# Congress Review

### Review of the virtual European Respiratory Society (ERS) International Congress 2020

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HE 30<sup>th</sup> anniversary of the European Respiratory Society (ERS) meeting was set to be a spectacle in Vienna, Austria, but no one could predict what the year had in stall for us. In response to the ongoing coronavirus disease (COVID-19) pandemic, the ERS made the decision to hold the 30<sup>th</sup> ERS International Congress virtually. Even with this unexpected turn of events, the society put together a platform that showcased research and facilitated discussion and interaction, which was attended by over 33,000 delegates.

In the 'Welcome to 30<sup>th</sup> Congress' section of the platform, the ERS President Thierry Troosters welcomed attendees to the event. Amongst many of his encouraging words, Prof Troosters highlighted how many professionals in the respiratory field had dedicated their lives to fighting the COVID-19 pandemic on the frontlines or have been involved in researching pharmacological and nonpharmacological treatments for the many patients affected by the disease. He further noted that: "The pandemic also showed the pivotal role of links to other country and regional societies. We exchange knowledge and help each other with dissemination of science around the pandemic in many of the disease areas covered by the society."

The scientific programme evolved to fit with the platform, with some sessions being available in multiple languages such as English, Spanish, and German. The society also added a day dedicated to the knowledge that is known so far about COVID-19, including COVID-19 prevention, management, and the impact on those with pre-existing lung conditions. In his welcome message, Prof Troosters thanked those who contributed to the meeting: "I'm grateful to those who have taken time, despite overburdened agendas, to contribute to the sharing of knowledge and initiation of scientific projects, moving the field forward at light speed."

Another new addition to the scientific programme this year were ALERT sessions,

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which combined the breaking news from recent, unpublished randomised clinical trials in easyaccess sessions. Furthermore, 'Live from the Clinic' sessions showed experts performing live procedures such as endoscopies, which was only possible due to the digital format.

Thousands of e-posters and abstracts were presented, which provided insight into the latest developments across all aspects of the respiratory field. Included in the following pages are summaries of a hand-selected collection of abstracts, written by the presenters themselves.

Prof Troosters acknowledged that we should not draw too much attention away from the ongoing efforts in preventative health, using smoking as an example, which has killed 15 times as many people in 2020 as COVID-19, adding that air pollution is still a pertinent issue for respiratory health. Even though the congress was held virtually this year, and thus had a very minimal carbon footprint, the society had great plans to hold a green face-to-face meeting, showcasing their commitment to minimising their ecological footprint.

Weighing in on the positives, Prof Troosters reminded attendees that: "The coronavirus has put some of our projects on hold, but facilitated others, for example, the transition towards a virtual format for our consultations, rehabilitation programmes, or even our congress. We will not waste this crisis and continue to build on the good things that came out of it."

We look forward to being able to attend what will sure to be another great meeting next year in Barcelona, Spain, until then, please enjoy the following review of the 30<sup>th</sup> ERS International Congress.



#### Personalised Asthma Care: Should we Prescribe According to Genetics?

GENETIC differences between children and adolescents with asthma may aid treatment selection for these patients; this is according to a study conducted at the University of Dundee, Dundee, UK, the results of which were reported at the ERS International Congress 2020 on the 8<sup>th</sup> September 2020.

In total, 241 patients aged between 12 and 18 years were enrolled in the trial. They were all being treated for asthma by their general practitioner and were randomly assigned to either a group that received treatment according to existing guidelines, or to a group that utilised personalised medicine techniques, in which they received treatment according to their genotype. To determine their genotype, the participants' inner cheek cells were tested for different versions of the  $\beta$ -2 adrenergic receptor *ADRB2* gene.

The  $\beta$ -2 adrenergic receptor is a common pharmacological target of asthma treatments, but previous research has shown that one in seven children have one or two copies of the altered versions of this gene; this can lead to the

medication having a negative effect on patients symptoms. Therefore, the personalised medicine group of this trial were treated with montelukast, rather than salmeterol.

Participants were followed for 1 year, during which quality of life, the severity of their symptoms, and the extent to which asthma limited their normal activities were assessed (on a scale of 1-7). When comparing the average scores for quality of life between the two groups, there was only an improvement of 0.16 seen in the personalised group. However, when specifically looking at those with two copies of the altered *ADRB2*, they found a 0.42 improvement.

Prof Mukhopadhyay, Brighton and Sussex Medical School, Brighton, UK, and leader of the study team, is hopeful about the implications of the results, especially as the genetic test kits cost \$20 USD: "These results are very promising because they show, for the first time, that it could be beneficial to test for certain genetic differences in children with asthma and select medication according to those differences."



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#### 'Long COVID': Heart and Lung Damage Could Improve with Time

CORONAVIRUS disease (COVID-19) has caused long-term heart and lung damage in many patients, but this has been shown to improve over time, as evidenced by a prospective followup study by researchers from the Tyrolean region in Austria. These results were presented at the ERS International Congress 2020 on 7<sup>th</sup> September 2020.

Conducted between 29<sup>th</sup> April and 9<sup>th</sup> June 2020, the study included 86 patients hospitalised with COVID-19 who were followed up at 6, 12, and 24 weeks, as well as after their discharge from the hospital. Clinical examinations, laboratory tests, CT scans, and echocardiograms were all carried out at every follow-up visit. The average age of participants was 61 years, 65% were male, 65% were overweight or obese, and almost 50% were current or former smokers.

At 6-weeks follow-up, 65% of the patients had at least one persistent symptom, the most common being breathlessness and coughing (47%). Using CT scanning, it was observed that 88% of patients had lung damage, deemed by the presence of ground-glass opacities. Echocardiogram analysis also showed that 59% of patients had dysfunction of the heart's left ventricle. At 12-weeks follow-up, some recovery was seen because lung damage was visible in 56% of participants and only 39% reported breathlessness. The 24-weeks follow-up has yet to be performed.

Dr Sabina Sahanic, The Medical University of Innsbruck, Innsbruck, Austria, and one of the authors of the study, summarised the findings: "The bad news is that people show lung impairment from COVID-19 weeks after discharge; the good news is that the impairment tends to ameliorate over time, which suggests the lungs have a mechanism for repairing themselves."

She concluded: "Knowing how patients have been affected long-term by the coronavirus might enable symptoms and lung damage to be treated much earlier and might have a significant impact on further medical recommendations and advice."

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### Bronchitis in Early Years as a Prediction Tool for Middle-Age Lung Health

LUNG problems in later life can be reliably predicted if the patient had bronchitis at least once before the age of 7 years; this is according to findings from the Tasmanian Longitudinal Health Study, which were released at the ERS International Congress 2020 on 4<sup>th</sup> September 2020.

Enrolled as children, 8,583 participants who were born in Tasmania in 1961 and started school in 1968 had their lung function initially assessed using a spirometer. The researchers took note of how much air they could breathe out forcibly in 1 second and the total volume of air exhaled, as well as establishing if they had been diagnosed with bronchitis or asthma by the age of 7 years.

The participants were followed up for an average of 46 years. In 2014, a total of 5,729 participants responded to a further survey and between 2012 and 2016, 3,609 participants completed an additional survey and 2,629 underwent a clinical examination that again used a spirometer to access lung function. Nonrecurrent, recurrent, or protracted recurrent episodes of bronchitis before the age of 7 years was associated with a 1.4-fold, 2.0-fold, and 3.2fold increased risk of pneumonia, respectively, by the time participants reached the average age of 53; a 1.3-fold, 2.7-fold, and 6.4-fold increased risk of ever having asthma, respectively; and a 1.3-fold, 2.0-fold, and 4.5-fold increased risk of currently having asthma, respectively.

Dr Jennifer Perret, a researcher at the University of Melbourne, Melbourne, Australia, analysed the findings: "The associations with asthma and pneumonia strengthened with increasing severity of childhood bronchitis."

However, she did stress that the results should be interpreted with caution: "There was no statistically significant link between childhood bronchitis and chronic bronchitis in middle-age. This was an unexpected finding and further study would be informative. We are currently exploring these associations."

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## What is the Cancer Risk of 'Social Smoking'?

MORE smokers are cutting back on their daily smoking, but the mortality and cancer risks of 'social smoking' remain substantially higher than for nonsmokers. News from a study by Columbia University Irving Medical Center, New York City, New York, USA, was presented at ERS International Congress 2020 on 1<sup>st</sup> September 2020.

'Social smokers', defined as those who smoke <10 cigarettes per day, represent an increased proportion of smokers in the USA, from 16% up to 27%, as many smokers have cut back or combined smoking with vaping. However, the risks from social smoking have not previously been well understood. Researchers analysed data from 18,730 people across ethnicities as a sample of the general population of the USA, to compare risk between social smokers, heavier smokers (>20 cigarettes per day), and nonsmokers. Participants, with an average age of 61 years, were followed for an average of 17 years.

The study found that, compared to nonsmokers, social smokers were 2.5 times more likely to die from respiratory diseases and 8.6 times as likely to die from lung cancer, even when controlling for age, sex, race, level of education, and body weight. Death from respiratory disease or lung cancer occurred in 3.3% and 4.7% of social smokers, respectively, compared with 10.1% and 12.9% of heavier smokers, and 1.8% and 0.6% of nonsmokers.

Addressing the value of these findings for clinicians at ERS International Congress 2020, Prof Jørgen Vestbo, Chair of the European Respiratory Advocacy Council and Professor of Respiratory Medicine, University of Manchester, Manchester, UK, emphasised: "It's clear that there is no safe level of smoking. This large study is important because it shows that smoking less will probably not have the effect that people are hoping for. We need to do all we can to support smokers to quit completely using evidence-based means."



#### Flavourings and Solvents Mix to Form New, Toxic Chemicals in e-Cigarettes

e-CIGARETTES have propelled into common use as a 'safe' alternative to tobacco smoking; however, recent evidence is questioning the real safety of these devices and the associated e-liquids. The case for such tobacco alternatives being unsafe was further supported by research presented at the ERS International Congress 2020 and reported in a press release dated 3<sup>rd</sup> September.

Flavourings are routinely added to e-liquids, and, according to manufacturers, are safe because they are vaporised by the e-cigarette; however, a recent study reported that they form new toxic chemicals by combining with the solvents, for which there are severe safety concerns.

In the toxicological studies, the researchers exposed cells that line the bronchi to chemicals that are commonly used as flavourings, for example vanillin and cinnamaldehyde, and explored the possible compounds formed when mixed with propylene glycol and vegetable glycerine, the main solvents used in e-liquids. "We consistently observed that the new chemicals formed from the flavours

and e-liquid solvents were more toxic than either of their parent compounds," noted author of the study Prof Sven-Eric Jordt, Duke University School of Medicine, Durham, North Carolina, USA. Additionally, TRPV1 and TRPA1, sensory irritant receptors in the bronchi responsible for numerous inflammatory responses, were activated by the new chemicals. Activation of these receptors can lead to issues in both the cardiovascular system, such as increased heart rate and irregular heartbeat in the predisposed, and pulmonary system, such as coughing and breathing difficulties due to increased secretions throughout the airways.

Upon further investigation, the researchers found that the newly formed chemicals caused the cells lining the bronchi to die, even if the chemicals were at low concentrations. Prof

Jordt commented: "This is the first demonstration that these new chemicals formed in e-liquids can damage and kill lung cells and probably do this by damaging their metabolism."

e In addition to listing the original chemicals, Prof Jordt called for manufacturers to list the chemicals formed when the flavourings are mixed with solvents. Furthermore, he noted that additional research into the toxicological properties of these chemical products should be

conducted, and regulators to be aware of their safety profile to assess the level of risk to health from e-cigarettes, with the aim for manufacturers to reduce the concentration of such chemicals in their product.

*"We consistently observed that the new chemicals formed from the flavours and e-liquid solvents were more toxic than either of their parent compounds"* 

### Heavy Metal Exposure in the Womb Associated With Childhood Asthma

CADMIUM is a heavy metal and its use is restricted in the European Union (EU) due to its known hazards to human health; however, exposure to cadmium can occur because it has been widely used in batteries and pigments, and is present in tobacco. According to new research presented at ERS International Congress 2020 and in a press release dated the 3<sup>rd</sup> September, higher concentrations of cadmium in the umbilical cord blood of newborns may increase the risk of developing childhood asthma and allergies.

In the study, the quantities of cadmium, manganese, and lead were measured in 706 females and their babies at the maternity units in Nancy and Poitiers in France. Blood samples were taken from the mothers during pregnancy and babies from their umbilical cord after delivery. During the 8-year follow-up period, the researchers noted if any of the children had developed asthma, allergic rhinitis, eczema, or food allergies, accounting for family medical history and smoking status of the parents.

At the time of delivery, the average level of cadmium in the mothers was 0.8  $\mu$ g/L and in the cord blood was 0.5  $\mu$ g/L. For cadmium, higher levels in the umbilical cord of babies (>0.7  $\mu$ g/L) were associated with a 24% increased risk of developing asthma. Interestingly, lower levels of

cadmium (<0.3  $\mu$ g/L) were associated with a 44% increase in risk of developing a food allergy. Manganese levels were linked to risk of eczema, a known risk factor for developing asthma: levels of >1.1  $\mu$ g/L in the mother's blood was associated with an increased risk of developing eczema, compared with levels <0.5  $\mu$ g/L.

"Our study doesn't tell us why this might be the case, but it could be that cadmium is interfering with babies' developing immune systems and we think this can have an impact on their allergic reactions in childhood," hypothesised the research presenter Prof Isabella Annesi-Maesano, Institut national de la santé et de la recherche médicale (INSERM) and Sorbonne Université, Paris, France.

Prof Daiana Stolz, ERS Education Council Chair, University Hospital Basel, Basel, Switzerland, commented on the findings: "It's particularly worrying to know that cadmium and other metals might be reaching unborn babies via the umbilical cord." She added that this study, along with the already known dangers of cadmium, supports extremely tight regulations of the use and disposal of products containing heavy metals.

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#### Novel App Measures Night-Time Coughing to Predict Asthma Deterioration

COUGHING at night, measured via a novel smartphone app, can indicate the severity of asthma progression according to research presented at ERS International Congress 2020 and a press release dated 25<sup>th</sup> August 2020.

"Smartphones have lots of potential to monitor different symptoms and detect changes early," stated research lead Dr Frank Rassouli, Cantonal Hospital St Gallen, St Gallen, Switzerland. The research group aimed to utilise technology and simple interventions to improve the management of chronic lung diseases such as asthma. Dr Rassouli noted that: "Until now, we haven't had a reliable tool for measuring peoples' asthma symptoms overnight, so we know very little about night-time coughing and what it means."

The study recruited 94 patients with asthma being treated at two Swiss clinics. Patients visited their clinics at the beginning and end of the study, where they were assessed on their usage of asthma treatments and symptoms, which included shortness of breath and the impact of asthma on their daily lives. For 29 days, patients slept with a smartphone in their bedroom and the app prompted them to report their night-time symptoms and measured the noise of their nighttime coughing.

Analysis of the data showed that while there was a discrepancy in the amount of night-time coughing from patient-to-patient, there was a strong correlation between increased nighttime coughing over the course of 1 week and subsequent worsening of asthma symptoms. "Our results suggest that night-time coughing can be measured fairly simply with a smartphone app and that an increase in coughing at night is an indicator that asthma is deteriorating," Dr Rassouli explained. He further stated that monitoring asthma is pivotal because early recognition of worsening symptoms would allow clinicians to adjust medication accordingly and prevent asthma attacks. This study showcases a potential new and easily accessible way to monitor signs of deteriorating asthma, and with this success the researchers are planning to test the same technology on patients with chronic obstructive pulmonary disease.

"Our results suggest that night-time coughing can be measured fairly simply with a smartphone app and that an increase in coughing at night is an indicator that asthma is deteriorating"

#### Low Levels of Air Pollution Linked to Asthma in Babies and Adults

BABIES raised in areas of higher levels of air pollution develop poorer lung function as children and teenagers, and adults exposed to low levels of air pollution over a prolonged time are more likely to develop asthma. These findings from two studies were reported at the ERS International Congress 2020 and in a press release dated 25<sup>th</sup> August 2020.

In the first study, lead by Dr Qi Zhao, IUF - Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany, 915 children from Munich and Wesel in Germany were tested for their breathing capabilities at the ages of 6, 10, or 15 years. Forced vital capacity and forced expiratory volume in 1 second were measured and compared with estimates of the levels of pollution in the areas the children lived in their first year of life. Factors associated with poorer lung function, such as whether the children's mothers smoked, were considered. Results found that the higher the babies air pollution exposure was, the worse their lung function was when they grew up. Dr Zhao concluded that: "Our results suggest that babies who grow up breathing polluted air, even at levels below European Union (EU) regulations, have poorer breathing as they grow into children and adults. This is worrying because previous research suggests that damage to lungs in the first year of life can affect respiratory health throughout life."

A separate study found that adults were also at risk. The study, which analysed 23,000 Danish nurses, found a correlation between long-term exposure to air pollution and the likelihood of being diagnosed with asthma. Levels of nitrogen dioxide (NO<sub>2</sub>) and particulate matter smaller than 2.5 microns (PM<sub>2.5</sub>) were compared to the levels of road traffic noise where the nurses lived, accounting for factors including smoking and obesity. While no link was found to noise pollution, air pollution increased the likelihood of asthma diagnosis. A 29% rise in asthma risk was associated to each 6.3  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> and a 16% rise in asthma risk for each 8.2  $\mu$ g/m<sup>3</sup> increase in NO<sub>2</sub>.

Compared to many European cities, the nurses were exposed to relatively low levels of air pollution; approximately 18.9  $\mu$ g/m<sup>3</sup> and 12.8  $\mu$ g/m<sup>3</sup> for PM<sub>2.5</sub> and NO<sub>2</sub>, respectively, and current European standard for PM<sub>2.5</sub> and NO<sub>2</sub> are 25.0  $\mu$ g/m<sup>3</sup> and 40.0  $\mu$ g/m<sup>3</sup>, respectively. Researcher Dr Shuo Liu, University of Copenhagen, Copenhagen, Denmark, asserted: "The fact that we found a link with asthma, even at relatively low levels of exposure, suggests that there is no safe threshold for air pollution. This is strong evidence that our regulations on air pollution need to be stricter if we want to prevent cases of asthma."

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#### Lung Microbiome Fungal Diversity Linked to Disease Severity

FUNGI present in the lung microbiome may regulate the inflammatory response in acute respiratory distress syndrome (ARDS), with less diversity linked to poorer outcomes. A study of mechanically ventilated patients was presented at ERS International Congress 2020 and in a press release dated the 24<sup>th</sup> August 2020.

Despite being outnumbered by bacteria as a part of the lung microbiome, fungi are known to

play a role in activating and regulating immune responses. Researchers at the University of Pittsburgh, Pittsburgh, Pennsylvania, USA, 202 analysed mechanically ventilated patients from October 2011 to September 2019; 21% had a diagnosis of ARDS. Nextgeneration sequencing of the DNA of the tracheal secretions of the patients revealed about 100 different species of fungi. Although species diversity was low in

all of the samples, for those patients where one species dominated the samples, diversity was very low.

ARDS was associated with very low species diversity; shock, sepsis, and organ failure were

associated with lower fungal diversity among the patients with ARDS. Reduced diversity was found to be associated with more severe lung injury, more intensive treatment, and elevated levels of the protein pentraxin-3 (an indicator of inflammation and disease severity).

Noel Britton, University of Pittsburgh, an author of the abstract, highlighted the value of the

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study: "The association of lower fungal diversity with clinical markers of disease severity is an important findina because it provides evidence for a relationship between the lung microbiome and clinical outcomes in critical illness." Discussing the future implications of the findings. Prof Tobias Welte, ERS Past President, and Hannover University School of Medicine, Hannover, Germany, said: "The finding from this study, that

less diversity in the mycobiome is linked to worse outcomes for patients with ARDS, is fascinating. It's too early to know what this might mean for patients and their doctors, but it has the potential to lead to new diagnostic tests and better treatments."



#### **Electronic Alerts Improve Asthma Management**

ELECTRONIC alerts can improve prescribing and asthma management in general practice. A UK study presented at ERS International Congress 2020 revealed the impact of an electronic alert system in general practitioner (GP) records.

Excessive prescription and use of short-acting reliever inhalers, such as salbutamol, can be an indicator of poorly controlled asthma, is a risk factor for asthma attacks, and has been implicated in asthma-related deaths. These short-acting reliever inhalers address asthma symptoms but do not improve the underlying inflammatory cause.

The study included 18,244 patients with asthma at 132 general practices in north-east London, UK, and involved adding an automatic, electronic alert that appeared on GP screens when accessing the electronic patient records for patients who had received three prescriptions for short-acting reliever inhalers within a 3-month period. The alert recommended an asthma review for the patient, to assess symptoms and improve asthma control. This intervention resulted in a 6% reduction in excessive prescribing of reliever inhalers in the 12 months following the first inclusion of the alerts, with asthma reviews increasing by 12% in the 3 months after the alerts. Within 6 months of the alerts being introduced, repeat prescribing of short-acting  $\beta$ 2 agonists reduced by 5% and exacerbations requiring oral steroid treatment reduced by 8%.

The value of these findings, and the intervention approach used, were highlighted by Dr Shauna McKibben. Institute of Population Health Sciences, Queen Mary University of London, London, UK, and clinical nurse specialist in asthma and allergy at Imperial College Healthcare NHS Trust, London, UK: "Excessive shortacting B2 agonists use is only one indicator for poor asthma control but the risks are not well understood by patients and are often overlooked by healthcare professionals. Further research into the development and robust evaluation of tools to support primary care staff in the management of people with asthma is essential to improve asthma control and reduce hospital admissions."

"Within 6 months of the alerts being introduced, repeat prescribing of short-acting β2 agonists reduced by 5% and exacerbations requiring oral steroid treatment reduced by 8%."