this, asthma has seen success with antibody treatments targeting type 2 inflammatory mediators, prompting exploration of their applicability in COPD.

Specifically, antibodies targeting IL-5 signaling, effective in certain asthma phenotypes, raise intriguing questions about their potential role in COPD. However, Prof. Papi shared conflicting findings regarding the impact of anti-IL-5 in COPD, emphasizing the need for more targeted studies in specific patient subgroups³.

Blocking IL-4 and IL-13 – a potential breakthrough

An encouraging breakthrough emerged in the form of blocking IL-4 and IL-13 signaling, showing



a promising 30% reduction in the annual exacerbation rate in a subgroup of COPD patients characterized by specific criteria⁴. This development marks a significant leap forward, especially for individuals on triple therapy still experiencing exacerbations.

Alarmins may recall history of smoking

Diving further into the exploration of alarmins' influence on COPD, studies on IL -33 inhibition revealed nuanced results. While there was no significant change in the overall exacerbation rate, a subgroup analysis showed a substantial reduction in frequency among former smokers⁵. Ongoing research is dedicated exclusively to this population, promising deeper insights.

Work in progress

Prof. Papi concludes that while treatments for type 2 inflammatory mediators in COPD have progressed, addressing non-type 2 inflammation remains a work in progress. With hope, future research will unveil treatments for non-type 2 inflammation in COPD, given that it represents the majority of cases.



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Mild to moderate asthma – mechanisms and phenotyping

Summary: Due to the variable nature of asthma the lung function can vary over time and between individuals; from normal to severely obstructed. Some factors are immediately reversed with bronchodilators, while others require long-term anti-inflammatory treatment. However, some manifestations are more or less irreversible. To be aware and act on underlying inflammation and hypersecretion is essential to prevent exacerbations and disease progression.

What do I need to know about mild and moderate asthma?

Hot topics of asthma in a clinical context were covered by Professor Celeste Porsbjerg (Copenhagen, Denmark) in a presentation titled *What do I need to know about the mechanisms and phenotyping of mild to moderate asthma?* This presentation included practical advise to clinicians working with asthma.



Reversibility of asthma manifestations may vary

Asthma patients are diverse, not only in disease severities, but also in underlying mechanisms driving the disease. Asthma is known for causing variable airflow obstruction, reversible in nature, but not all factors contributing to the manifestation of the disease display the same reversibility¹. Understanding the patient's specificities is key to effectively find the most suitable treatment.

Immune hyperresponsiveness of airway epithelium

The airway epithelium was described as having a key role in the asthma pathology. In addition to the barrier function, the epithelium can be considered the origin of the immune "hyperresponsiveness" seen in asthmatic patients. The inflammatory response and induced inflammation are the result of exposure to an otherwise harmless agent. The inflammatory response could lead to asthma exacerbations, highlighting the interest in the airway epithelium.^{1,2} The structural changes that drive airway remodelling and airway hypersecretion are derived from airway epithelium.

Understanding hyperresponsiveness type

Airway remodelling and airway hypersecretion are two components of asthma that might not be fully reversible with treatment, and airway hypersecretion could potentially accelerate loss of lung function^{1,2}. Immune hyperresponsiveness and airway hyperresponsiveness are two different things, and Professor Porsbjerg highlighted the importance of differentiating between them. Some patients never experience exacerbations, while exacerbations among other patients are the predominant feature of their disease.

Blood versus sputum eosinophils

The most widely used biomarkers for assessing T2 inflammation are blood eosinophils and FeNO. Nevertheless, sputum eosinophils is the golden



standard method but does not necessarily correlate with blood eosinophil counts. Normal blood eosinophil values are seen in 1 out of 3 patients with elevated sputum eosinophils. Therefore, blood eosinophils may be a poor measure for inflammation. Induced sputum analysis, as well as adherence to treatment, should be considered and evaluated, respectively.³

Allergies and asthma control

A final reminder regarding allergies: Besides evaluating if T2 inflammation is present, clinicians could potentially help a great number of asthma patients by also considering the probability of concurrent allergy. Uncontrolled allergic rhinitis causes poor asthma control and treating allergic rhinitis adequately improves asthma control. In the same manner, allergen immunotherapy is shown to reduce the need for asthma treatment and can also prevent progression of asthma.⁴

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